

Withdrawal/Redaction Sheet

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. resume	re: Michael Cohen (partial) (1 page)	n.d.	P6/b(6)
002. resume	re: William Roper (partial) (1 page)	03/03/1999	P6/b(6)
003. bio	re: Joseph Pizzorno (partial) (1 page)	03/02/1999	P6/b(6)
004. resume	re: Guy Riekeman (partial) (1 page)	03/23/1999	P6/b(6)

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Clinton Presidential Records
Domestic Policy Council
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FOLDER TITLE:

Alternative Medicine [Folder 7]

2012-0463-S

rc712

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

- P1 National Security Classified Information [(a)(1) of the PRA]
- P2 Relating to the appointment to Federal office [(a)(2) of the PRA]
- P3 Release would violate a Federal statute [(a)(3) of the PRA]
- P4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
- P5 Release would disclose confidential advice between the President and his advisors, or between such advisors [(a)(5) of the PRA]
- P6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Personal record misfile defined in accordance with 44 U.S.C. 2201(3).

RR. Document will be reviewed upon request.

Freedom of Information Act - [5 U.S.C. 552(b)]

- b(1) National security classified information [(b)(1) of the FOIA]
- b(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
- b(3) Release would violate a Federal statute [(b)(3) of the FOIA]
- b(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
- b(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
- b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
- b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
- b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

Withdrawal/Redaction Marker

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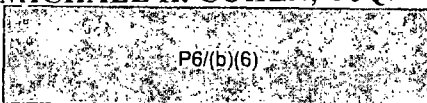
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EDUCATION

- 1988-1990 **University of Iowa, Iowa Writers' Workshop**
 M.F.A. Thesis: *A Book Full of Surprises*.
- 1987-1988 **University of California, Berkeley, Haas School of Management**
 M.B.A. Thesis: *Regulated Industries*.
- 1984-1986 **University of California, Berkeley, Boalt Hall School of Law**
 J.D.
 Member, *California Law Review*; Editor, Book Review.
- 1983-1984 **Boston University, School of Law**
 G. Joseph Tauro Distinguished Scholar (top 2%).
 C.J.S. and Am.Jur Awards; invited onto *Boston University Law Review*.
- 1979-1983 **Columbia University, Columbia College**
 B.A. (concentration in political science).

ACADEMIC APPOINTMENTS AND TEACHING

- 1999 **University of California, Los Angeles School of Medicine**
 Guest lecture: *Legal and Ethical Issues in Integrative Medicine* (Center for East-West Medicine)
- University of California, Irvine College of Medicine**
 Guest lectures: *Legal and Ethical Issues in Integrative Medicine*
 Body-Mind-Spirit Medicine (Department of Anatomy & Neurobiology)
- 1996-1999 **Chapman University School of Law**
 Associate Professor of Law
 Civil Procedure, Conflicts of Laws, Constitutional Law, Criminal Law, Health
 Care Law, Advanced Health Care Law.
- 1993-1996 **Widener University School of Law**
 Associate Professor of Law
 Civil Procedure, Insurance Law, Legal Research and Writing, Seminar on
 Regulation of Complementary and Alternative Medicine.
- 1992-1993 **Brooklyn Law School**
 Adjunct Instructor
 Legal Writing, Moot Court.

LEGAL EXPERIENCE

- 1992-1993 **Shereff, Friedman, Hoffman & Goodman**, New York
Associate
Litigation experience in Constitutional, white-collar crime, and securities fraud cases.
- 1990-1992 **Davis, Polk & Wardwell**, New York.
Associate
Experience in securities, mergers and acquisitions and banking groups within the corporate department; *pro bono* experience including libel, copyright and contract cases. Responsibilities included drafting and negotiating agreements, handling SEC filings and other regulatory matters, drafting legal memoranda and firm opinions, handling closings, and managing medium-sized transactions.
- 1986-1987 **United States District Court, Southern District of New York, Honorable Thomas P. Griesa**
Law Clerk
Responsibilities included drafting bench opinions, assisting in civil hearings, trials, and settlement conferences, and assisting in criminal trials and sentencing hearings.
- 1986 **Gibson, Dunn & Crutcher**, Los Angeles and Newport Beach.
Summer Associate
Litigation and transactional experience; practice areas included securities and real estate.

Bar Admissions

Massachusetts (Jan. 28, 1988).
New York (June 28, 1988).

PUBLICATIONS

Books and Book Chapters

- **COMPLEMENTARY AND ALTERNATIVE MEDICINE: LEGAL BOUNDARIES AND REGULATORY PERSPECTIVES** (Baltimore: Johns Hopkins University Press, 1998).
- **CREATIVE WRITING FOR LAWYERS** (New York: Citadel Press, Carol Publishing Group, 1991).
- **INTEGRATIVE HEALTH CARE: ESSAYS IN LAW AND 21-CENTURY MEDICINE** (in peer review).
- **MILLENNIAL MEDICINE: CLINICAL, ETHICAL, AND LEGAL DIMENSIONS OF SPIRITUAL HEALING** (in progress).
- ***Legal Authority and Holistic Health***, in **TEXTBOOK ON COMPLEMENTARY AND ALTERNATIVE MEDICINE** (Baltimore: William & Wilkins, Wayne Jonas & Jeff Levin eds., forthcoming 1999).
- ***Third-Party Reimbursement for Complementary and Alternative Medicine; Legal Rules***

Affecting Complementary and Alternative Medicine: Malpractice and Vicarious Liability; Federal Regulation of Complementary and Alternative Medicine Through Health and Insurance Fraud Legislation; The Federal Role in Regulating Access to Complementary and Alternative Medicine; in ENCYCLOPEDIA OF COMPLEMENTARY HEALTH PRACTICES (New York: Springer Publishing Co., 1999).

Law Review Articles

- ***U.S. Dietary Supplements Regulation: Belief Systems and Legal Rules***, HASTINGS WOMEN'S LAW JOURNAL (under submission for Spring 1999).
- ***Holistic Health Care: Including Complementary and Alternative Medicine in Insurance and Regulatory Schemes***, 38 ARIZ. L. REV. 83 (1996).
- ***A Fixed Star in Health Care Reform: The Emerging Paradigm of Holistic Healing***, 27 ARIZ. STATE L. J. 79 (1995).
- ***Malpractice and Vicarious Liability for Providers of Complementary and Alternative Medicine***, BENDER'S HEALTH CARE MONTHLY 3 (July 1996).
- ***Toward a Bioethics of Compassion***, 28 IND. L. J. 667 (1995).
- ***Reconstructing the Implied Covenant of Good Faith and Fair Dealing as a Tort***, 73 CALIF. L. REV. 1291 (1985).

Additional Articles

- ***Insurance Coverage of Alternative Medicine***, INTELLECTUAL CAPITAL, www.intellectualcapital.com (March 25, 1999).
- ***Setting Up A Holistic Health Care Clinic: Legal Implications***, INTEGRATIVE MED. CONSULT (forthcoming, April 1999).
- ***Medicine in "Flatland:" A Tale of Two Dimensions***, ALT. & COMP. THERAP. (forthcoming, March 1999).
- ***Malpractice Considerations Affecting the Clinical Integration of Complementary and Alternative Medicine***, CURRENT PRACTICE OF MEDICINE (forthcoming, March 1999).
- ***Changing U.S. Dietary Supplements Regulation: Belief, Values, Policies***, 2:2 ALT. HEALTHCARE MGT. 16 (March 1999).
- ***An Indigenous Mexican Healer: A Personal Encounter***, 2:2 ALT. HEALTHCARE MGT. 24 (March 1999).
- ***Referral to Complementary and Alternative Medicine Providers: A Physician's Liability***, INTEGRATIVE MED. CONSULT 44 (March 1, 1999).
- ***Complementary and Alternative Medicine Policy: The Future of Regulation***, 5:1 ALT. & COMP.

THERAP. 50 (Feb. 1999).

- ***Sex, Scandal and Spirituality***, 4:6 ALT. & COMP. THERAP. 435 (Dec. 1998).
- ***Examining The Legal Status of Energy Healing***, 1:2 ALT. HEALTHCARE MGT. 14 (Nov. 1998) and 2:1 (Jan. 1999).
- ***Integrating Complementary and Alternative Therapies: Strategic Advice for Health Care Institutions***, 1:1 ALT. HEALTHCARE MGT. 10 (Sept. 1998).
- ***Complementary Medicine: Legal Status of the Nonlicensed Provider in the United States***, 4:3 COMP. THER. IN NURS. & MIDWIF. 99 (Aug. 1997).
- ***Scope of Practice Limitations on Unconventional Providers: The Case of Chiropractic***, 2:2 ALT. & COMP. THERAP. 110 (1996).
- ***Guaranteeing Freedom of Access to Healing: The Access to Medical Treatment Act of 1995***, 1:6 ALT. & COMP. THERAP. 408 (1995).
- ***Legal Ramifications of Homeopathy***, 1:4 J. ALT. & COMP. MED. (1995).
- ***Expanding Legal Paradigms to Incorporate Subtle Energies***, 6:1 SUB. ENERG. 99 (1995).
- ***The Impact of Complementary and Alternative Medicine on Informed Consent*** (in progress).

SPEAKING ENGAGEMENTS

1999

- ***Overview of Licensing and Credentialing***, Center for Bioethics, University of Pennsylvania/NIH Center for Complementary and Alternative Medicine (Philadelphia, November 9-12).
- ***Complementary and Alternative Medicine Legal Issues***, Stanford University School of Medicine and Harvard Medical School (San Francisco, October 15-17).
- ***Legal and Regulatory Issues in Integrative Care: Risk Management Solutions for Business Development and Clinical Practice***, Practice Management for Integrative Medicine (San Francisco, June 3-4).
- ***Freedom of Choice in Health Care***, Comprehensive Cancer Care Conference II: Integrating Complementary and Alternative Therapies (Arlington, Virginia, June 9-12).
- ***Malpractice and Informed Consent in Integrative Medicine***, First International Conference on Integrative Medicine (Seattle, April 30-May 2).
- ***Complementary and Alternative Medicine Policy***, Society of Air Force Physicians (Berkeley, California, April 6).

- ***Malpractice/Informed Consent Issues in Integrative Medicine***, Harvard Medical School, Alternative Medicine: Implications for Clinical Practice (Boston, February 1999) (informal interest group).
- ***Evaluating U.S. Dietary Supplements Regulation***, Symposium, Hastings Women's Law Journal (San Francisco, February 6).

1998

- ***Legal and Regulatory Issues Affecting the Practice of Tibetan Medicine*** (Panel, Moderator); ***The Role of U.S. Law in Tibetan-American Medical Exchange***, First International Congress on Tibetan Medicine: Revealing the Art of the Medicine Buddha (Washington, D.C., November).
- ***Legal and Ethical Perspectives on Complementary and Alternative Medicine***, Bioethical Issues Committee, Association of the Bar for the City of New York (New York, November).
- ***Regulation of Complementary and Alternative Medicine***, Health Law & Policy Program, Seton Hall Law School (Newark, N.J., November).
- ***Complementary Medicine and the Courts***; Panel, ***Legislative Issues for Complementary Care Practitioners***, American Preventive Medical Association/Emord & Associates Legal Seminar (Arlington, VA, October).
- ***Integrative Medicine: Practical Applications for Practice Management (Outcomes Analysis, Billing & Reimbursement)*** (Panel, Fourth Annual Congress on Alternative and Complementary Therapies (Arlington, VA, October).
- ***Legal Aspects of Alternative Medicine Therapies***, Whittier Law School (Costa Mesa, California, October).
- ***Integrating Spirituality into Medicine: A Healer's Perspective***, Kindred Spirits (Washington, D.C., June).
- ***Legal and Ethical Reflections on the Practice of Homeopathy***, National Center for Homeopathy (San Diego, California, March).
- ***Complementary and Alternative Medicine: Legal Boundaries and Regulatory Perspectives***, Chapman University (Orange, California, March).

1991-1997

- ***Developing a Complementary Care Center***, University of California, Irvine, School of Medicine (December 1997).
- ***Legal Issues in Complementary Medicine***, Chapman University School of Law (Dec. 1997).
- ***Practice Issues in Clinical Nutrition***, Health Professionals Seminar, Body Wise International (Newport Beach, CA, October 1996).

- ***Overview of Malpractice and Reimbursement Issues for the Practitioner***, Chair, Legal Panel, Second International Congress on Complementary & Alternative Therapies (Washington, D.C., June 1996).
- ***Managing Practice Risks, Obtaining Reimbursement: An Overview***, Second International Congress on Complementary & Alternative Therapies (Washington, D.C., June 1996).
- ***Legal Obstacles & Opportunities in an Integrated Health Care System***, Annual Meeting, International Society for the Study of Subtle Energies & Energy Medicine (Boulder, 1996).
- ***Legal Ramifications of Energy Medicine***, Annual Meeting, International Society for the Study of Subtle Energies & Energy Medicine (Boulder, June 1995).
- ***Healing and Holistic Justice***, Annual Meeting, International Alliance of Holistic Lawyers (Burlington, Vermont, May 1995).
- ***The Emerging Paradigm of Holistic Healing***, Medical Institute for Law Faculty, Cleveland-Marshall College of Law, Cleveland State University/Cleveland Clinic (June 1994).
- ***From Briefs to Bestsellers***, New York City Bar Association (New York City, April 1991).

ADDITIONAL PROFESSIONAL CONFERENCES

- Cancer Care: Integrating Complementary and Alternative Therapies (Arlington, VA, June 1998).
- AALS Health Law Teachers' Conference (Houston, June 1998).
- Whole World Health Forum (Los Angeles, March 1998).
- AALS Annual Meeting (San Francisco, January 1998).
- Health Freedom Legislative Summit (Reston, Virginia, December 1996).
- III World Congress of Bioethics (San Francisco, November 1996).
- Alternative Medicine and Managed Care (San Francisco, September 1996).
- AALS Conference, New Ideas for Experienced Teachers (Minneapolis, MN, June 1995).
- AALS Conference, Civil Procedure (Washington, D.C., June 1995).
- First International Congress on Complementary & Alternative Therapies (Washington, D.C., May 1995).
- American Society of Law, Medicine & Ethics, Ethics Committees & The Elderly (New York City, January 1995).

- AALS Health Law Conference (Washington, D.C., March 1994).
- AALS Annual Meeting (Orlando, FL, December 1993).

OTHER ACTIVITIES

- Board of Advisors, Compassion in Action (San Francisco chapter, 1999-present).
- Legal Editor, Alternative Healthcare Management (1998-present).
- Co-Editor, column, "Legal Matters," Alternative & Complementary Therapies (Larchmont, New York: Mary Ann Liebert, Inc., 1995-96, 1998-present).
- Board of Directors, American Preventive Medical Association (Great Falls, Virginia, 1995-1997).
- Board of Directors, American Preventive Medical Association Education & Legal Foundation (Great Falls, Virginia, 1995-present).
- Board of Directors, New Creek Foundation for Research and Education on Low Impact Therapy and Evaluation (Alexandria, Virginia, 1996-1997).
- Board of Directors, Global Community (New York, New York, 1994-96).
- Compassion In Action, training (VA Hospital, L.A.; hospice volunteer work) (July 1998).
- Barbara Brennan School of Healing (New York, 1992-1996).

MEDIA APPEARANCES

- "Here's To Your Health (with Deborah Ray and Ronald Carrow, M.D.)" (radio, national syndication, March 1998).
- "Here's To Your Health" (September 1998).
- "Here's To Your Health" (February 1999).
- "Total Health Talk" (cable television, Los Angeles, taping March 1998).
- "The Alternative Medicine Show" (cable television, D.C. area, taping June 1998).
- The American Health Network (cable television, national syndication, taping June 1998).
- "Beyond Wellness" (radio, Palm Springs, July 1998).

John Weeks***Experience in Integration of Healthcare Alternatives: 1983-1999***

Publisher-Editor, THE INTEGRATOR for the Business of Alternative Medicine
Principal, Integration Strategies for Natural Healthcare

3345 59th Avenue Southwest, Seattle, WA 98116
206-933-7983; FAX 206-933-7984; pinhcp@aol.com

Overview

John Weeks is viewed by diverse stakeholders as one of the nation's most knowledgeable authorities on the practical business of complementary and alternative medicine integration. He has been called an "expert in alternative medicine" by *Medical Economics* and an "alternative care (integration) guru" by *Modern Healthcare*. For three years, Weeks has produced a monthly newsletter, *THE INTEGRATOR for the Business of Alternative Medicine*. The newsletter is widely viewed, in the words of Lee Ballance, MD, of the Kaiser Permanente alternative medicine committee, as "the single most up-to-date, insightful and comprehensive source on what's actually going on in integration." *THE INTEGRATOR* focuses on the nuts and bolts of delivering and paying for alternative medicine services. The newsletter's pioneering information sharing reports include the ongoing *INTEGRATOR Integrative Clinic Benchmarking Survey* and the annual *INTEGRATOR CAM Network Executive Survey*.

THE INTEGRATOR is informed by Weeks' long-time, hands-on experience in the field. Since 1993, when he formed *Integration Strategies for Natural Healthcare*, he has worked full-time consulting, writing and speaking in CAM integration. His clients have included government agencies at all levels (US AHCPR, US Bureau of Primary Health Care, Arizona Department of Health, Washington State Office of the Insurance Commissioner, King County Department of Public Health, Beach Cities Health District (CA)), health systems (St. Joseph Health System (CA), Deaconess (IN), Sisters of Providence (OR), Catholic Health Initiatives (CO), Baptist-St. Vincent (FL)), HMOs (PacificCare of WA, First Choice, American Specialty Health Plans), physician groups, alternative provider network services organizations, and CAM professions.

Prior to establishing his business, Weeks served a decade (1983-1993) in the maturation of the alternative medicine movement. He held positions as vice president for Bastyr University and as board member for the American Herbal Products Association. His writing has appeared in diverse publications, both peer-reviewed and industry, including *Health Forum Journal*, *Physician Executive*, *Drug Benefit Trends* and Andrew Weil's *Integrative Medicine*. He has contributed chapters on alternative medicine integration for *Best Practices in Medical Management* (Peter R. Kongstvedt, editor, Aspen Publishing), and *Current Medicine* (Mark Micozzi, MD, PhD, editor) and the planned *Textbook of Complementary and Alternative Medicine* (Wayne Jonas, MD, co-editor, Williams and Wilkins). Weeks and *THE INTEGRATOR* are widely cited sources in the mainstream, business and medical media. His prior professional experience was in journalism, politics and organizing. Weeks attended Stanford University for three years, studying history.

Consulting on CAM Integration Initiatives: 1994-1999

Catholic Health Initiatives (Denver, CO). Day-long consultation with national CAM team.

Stanford University, Complementary and Alternative Medicine Program (Palo Alto, CA). Contracted paper for Kenneth R. Pelletier, PhD, MD (hc) on coverage issues and developments.

INTEGRATOR INDUSTRY/HEALTH Subscription, a combined information and consultative service (\$1000/yr.) offered beginning December 1998 and subscribed by 40 health systems, CAM professional organizations, academic medical centers and CAM businesses, as of March 15, 1999.

John Weeks: Experience in Integration of Healthcare Alternatives

Beach Cities Health District (CA). Day-long consultation on integrative clinic strategies.

Condell Medical Center (Chicago, IL). Workshop presentation to trustees and executive team.

St. Joseph Health Care (Orange, CA). Strategic planning, including: presentation to executive team; survey development; focus on the value of CAM in creating health in the population served.

Office of the Insurance Commissioner, Washington State. Co-facilitator and co-developer of a year-long series of seven, half-day interactive workshops on clinical issues in integration and coverage involving medical directors of six of the state's health plans, five physician groups and selected leaders of CAM professions (DC, LAc, LMP, LM, ND) and co-funded by the involved organizations.

Price Waterhouse (Arlington, VA). Contracted to develop and head an outside expert panel as part of a three-armed proposal team, which also included the Lewin Group, on an alternative medicine proposal for the Veteran's Health Administration.

HealthNotes (Portland, Oregon). Background paper and consultation on the state of CAM integration and marketing opportunities for online/CD ROM CAM firm.

WellSpace (Boston, MA). Advisory capacity for national clinic network.

Baptist/St. Vincent Healthcare System (Jacksonville, FL). Strategic planning; physician and consumer surveys; marketing.

Bureau of Primary Health Care, US HRSA (Rockville, MD). Working group on complementary medicine and alternative health practices for the underserved.

American Centers for Health and Medicine/Catholic Healthcare West (Phoenix, AZ). Physician education, special projects, natural products quality.

American WholeHealth Networks (Hartland, WI). Information on developing benefits for services of LAc, ND, massage, MD-homeopaths, including credentialing, pricing, coding, management; used as basis for successfully securing contracts in AZ and WA.

Midwives Association of Washington State (Seattle, WA). Strategic planning; outreach to insurers.

General Nutrition Centers/Nature's Northwest (Portland, OR). Development of linked, not-for-profit selfcare centers and health education and disease management programs which integrate alternative methods; liaison to complementary medical institutions; program development; strategies with payers and complementary providers.

Medalia HealthCare/Sisters of Providence Health System (Seattle, WA). Strategic planning, survey of conventional providers, survey of CAM providers, complementary care network development, utilization review and program implementation for PCP network.

Deaconess Hospital (Evansville, IN) Feasibility study, provider survey, consumer survey, strategic planning.

PacificCare of Washington (Mercer Island, WA). Provider selection, credentialing standards, coding, network development and utilization plan for LAc, ND, LMP providers.

Unified Physicians of Washington (Federal Way, WA). CAM credentialing standards, network development, benefit definition.

American Specialty Health Plans (Los Angeles, CA). Information on naturopathic benefits.

John Weeks: Experience in Integration of Healthcare Alternatives

First Choice Health Network (Seattle, WA). CAM credentialing standards, statewide network development, benefit definition.

Arizona Department of Health Services (Phoenix, AZ). Development of workshop involving conventional and complementary providers and public health officials toward establishing an integrated public health clinic; lead-off presentation.

CommonWell (Boston, MA). Strategic planning.

King County Department of Public Health/Natural Medicine Clinic (Seattle, WA). Resource development, RFP guidance for first integrated conventional/natural medicine clinic in the public health arena.

American Association of Naturopathic Physicians (Seattle, WA). Develop and facilitate national summit on reimbursement and quality management issues. White Paper: *Naturopathic Medicine and Managed Care*.

Bastyr University (Bothell, WA). Strategic responses to managed care and insurance issues; instructor on business issues.

Behavioral Health Alliance (Seattle, WA) and Peninsula Mental Health Providers Association, (Bremerton, WA). Marketing and organizational development.

Bezwecken (Portland, OR). grant funded project to educate and network naturopathic leaders nationwide on efforts to gain more inclusion and integration into health care plans.

Connecticut Society of Naturopathic Physicians (Middletown, CT). Outreach to payers.

Hawaii Society of Naturopathic Physicians (Kailua-Kona, HI). Outreach to payers.

American Naturopathic Independent Physicians Association (Portland, OR). Outreach to managed care organizations, provider education.

Writing & Research

THE INTEGRATOR for the Business of Alternative Medicine (formerly *St. Anthony's Alternative Medicine Integration and Coverage*) Publisher-Editor for 8-12 page monthly on integration and coverage strategies. August 1996 – present.

"Operational Issues in Incorporating Complementary and Alternative Therapies and Providers in Benefit Plans and Managed Care Organizations", unpublished paper contracted for a workshop entitled "Complementary and Alternative Medicine: Issues Impacting Coverage Decisions," co-sponsored by the NIH Office of Alternative Medicine, US Agency for Health Care Policy and Research, and the Arizona Prevention Center at the University of Arizona Health Sciences Center, October 9, 1996; 82 pages.

"Utilization, Patient Satisfaction and Potential Cost Implications from Acupuncture, Massage and Naturopathic Medicine Services in a PPO Plan and an HMO Benefit Design," co-author. Submitted for publication, 1999.

"Integration as Community Organizing: Toward a Model for Optimizing Relationships between Networks of Conventional and Alternative Providers," with Richard Layton, MD. *Integrative Medicine*, Vol. 1, No. 1, Andrew Weil, MD, editor. Spring 1998.

"Trends in Developing the Integrative Medicine Clinic" for *The Physician Executive*, November-December 1998, Vol 24, Issue #6, 18-19.

John Weeks: Experience in Integration of Healthcare Alternatives

"On the Outside Moving In: Will the Alternative Medicine Integration Movement Shape US Healthcare?" Healthcare Forum Journal, November-December 1998, cover story, 14-19.

Best Practices in Medical Management (Peter R. Kongstvedt, Aspen Publishing), contributor of chapter on operational issues and models in CAM integration. 1998.

"Managed Care Meets Alternative Medicine: Reflections on Overcoming the Polarization," *Alternative and Complementary Therapies*, Vol. 3, No. 1., February 1997.

Textbook of Complementary and Alternative Medicine (Williams and Wilkins, 1998), editor, Wayne Jonas, MD, Director, NIH OAM; contributor of chapter entitled "The Insurance Industry and Complementary and Alternative Medicine."

"The Emerging Role of Alternative and Complementary Medicine in Managed Care," *Drug Benefit Trends/Medscape*. Volume 9, Number 4, April 1997.

Townsend Letter for Doctors, Port Townsend, WA. Monthly column, "Charting the Mainstream". Review of trends in mainstream medicine for a leading national alternative medical publication. January 1995-present.

"Marrying the Medicines", feature in the Sunday *Seattle Times-PI* on the first year of the WA mandate requiring plans to include "every category of provider". April 6, 1997.

The Synergizer. Quarterly newsletter (6-8) pages on managed care and integration topics related to naturopathic medicine (1994-1996).

Southwest College Press Journal, Phoenix, AZ. *Report on a Pilot Survey of Naturopathic Patients: Developing Useful Data for the Reimbursement Arena*, August 1996. Based on a patient survey administered to thirty consecutive patient in each of five naturopathic practices.

Presentations Completed or Scheduled

National Managed Health Care Congress West. Track chair, moderator and presenter. Los Angeles, CA. October 18-20, 1999.

Stanford University Medical School-Harvard University Medical School. "Complementary and Alternative Medicine: Practical Medicine and Evaluations." San Francisco, CA. October 15-17.

University of Arizona School of Medicine, Program in Integration. "Mainstreaming Integrative Medicine: State of the Art." Presenting with Andrew Weil, MD, and Tracy Gaudet, MD, in a three hour, multi-site video-conferenced workshop. July 28, 1999.

Nutracon 1999. Presentation on strategies for covering and integrating botanicals into managed care and health system initiatives. Las Vegas, Nevada. July 12, 1999.

American Association of Health Plans, annual Institute. Trends in Alternative Medicine Integration. San Francisco, CA. June 22, 1999.

Solutions in Integrative Medicine/CambridgeHealth Resources. Integrative clinic business strategies. San Francisco, CA. June 3-4, 1999.

International Conference on Integrative Medicine. "Our Integration Models: Are They Working? What Can We Expect? National Trends in the Business of Integration." Seattle, WA. April 30, 1999.

John Weeks: Experience in Integration of Healthcare Alternatives

National Managed Health Care Congress. Track chair for alternative medicine, moderator. Moderator of debate on the role of CAM in managed care. Atlanta, GA. March 29 - April 1, 1999.

Harvard Medical School. Alternative Medicine: Implications for Clinical Practice. "Billing, Reimbursement and Network Strategies." Boston, MA/ February 28-March 3, 1999.

Healthcare Forum Best Practices Meeting. Presentation on Washington's Clinician Workgroup on Integration of CAM. Honolulu, HI, February 10-13, 1999.

Institute for Alternative Futures. Foresight Seminar on Complementary and Alternative Approaches. Rayburn House Office Building, US Congress. February 9, 1999.

Washington Chapter, American Massage Therapy Association. Annual meeting keynote. Seattle, WA. January 23, 1999.

Washington Association of Naturopathic Physicians. Keynote: "The Naturopathic Profession and Healthcare Reform: Political Application of a Homeopathic Dose?" Seattle, WA, November 13, 1998.

American Massage Therapy Association, keynote presentation at annual national meeting. Washington, DC, October 29, 1998. Keynote presentation at Washington State Chapter: January 23, 1999.

National Managed Health Care Congress West.. Developer/moderator of day-long track on alternatives. Lead-off presentation. November 18, 1998. Los Angeles, CA.

4th Annual Congress on Alternative and Complementary Therapies (Mary Ann Liebert-BioConferences International). Co-developer and presenter, Integrated Clinic Track: "What Goes First? What Yields? Merging Alternatives into the Mainstream Delivery System." Arlington, VA, October 2-4.

American Association of Health Plans. Mainstreaming the Alternatives. Panel with representatives of Group Health Cooperative and Oxford Health Plans. June 15, 1998. Boston, MA.

Healthcare Forum Annual Summit. Mainstreaming Alternative Medicine: Lessons from the Frontline. Pre-conference workshop. San Diego, CA, May 2, 1998.

Loudoun Healthcare System. Three hour morning seminar on integration issues at system annual retreat. Leesburg, VA, April 26, 1998.

National Managed Health Care Congress, moderator or presenter on three panels on integration topics. Atlanta, GA, April 20-23, 1998.

Casa Colina World Whole Health Forum, Integrated Care: An Industry Primer for Better Managed Care and Healthier Communities. Los Angeles, CA, March 25, 1998.

Medicode Annual Summit, session entitled "Working with Conventional and Alternative providers to Maximize the Value of Integrated Care." Salt Lake City, UT, March 9-10, 1998.

Washington Health Legislative & Policy Forum, "The Consumer's Role in Coverage Decisions." December 4, 1997.

National Managed Health Care Congress, pre-conference symposium, "Alternative Medicine and Managed Care." Los Angeles, CA, November 3, 1997.

Midwives Alliance of North America, annual conference. Seattle, WA, November 2, 1997

Bureau of Primary Health Care, HRSA: "BPHC and Complementary Medicine and Alternative Health Practices: A New Medical Paradigm for Improving the health Status of Underserved Populations". Panel on finance, marketing and managed care issues. Rockville, MD, September 25-26, 1997.

John Weeks: Experience in Integration of Healthcare Alternatives

3rd Annual Congress on Alternative Therapies, Mary Ann Liebert. Presentation on opportunities for coverage; panelist on integration strategies. Arlington, VA, September 6-8, 1997.

American Association of Health Plans, annual Institute, 'Integration and Coverage Issues in Complementary Medicine.' Program chair and presenter. Seattle, June 23, 1997.

National Managed Health Care Disease Management Congress, panelist on CAM. New York City, New York, June 16, 1997.

Employee Benefits Planning Association, Pacific Northwest Chapter, annual conference. Presentation on CAM coverage and integration issues. Seattle, WA, June 3, 1997.

National Acupuncture and Oriental Medicine Alliance Annual Conference, 'Interfacing with National Policy' and 'The Washington State Experiment.' Arlington, VA, May 3, 1997.

Sisters of Providence Health System, 'National Integration Status and the Medicaid Strategy.' Seattle, WA, April 29, 1997.

Cambridge Healthtech Institute, pre-conference session: 'Report from the NIH OAM/AHCPR Workshop on Reimbursement of Complementary Providers and Therapies'. San Diego, February 3-4, 1997.

Policy and Issues Forum, National Association of Community Health Centers, panelist on 'Closing Health Status Gaps: Alternative Health Practices -- New Paradigms in Primary Health Care Delivery,' Washington, D.C., March 24, 1997.

'Integrating Alternative Medicine into Managed Care,' pre-conference symposium, National Managed Health Care Congress West, January 28, 1997.

AIC Conferences: 'Developing, Operating and Integrating Complementary and Alternative Medicine.'

Presentation: 'Engaging Providers in the Opportunities in Complementary Care.' Atlanta, GA, November 21-22, 1996.

Midwives Association of Washington State, annual conference presentation on trends in reimbursement. October 11, 1996.

NIH OAM/AHCPR invitational workshop: 'Complementary and Alternative Medicine: Issues Impacting Coverage Decisions.' Paper on operational issues. October 9, 1996.

Institute for International Research, New York, NY. Conference co-chair and presenter, 'Integrating Complementary Medicine and Managed Care.' Presentation on the Washington State experience. Washington, DC, October 7-8, 1996.

American Association of Naturopathic Physicians, Seattle, WA, 1996 National Convention. 'Integrating Naturopathic Medicine into the Reimbursement System: Part I -- Basic Issues for the Naturopathic Provider and Profession; Part II -- Case Studies on Health Plan Strategies', September 5-6, 1996.

Drug Information Association, 32nd Annual Meeting. 'The Emerging Role of Alternative/Complementary Medicine in Managed Health Care.' San Diego, CA, June 11, 1996.

Evergreen Hospital/Community Health Care Alternative Medicine Task Force, Kirkland, WA. 'Reimbursement of Alternative Medicine,' May 20, 1996.

Association of Healthcare Administrative Assistants. Topic: 'Health Plans, Hospitals and the Every Category of Provider Legislation.' April 19, 1996.

Acupuncture program, Bastyr University. Guest lecturer on managed care integration strategies, 3rd year students. March 1996.

John Weeks: Experience in Integration of Healthcare Alternatives

Washington Association of Naturopathic Physicians. Keynote presenter, "Managed Care Principles and Naturopathic Practices," Winter Insurance Conference, January 27-28, 1996.

Providence/Medalia Health Plans. Panelist on integrating complementary providers into the health system. January 18, 1996.

Office of Congressman Bernie Sanders. Alternative Medicine and Insurance Coverage. Conference title: "Alternative Medicine in the Green Mountain State," Randolph, VT, January 14, 1996.

Office of the Insurance Commissioner, Washington State: "Workshop for Providers" on the state's new "every category of provider" law. Seattle, WA, December 14, 1995.

Institute for International Research (NY), "Managed Care and Natural Medicine: Strange Bed-Fellows of Future Medicine?", and "Engaging the Challenges of Integrating Alternative Providers". Conference title: "Integrating Managed Care and Alternative Medicine." San Francisco, CA, December 7-8, 1995.

Bastyr University, Strategic Planning Retreat. Managed care and reimbursement issues. November 1995.

Arizona Naturopathic Medical Association, Tucson, AZ. "Naturopathic Medicine and Managed Care," November 19, 1995.

Quoted Media Resource on Integration Topics

"Nation Embracing Alternative Medicine," cover story, *USA Today*. November 11, 1998, 1-2.

"HMOs Open to Alternatives," *Modern Healthcare*. September 7, 1998. Cover story.

"Insurers look at merits of covering more non-traditional health care", by Judi Russell, *New Orleans CityBusiness*, June 15, 1998

"Expanding Coverage Signals Growing Demand, Acceptance for Alternative Care," *Medicine and Health*, (Faulkner & Gray). Volume 52, No. 18, May 4, 1998.

"Health Plans, Providers, Struggle for Quality in Alternative Medicine," *The Quality Letter for Healthcare Leaders* (Capitol Publications). Volume 10, Number 5, May 1998. Similar articles in two other Capitol publications, *Medical Guidelines and Outcomes Research*, May 14, 1998, Volume 9, Number 10, and *Executive Solutions for Healthcare Management*, Volume 1, Issue 3, May 1998..

"Insuring Wellness" in *IDEA Health and Fitness Source*. February 1998, page 68.

"20/20 on 2020", one of eight selected leaders asked to comment on seven questions on health care in the year 2020. *Best's Review*, January 1998.

"The Building Blocks of an Alternative Medicine Program" by Daniel Stern. *HealthPlan* (AAHP), January-February 1998.

"MCOs Integrating Alternative Care" by Diane West. *National Underwriter*, November 10, 1997. Page 1, 58.

"Gold in Goldenseal" by Michele Bitoun Blecher. *Hospitals and Health Networks*, October 20, 1997, 50-52.

"Get Yourself Covered" by Lorraine Calvacca. *Natural Health*, September-October 1997, 26.

"Health Providers See Point of Offering Acupuncture," *San Francisco Chronicle*. September 22, 1997.

John Weeks: Experience in Integration of Healthcare Alternatives

"Integrated medicine' could boost your income" by Deborah Grandinetti. *Medical Economics*, September 8, 1997, 73-99.

"Fringe Benefits: Insurers Begin Covering Alternative Medicine" by Daniel Stem. *LAN/Life Association News*, September 1997, 103-110.

"Insurance Coverage of Complementary and Alternative Medicine in Washington State" by Mark Schulte. *Healing Arts Report*, Volume 1. Fall 1997.

"MCOs increasingly embracing alternative care in response to consumer demand" in *Managed Care Outlook*, July 11, 1997.

"Insurers giving alternative health services new look" by Tom Philip. *Sacramento Bee*, July 5, 1997, page A1, A16.

"Demand for Alternative Care Not Quashed by Washington Ruling." *American Medical News*, June 7, 1997.

"Consumers Lead Way toward Integrated Health Care" in *Nutrition Business Journal*, June 1997. Various article in 18 page issue.

"A Health Insurance Revolution" by Jan Goodwin. *New Age Journal*, March/April 1997, 95-100.

"Alternative Medicine Moves into the Mainstream" by Lynna Goch. *Best's Review (Life/Health)*, March 1997, 84-88.

John Weeks: Experience in Integration of Healthcare Alternatives

Related Professional Experience

1978-1983 Politics and Journalism. Diverse positions (WA State Senate Legislative Aide, State Senate; PR consultant and organizer to diverse groups, including Wein Airlines Pilots Association and Eastern Washington wheat farmers). Extensive freelance writing on politics, international trade.

1983-1989 Bastyr University. Vice President for External Affairs. Created and developed the national and local presence and support for the institution which became, during this period, the first multi-disciplinary institution of natural medicine to gain formal accreditation status with a regional accrediting agency (media, political, industry and alumni relations; fundraising.) Grew contributed funding from \$20,000 in 1983 to over \$400,000 in 1989 (\$210,000 cash and the remainder in pledges).

1986-1989 American Herbal Products Association, Board of Directors. Worked with the board, 1986-1989. Elected to the board 1989.

1989-1993 American Association of Naturopathic Physicians. Executive Director. Grew the organization's operating budget from \$40,000 to \$280,000 and membership from 170-450. Also served as National Affairs Director and principal media relations coordinator. Successfully lobbied the first Congressional support for a naturopathic initiatives and appointments.

Related Awards and Acknowledgments

1999 Advisory Committee Member, Healthier Community Best Practices Forum, The Healthcare Forum Foundation (Health infoSource/American Hospital Association).

1998 Selected as a member of the National Advisory Board and track chair for alternative medicine for the National Managed Health Care Congress.

1998 Selected by the insurance industry monthly *Best's Review* as one of six industry leaders to answer questions about the future of health insurance for a "20/20 on 2020" feature.

1997 Selected by the US Bureau of Primary Health Care to serve on a working group on Complementary Medicine and Alternative Health Practices.

1997 Only non-insurance carrier, non-complementary provider representative asked by the Washington State Office of the Insurance Commissioner to participate in a series of meetings to create understanding between the parties following the state's mandate to cover "every category of provider"

1996 Invited to present a paper on the operational issues in integration at the seminal federal workshop (NIH OAM/AHCPR co-sponsors) on coverage issues in alternative and complementary medicine, Tucson, AZ

1994 Special recognition, Washington Mental Health Counselors Association

1993 Recognition for leadership, American Association of Naturopathic Physicians, AANP Convention (Portland, OR)

1993 One of 23 national leaders in alternative medicine invited by the Office of First Lady Hillary Rodham Clinton to a special meeting at the White House on the role of alternative therapies in health reform

1990 Honorary doctorate, Bastyr University

1989 Honored for contribution, American Herbal Products Association, AHPA meeting

1989 Special recognition for instrumental role in achieving first institutional accreditation of a multi-disciplinary college of natural medicine through a regional accrediting agency, Bastyr University

1988 Special recognition for public education and public relations, AANP

Bio-Brief Of

Marc S. Micozzi, M.D., Ph.D.

Dr. Micozzi is the Executive Director of the College of Physicians of Philadelphia. Prior to joining the College, Dr. Micozzi was the founding Director of the National Museum of Health and Medicine and a Distinguished Scientist with the American Registry of Pathology in Washington, D.C. He is the author of **Fundamentals of Complementary and Alternative Medicine**, the first textbook on this subject for physicians and medical students. He was the founding editor of **The Journal of Alternative and Complementary Medicine**. Dr. Micozzi has worked to foster communication and cooperation between mainstream and alternative medicine on issues of policy research and education.

Dr. Micozzi earned an M.D. (1979) and a Ph.D. in biomedical anthropology and epidemiology (1984) from the University of Pennsylvania. He also did his medical residency at Pennsylvania Hospital. During 1984-1986, he was a Senior Investigator at the National Cancer Institute. From 1986 to 1995, Dr. Micozzi also served as Adjunct Professor at the Uniformed Services University of the Health Sciences in Bethesda, Maryland.

Dr. Micozzi has presented more than 120 scholarly papers at professional conferences and is the author of over 130 scientific publications. His work has appeared in a number of distinguished publications, including the **New England Journal of Medicine**; the **American Journal of Public Health**; the **Journal of the National Cancer Institute**; and the **Journal of the American Medical Association**. He has published several books and edited volumes on diet and nutrition, cancer prevention research, medical anthropology and complementary therapies in medicine. Dr. Micozzi serves as an Adjunct Professor in the Department of Medicine at the University of Pennsylvania. He is also a member of the Penn Medical Alumni Council.

Laura Patton, MD

1100 Olive Way, Suite 1800
Seattle WA 98101

Phone: (206) 442-4145
Fax: (206) 442-4071
E-mail: patton.l@ghc.org

Education:

1975-1979	University of Washington School of Medicine	Seattle, WA
1970-1971	University of California Certificate in Physical Therapy	San Francisco, CA
1966-1970	Duke University BA Zoology	Durham, NC

Postgraduate Training:

1979-1982	University of Washington Residency in Family Practice	Seattle, WA
	Board Certification 7/82 Re-certification 7/89, 7/95	

Practice Experience:

	Group Health Cooperative of Puget Sound	
1991-Present	University Medical Center	Seattle, WA
1988-1991	Lynnwood Medical Center	Lynnwood, WA
1982-1988	Everett Medical Center	Everett, WA

Administrative Experience:

7/96-Present	Clinical Director, Alternative Services Responsible for directing program offering chiropractic, acupuncture, massage therapy and naturopathy to approximately 500,000 consumers. Oversees provider education, utilization management, credentialing and quality assurance.
1990-7/96	Medical Director, Options Health Care Responsible for medical coverage policies and decisions for 47,000 enrollees in a point of service plan.

- 1987-1990 Regional Director, Purchased Patient Services
Responsible for provider contracting in Everett and GHC's East District.
Annually developed and monitored multimillion dollar budget.
- 1988-1991 Chair, Utilization Management Committee
Eastside Hospital
- 1986-1988 Chair, Utilization Management Committee
Everett Medical Center
- 1986-Present Clinical Associate Professor
University of Washington School of Medicine

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
002. resume	re: William Roper (partial) (1 page)	03/03/1999	P6/b(6)

COLLECTION:

Clinton Presidential Records
Domestic Policy Council
Devorah Adler
OA/Box Number: 20472

FOLDER TITLE:

Alternative Medicine [Folder 7]

2012-0463-S

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RESTRICTION CODES

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- P6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

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Freedom of Information Act - [5 U.S.C. 552(b)]

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- b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
- b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
- b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

HP

WILLIAM L. ROPER, MD, MPH
Curriculum Vitae

1. **Name:**

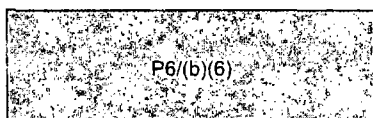
William Lee Roper

2. **Business Address:**

School of Public Health
The University of North Carolina at Chapel Hill
170 Rosenau Hall, Campus Box #7400
Chapel Hill, NC 27599-7400

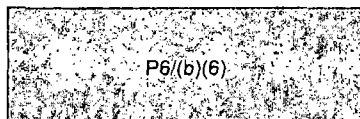
Tel 919.966.3215
Fax 919.966.7678
Email bill_roper@unc.edu

Home Address:



[0021]

3. **Date and Place of Birth:**



4. **Family:**

Spouse
Maryann Jedziniak Roper

Son
William L. Roper, Jr. (Will)

5. **Professional Experience:**

1997-	Dean and Professor of Health Policy and Administration, School of Public Health, The University of North Carolina at Chapel Hill
1997 -	Professor of Pediatrics, School of Medicine, The University of North Carolina at Chapel Hill
1994-97	Senior Vice President, Prudential HealthCare, Roseland, New Jersey
1993-95	President, The Prudential Center for Health Care Research, Atlanta, Georgia
1990-93	Director, Centers for Disease Control and Prevention, Atlanta, Georgia

1989-93 Deputy Assistant to the President for Domestic Policy,
and Director, White House Office of Policy Development,
The White House, Washington, DC
1986-89 Administrator, Health Care Financing Administration, Washington, DC
1983-86 Special Assistant to the President for Health Policy, The White House,
Washington, DC
1982-83 White House Fellow, The White House, Washington, DC
1981-83 Assistant State Health Officer, Alabama Department of Public Health,
Birmingham, Alabama
(on leave 9/82-8/83)
1977-83 Health Officer, Jefferson County Department of Health, Birmingham,
Alabama (on leave 9/82-8/83)

6. Professional Training:

1974-77 Resident in Pediatrics, University of Colorado Medical Center
1975-76 Community Fellow, Department of Health and Hospitals,
City and County of Denver, Colorado

7. Education:

1968 AA, Florida College
1968 University of Michigan
1970 BS, University of Alabama
1974 MD, School of Medicine, University of Alabama
1981 MPH, School of Public Health, University of Alabama at Birmingham

8. Other Professional Activities:

Immediate-Past President, Association for Health Services Research
Chairman, Partnership for Prevention
Member, Institute of Medicine, National Academy of Sciences

9. Memberships:

American Academy of Pediatrics
American Medical Association
American Public Health Association

10. Honors and Awards:

Florida College:

Phi Theta Kappa

Who's Who Among Students in American Junior Colleges

University of Alabama:

Phi Beta Kappa

Outstanding Senior in Chemistry

Distinguished Undergraduate Scholar
of the College of Arts and Sciences

University of Alabama School of Medicine:

State Merit Scholar

Alpha Omega Alpha

Association for Health Services Research:

President's Award (1989)

Fellow (1996)

University of Alabama at Birmingham School of Public Health:

Alumnus of the Year Award (1990)

Institute of Medicine, National Academy of Sciences:

Elected Member (1990)

U.S. Public Health Service:

Distinguished Service Medal (1990)

Meritorious Service Medal (1991)

Exemplary Service Medal (1992)

Surgeon General's Medallion (1993)

University of Alabama School of Medicine

Distinguished Alumnus (1991)

National Association of Health Data Organizations:

Award of Excellence (1991)

Phi Theta Kappa:

National Alumnus of the Year Award (1991)

Emory University School of Medicine:

Alumni Association's Award for Distinguished
Professional Achievement (1993)

University of Alabama at Birmingham:

Distinguished Alumnus Award (1994)

11. Published Writings:

Roper, W.L.: Pasteur and rabies. Alabama Journal of Medical Sciences, 11:57-62, 1974.

Altenburger, K.A., Jedziniak, M.T., Roper, W.L., and Hernandez, J.: Complete congenital heart block and hydrops fetalis. Journal of Pediatrics, 91:618-620, 1977.

Holmes, J.R., Plunkett, T., Pate, P., Roper, W.L., and Alexander, W.J.: Emetic food poisoning due to *Bacillus cereus*. Archives of Internal Medicine, 141:766-767, 1981.

Roper, W.L., Bridgers, W.F.: Organizations and activities of local public health departments in Alabama. Alabama Journal of Medical Sciences, 20:208-216, 1983.

Roper, W.L.: New physicians in a changing health care system. Alabama Journal of Medical Sciences, 22:315, 316, 1985.

Alexander, W.J., Holmes, J.R., Shaw, J.F.E., Riley, W.E., and Roper, W.L.: Norwalk virus outbreak at a college campus. Southern Medical Journal, 79:33-36, 1986.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 258:747, 1987.

Roper, W.L.: Health policy priorities under the Reagan Administration. The Changing Health Care Market, Employee Benefit Research Institute, 133-142, 1987.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 258:3489, 1987.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 259:471, 1988.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 259:1776, 1988.

Roper, W.L.: Balancing efficiency and quality-toward market-based health care. Notre Dame Journal of Law, Ethics & Public Policy, 3:169-186, 1988.

Roper, W.L., Winkenwerder, W.: Enhancing freedom and fairness through Medicare's private health plan option. HMO Practice, 2:66-68, 1988.

Roper, W.L., Hackbarth, G. M.: HCFA's agenda for promoting high-quality care. Health Affairs, 7:91-98, 1988.

Roper, W.L., Winkenwerder, W.: Making fair decisions about financing care for persons with AIDS. Public Health Reports, 103:305-308, 1988.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 259:3530, 1988.

Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 260:609, 1988.

Roper, W.L.: Sounding board—perspectives on physician-payment reform. The New England Journal of Medicine, 319:865-867, 1988.

- Roper, W.L.: The resource-based relative value scale: a methodological and policy evaluation. Journal of the American Medical Association, 260:2444-2446, 1988.
- Roper, W.L., Winkenwerder, W., Hackbarth, G. M., Krakauer, H.: Effectiveness in health care: an initiative to evaluate and improve medical practice. The New England Journal of Medicine, 319:1197-1202, 1988.
- Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 260:2482, 1988.
- Roper, W.L.: From the Health Care Financing Administration. Journal of the American Medical Association, 261:197, 1989.
- Roper, W.L.: Letter to the editor. The New England Journal of Medicine, 320:1086, 1989.
- Roper, W.L.: Commentary: Financing health care: A view from the White House. Health Affairs, 8:97-102, 1989.
- Roper, W. L.: Toward Better Public Health, three speeches delivered in spring 1990, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control.
- Roper, W.L.: National policy perspectives: making prevention a practical reality. Academic Medicine, 65(12): 1990.
- Roper, W.L.: Response to Robert G. Evans. The 1990 Institute of Medicine Rosenthal Lectures: Improving Access to Affordable Health Care, 48-52, 1990.
- Roper, W.L.: Preface, Teenage health teaching modules evaluation. Journal of School Health, 61(1), January 1991.
- Roper, W.L.: Current approaches to prevention of HIV infections. Public Health Reports, 106(2):111, 1991.
- Roper, W.L.: Making smoking prevention a reality. Journal of the American Medical Association, 266(22):3188-89, 1991.
- Roper, W.L.: A comprehensive HIV prevention program (editorial). Public Health Reports, 106(6):601, 1991.
- Snider, D.E.Jr., Roper, W.L.: The new tuberculosis. New England Journal of Medicine, 326(10):703-5, 1992.
- Roper, W.L.: HIV epidemic. Bulletin of the New York Academy of Medicine, 68(2):207-212, 1992.

Roper, W.L.: Americans with Disabilities Act: Lessons for the future. Health Affairs, 11(3):257-258, 1992.

Roper, W.L., Baker, E.L., Dyal, W.W., Nicola, R.M.: Strengthening the public health system. Public Health Reports, 107(6):609-615, 1992.

Roper, W.L.: Book review: A Pound of Prevention, the Case for Universal Maternity Care in the U.S., by Jonathan B. Kotch, et al. New England Journal of Medicine, 327(20):1463, 1992.

Roper, W.L.: Letter to the Editor: Breast Cancer. New England Journal of Medicine, 327(24):1755, 1992.

Roper, W.L., Peterson, H.B., Curran, J.W.: Commentary: Condoms and HIV/STD Prevention--Clarifying the Message. American Journal of Public Health, 83(4):501-3, 1993.

Roper, W.L.: Health Communication Takes on New Dimensions at CDC. Public Health Reports, 108(2):179-183, 1993.

Roper, W.L.: The Rationale for a Universal Infant Hepatitis B Vaccination Program. Leonard Davis Institute Health Policy & Research Quarterly, 3(1):3, 1993.

Roper, W.L., Cates, W., Jr.: Managerial Epidemiology: The Basic Science for Health Reform. Journal of Health Administration Education, 11(4):621, 1993.

Mercy, J.A., Rosenberg, M.L., Powell, K.E., Broome, C.V., and Roper, W.L.: Public Health Policy for Preventing Violence. Health Affairs, 12(4):7-29, 1993.

Roper, W.L., Thacker, S.B.: Doing Good Before There's Harm. Annals of the New York Academy of Sciences, 703:33-39, 1993.

Roper, W.L.: Quality Measurement and Improvement. Health Affairs, 13(1):250-251, 1994.

Thacker, S.B., Koplan, J.P., Taylor, W.R., Hinman, A.R., Katz, M.F., Roper, W.L.: Assessing Prevention Effectiveness—Using Data to Drive Program Decisions. Public Health Reports, 109(2):187-194, 1994.

Roper, W.L., Koplan, J.P., Stinnett, A.A.: Public Health in the New American Health System. Frontiers of Health Services Management, 10(4):32-36, 1994.

Roper, W.L.: Foreword: Ranking Hospitals and Physicians: The Use and Misuse of Performance Data. Faulkner & Gray's Medical Outcomes and Practice Guidelines Library, 3:ix-x, 1994.

Roper, W.L., Thacker, S.B., Teutsch, S.M.: Translating Science into Practice in Child Day-Care Settings. Pediatrics, 94(6):1112-1114, 1994.

Koplan, J.P., Roper, W.L., Udvarhelyi, I.S.: Outcomes Research: Perspective of the Prudential Insurance Company of America. Faulkner & Gray's Medical Outcomes and Practice Guidelines Library, 2:19-23, 1994.

Roper, W.L.: Book review: Medical Gridlock and Health Reform. The New England Journal of Medicine, 331(21): 1462-63, 1994.

Roper, W.L.: Quality Assurance in the Competitive Marketplace. Health Affairs, (14)1:120-121, 1995.

Roper, W.L.: What does the future hold? The Problem that Won't Go Away: Reforming U.S. Health Care Financing, H.J. Aaron, ed., The Brookings Institution, Washington, D.C. 1996.

Roper, W.L.: Can the Marketplace Assure Quality of Care? Looking Back, Looking Forward . . . "Staying Power" Issues in Health Care Reform, The Richard and Hinda Rosenthal Lectures, 1994-1995, National Academy Press, 1996.

Roper, W.L., Gordon, R.L., Baker, E.L., Omenn, G.S.: Prevention and the Reforming U.S. Health Care System: Changing Roles and Responsibilities for Public Health. Annual Review of Public Health, 17:489-509, 1996.

Roper, W.L.: What Is Quality and Why Is It Critical To Managed Care? Faulkner & Gray's Quality in Managed Care Series -- Communicating The Quality Message, 1:17-30, 1996.

Roper, W.L., Cutler, C.M.: Health Plan Accountability and Reporting: Issues and Challenges. Health Affairs, (17)2:152-155, 1998.

Roper, W.L.: Foreword: Clinical Preventive Services Research. American Journal of Preventive Medicine, 14(4):300-301, 1998.

Withdrawal/Redaction Marker

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
003. bio	re: Joseph Pizzorno (partial) (1 page)	03/02/1999	P6/b(6)

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Domestic Policy Council
Devorah Adler
OA/Box Number: 20472

FOLDER TITLE:

Alternative Medicine [Folder 7]

2012-0463-S

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RESTRICTION CODES

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- b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
- b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

Praca

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[003]

A leader in the field of natural medicine, Dr. Pizzorno is a practical visionary. His uniting the healing traditions of natural medicine with the rigors of the scientific method has resulted in major advances. Co-founder and founding president of Bastyr University, he has lead Bastyr to become the first ever accredited, multidisciplinary university of natural medicine in the United States (and the English-speaking world) and set the standard of educational excellence for institutions of natural medicine throughout the world. Under his leadership, Bastyr University was one of the first institutions chosen as an National Institutes of Health Office of Alternative Medicine Center for Alternative Medicine Research. As senior editor and co-author of the internationally-acclaimed *A Textbook of Natural Medicine* and member of several editorial boards, he has helped define the standard of care for natural medicine, establish the importance of critical thinking in scientific evaluating the validity of natural medicine, and pushed forward the frontiers of our understanding of healing. As lecturer, best-selling co-author of the *Encyclopedia of Natural Medicine* (400,000 copies, six languages), researcher and expert spokesman, he has introduced and taught credible natural medicine to medical and lay audiences throughout the United States, South Pacific and Europe.

An expert in natural medicine (and licensed as a naturopathic physician and, previously, as a midwife), he actively works with the media (over 100 national media interviews a year) and county, state and federal legislatures and regulatory agencies to establish the appropriate role for natural medicine in health care. Dr. Pizzorno presented the role of naturopathic medicine in health care to First Lady Hillary Clinton's Health Care Reform Taskforce, was appointed to the U.S. Congress's Office of Technology Assessment's Advisory Panel on the Safety and Efficacy of Dietary Supplements, and has provided expert advice to the U.S. Federal Trade Commission. Dr. Pizzorno is Senior Medical Advisor for the *Journal Alternative & Complementary Therapies*.

In January 1996, Dr. Pizzorno debated natural medicine on national radio (CBS) and television (Good Morning America) programs, was the featured personality in the February 1996 issue of *Natural Health Magazine*, in May appointed to the King County Board of Health, the first natural medicine practitioner to be appointed to such a position (reappointed to a three year term in December), and, in June, appointed to the ad hoc advisory committee for the NIH Office of Dietary Supplements. In September, the American Association of Naturopathic Physicians Honored Dr. Pizzorno as the first recipient of the Benedict Lust Award (founder in 1896 of the naturopathic profession) and in October the *Seattle* magazine recognized him as one of the city's top 20 national intellectual leaders. His newest book, *Total Wellness*, was released by Prima last year.

In 1997, a few of Dr. Pizzorno speaking engagements include: the Ecological Farming conference in Monterey, the World President's Organization in Key Largo, the American College for the Advancement of Medicine in Tampa, the National Council of State Nursing Boards annual convention in Chicago, the Washington State Teamsters Welfare Trust, the International Spa & Fitness Association annual conference in Banff, and the annual meeting of the American Public Health Association in Indianapolis. New editions of the textbook *Natural Medicine* (Chrchill-Livingstone) and *The Encyclopedia of Natural Medicine* (Prima) will be released in 1998.



Office of the President

RESUME

Dr. Guy Riekeman is the President of Palmer College of Chiropractic, the 101-year-old Fountainhead of the profession. Over the years, he has founded numerous international organizations dedicated to creating a passionate way of being powerful in the world through vision and commitment with integrity. He is a pioneer in patient education utilizing video and computer technology. He has worked with Peter Graves, Dick Cavett, Lorne Green, Jack Perkins and many more to bring health and Chiropractic to patients and lay audiences via national television. From audiences of over 7000 to intimate experiential courses in integrity presented at his conference facility and Ranch in Colorado, he has dedicated the past 25 years to increasing peoples' awareness of the responsibilities and outcomes of the choices they make. He has become one of the most sought after speakers in the world on health, Chiropractic and leadership. He is the writer, producer and director of the Chiropractic Documentary which brought Chiropractic's message, via national television, into the homes and minds of millions of people in 1995. He was a member of the Chiropractic Centennial Foundation and a keynote speaker at both the Washington, D.C., and Davenport, Iowa, events. He is a Fellow in the Palmer and Palmer West Academies and has received the coveted Doctor of Chiropractic Humanities degree. Possessing dynamic insights that cut to the core of peoples' issues, Dr. Riekeman speaks to the place of personal truth and power inside each of us.

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Curriculum Vitae

Riekeman, Guy F., D.C.

Personal Information

[004]

Education

D.C. Graduated Cum Laude Palmer College of Chiropractic, Davenport, Iowa 1972
Studied Cinema and Television Arts, University of California, Los Angeles, 1984-87

Doctor of Chiropractic Humanities degree from Palmer College of Chiropractic, 1997

- 1972 Graduates Palmer College with academic honors and receives the Clinical Excellence Award
- 1973 Published in the Berkeley Health Handbook
- 1975 Becomes Vice-President of Sherman Chiropractic College
- 1977 Co-founds Renaissance International; a professional seminar which produced the first ever educational programs for patients on video with stars such as Peter Graves, Lorne Greene, Dick Cavett, Tony Franciosa, and others
- 1978-94 Conducts 20 world tours speaking on Chiropractic research and patient education
- 1980 Co-produces film - Introduction to Chiropractic, featuring Peter Graves
- 1981 Co-produces film - Report of Findings by Dr. Russell Erhardt
- 1981 Writes and publishes articles on Chiropractic research as it relates to new concepts of the Vertebral Subluxation Complex and spinal rehabilitative care
- 1983 Produces film on Chiropractic research with spokespersons Jayne Kennedy, Lorne Greene, and Tony Franciosa; featuring geneticist Dr. R. Pero, Dr. C. Suh, author Suzanne Arms, and others
- 1984 Co-founds the Chiropractic Basic Science Research Foundation with Dr. Flesia and R. Pero, Ph.D.
- 1984 Initiates research project at the Preventive Medicine Institute which measured the impact of Chiropractic care on genetic markers for cancer, gene repair, etc.
- 1984-86 Organizes a three-day research symposium featuring medical, scientific and Chiropractic research from both the free and iron curtain worlds
- 1985 Writes, directs and produces a one-hour TV pilot with Dick Cavett, Mary Crosby, Diane Schuur, Sally Ride, and others

- 1985 Writes and produces 13 commercials, public service announcements and great moments in Chiropractic history for national media use
- 1986 Writes and produces an eight-minute Chiropractic cartoon for children with music by Lionel Richie
- 1986 Writes and publishes Chiropractic educational programs for children
- 1986 Founds the 10 Strategies Seminar; a post-graduate seminar on practice management for chiropractors using Disney Principles
- 1987 Writes and produces a 10-minute video tape for prospective patients
- 1987 Co-founds and organizes the board for the International Association of Chiropractic Assistants
- 1987 Co-founds Quantum; a seminar on personal development featuring resort locations and world-class speakers
- 1987 Co-founds Quest; a post-graduate seminar for practice and personal growth; becomes one of the most successful programs ever in Chiropractic
- 1989 Produces a new education program for patients (This patient video tape wins the Screen Actors Guild Silver Screen Award)
- 1990 Produces the 10 Strategies audio tape seminar
- 1990 Produces a nine-hour audio program - Make Your Life Extraordinary
- 1990 Creates the WORKSHOPS; The first management program for the Wellness Care Office
- 1991 Joins continuing educational extension faculty of two Chiropractic Colleges
- 1991 Keynote speaker at intraprofessional-international conference on Wellness Care in Viareggio, Italy
- 1992 Produces three videos for Patient Education - The National Health Forum, Report of Findings, progress Exam Report (The videos win an award for computer animation)
- 1993-95 Heads the Chiropractic Centennial Foundation Media Committee, produces CCF promotional video, documentary, audio tape library
- 1996 Is named a Fellow by Palmer College of Chiropractic-West
- 1997 Is honored with a Doctor of Chiropractic Humanities degree from Palmer College of Chiropractic
- 1997 Named the Executive Director of the Palmer Institute for Professional Advancement
- 1998 Named Eighth President of Palmer College of Chiropractic

Papers Published by Dr. Riekeman

Chiropractic and Wellness Care. Berkeley Health Handbook. 1973
A Breakthrough to Excellence. AHHA magazine. Fall edition 1991
What is Wellness Care. Clinical Chiropractic. January 1992

The Wave. Clinical Chiropractic. April 1993

Changing the World. Clinical Chiropractic. July 1993

The Seven Disciplines of Excellence. Clinical Chiropractic. January 1994

Goosebumps. The Chiropractic Journal. August 1996

Alterations Are Ahead at the OAM

AS THE OFFICE of Alternative Medicine (OAM) at the National Institutes of Health (NIH) celebrates its sixth year since its establishment by Congress, it faces some major changes.

Congress has given the office increased status and authority by naming it the National Center for Complementary and Alternative Medicine and has increased its budget from the current \$20 million to \$50 million. The provisions are included in the appropriations legislation for the Department of Health and Human Services. The action means that the newly named Alternative Medicine Center will be in a position to fund its research grants and other projects directly. As an office, its projects can only be funded through collaboration with other institutes or outside agencies.

Also, a change in leadership is pending. Wayne Jonas, MD, who has been serving as director of the OAM since 1995 on a 3-year detail from the military, leaves at the end of the year. A search for a new director, preferably an experienced world-class clinical trialist, says the NIH, is under way.

From Exploration to Evidence

Meanwhile, research supported by the office is moving from exploratory phases to evidence-producing studies. The OAM has funded 13 research centers at universities and other institutions throughout the United States that are conducting 50 different research projects. These have stimulated a wide interest in studies into complementary (or, in the terms used sometimes additively and sometimes instead, alternative or integrative) medicine. The OAM has started a number of large clinical trials that, experts say, will stimulate further research in the field. The centers and the trials together will provide new opportunities for training researchers in alternative medicine studies.

"In 10 years," predicted Jonas, "the Office of Alternative Medicine will be a thriving organizational entity working closely with other NIH components."

Other federal agencies, academic centers, private organizations, and the public to facilitate quality research that integrates complementary and alternative medicine and conventional healing approaches.

The biggest change since the OAM began is in attitudes toward alternative medicine, said William R. Harlan, MD,

associate director of the NIH's Office of Disease Prevention. (Organizationally the office is under the supervision of NIH Director Harold Varmus, who named Harlan as his liaison to the OAM.) "Those in conventional research and medical practitioners have become very interested in alternative medicine and in doing research in it. It is now recognized that there are a lot of promising therapies that need to be tested in the most appropriate manner. What is important to the efforts around here is that the institute directors and Varmus himself are interested. Without that a lot of research cannot proceed."

The office's largest investment in research is the support of a number of cen-

ters of research into complementary medicine. "They aren't the only research centers we have funded," says Jonas, "but it's where we have put the bulk of our resources. Initially, there needs to be a lot of developmental work, pilot studies, to identify the most promising and testable hypotheses and to collect the data necessary to decide where you should invest more money and do more definitive clinical trials."

Each university or institutional center focuses on a clinical area, covering the safety and efficacy of alternative medical practices on asthma, AIDS, cancer, pain, addictions, aging, stroke, cardiovascular diseases, and pediatric conditions.

Institution-Affiliated Centers of Research on Alternative Medicine

Institution and Location	Name of Center	Specialty of Center
Bastyr University Bethel, Wash.	Bastyr University AIDS Research Center	HIV/AIDS
Columbia University New York	Center for Complementary and Alternative Medicine Research in Women's Health	Women's health issues
Harvard Medical School, Beth Israel Hospital Deaconess Medical Center Boston	Center for Alternative Medicine Research	General medical conditions
Kessler Institute for Rehabilitation West Orange, NJ	Center for Research in Complementary and Alternative Medicine for Stroke and Neurological Disorders	Stroke and neurological conditions
Palmer Center for Chiropractic Research Davenport, Iowa	Consortial Center for Chiropractic Research	Chiropractic
Stanford University Palo Alto, Calif.	Complementary and Alternative Medicine Program at Stanford	Aging
University of Arizona Health Sciences Center Tucson	Program in Integrative Medicine	Pediatric conditions
University of California, Davis Davis, Calif.	Center for Alternative Medicine Research in Asthma and Immunology	Asthma, allergy, and immunology
University of Maryland School of Medicine Baltimore	Center for Alternative Medicine Pain Research and Evaluation	Pain
University of Michigan Ann Arbor	University of Michigan Complementary and Alternative Medicine Research Center for Cardiovascular Diseases	Cardiovascular diseases
University of Minnesota Medical School Minneapolis	Center for Addiction and Alternative Medicine Research	Addiction
University of Texas Health Science Center Houston	University of Texas Center for Alternative Medicine	Stroke and neurological conditions
University of Virginia Charlottesville	University of Virginia Center for the Study of Complementary and Alternative Therapies	General medical conditions

"These centers will bear a lot of fruit in the years ahead," predicted James Gordon, MD, chair of the OAM's advisory council for its first 4 years. "They are serving as places to encourage and to provide technical assistance to those who may be interested in doing research in these areas. They bring a nucleus of researchers, clinicians, and epidemiologists together to try to figure out how to tackle a particular problem: how can we integrate some of these alternative therapies into treatment, how can they be studied, and how can we look at both the clinical results and the basic science. Even more important, their very existence stimulates interest. Other places are starting similar centers even without NIH funds." Gordon is associate professor of medicine in the Department of Community and Family Medicine at Georgetown University School of Medicine.

Asking the Right Questions

The centers are selected because they are staffed by individuals with scientific expertise and an understanding of alternative medicine practices. These researchers can formulate the appropriate questions, and they have the capacity to execute the studies, said Jonas, citing an early study by one of the centers that developed models to test the effect of acupuncture on osteoarthritis. From that work, a large, multicenter randomized controlled trial has been designed. Applications for this trial have been reviewed, and one trial has been selected and funded, Jonas said.

In addition to this trial, others include the much-publicized study, now being

conducted by the National Institute of Mental Health, of using St John's wort (hypericum) to treat depression; a large trial to test the popular dietary supplement glucosamine for treating arthritis, for which contract proposals are now out soliciting applications; and a planned trial of acupuncture's effect on depression.

Some 60% of the inquiries the OAM receives deal with cancer. "It's by far the largest single condition people ask about. National surveys show that approximately half of cancer patients will use some kind of unconventional therapy, so it's an important issue for the medical community to address. We have been trying to develop a dialogue between those in alternative medicine and those in conventional medicine who are willing to work on cancer," said Jonas.

After discussions with the National Cancer Institute (NCI), both groups agreed that the present structure of cancer centers and oncology groups the institute already has in place is the best way to do the research. "What we needed to do was make sure that the alternative medicine field was represented on an ongoing basis," said Jonas. To this end, the OAM has formed a knowledgeable advisory panel representing the conventional and complementary medicine arenas that will make recommendations on what to test and will assist in evaluating claims of efficacy related to therapies for cancer. The panel will provide the expertise and advice needed by both NCI and OAM for evaluating alternative medicine interventions. "We've started this with two projects, one an evaluation of shark car-

tilage and the other a complex nutritional program," said Jonas.

"The point is that we now have a system, and this cancer advisory panel is one element, providing input and dialogue along the line that moves research forward without compromising the science." He suggested that a similar system might be developed in other areas, projecting possible collaborations with NIH scientists in which those who are knowledgeable about alternative medical practices will identify the most promising topics for testing in an appropriate and rigorous manner.

With the assistance of the evidence-based practice centers at the Agency for Health Care Policy and Research, the OAM is reviewing and evaluating published data on the effects of milk thistle on liver disease and on cholesterol and hypertension. Jonas noted that there have been a number of controlled trials with this substance, and "we want to look at the evidence and make an assessment of how good it is."

He commented that "it was recently reported that garlic didn't appear to lower cholesterol, which contradicts other studies that show it does [*JAMA*. 1998;279:1900-1902]. So this needs to be looked at."

"Whether the office becomes a center or not, it bodes well for the general enterprise in terms of investigating the alternative modalities of treatment and in trying to bring them into the mainstream of medicine as they prove efficacious," said NIH's Harlan. "I think we are going to see a tremendous expansion of that effort."—by Charles Marwick

FDA Never Promised an Herb Garden— But Sellers and Buyers Eager to See One Grow

PERHAPS OPPONENTS and skeptics of the safety and efficacy of medicinal herbs should take echinacea to improve their immune systems so they can ward off the growing deluge of requests from consumers for these alternative medicines.

That's not to say that consumer fashion overrides any scientific and medical discussions about what does and does not help in preventing or treating diseases, but it does mean the debate isn't happening in a vacuum—that physicians are seeing patients who want or are already taking medicinal herbs for treatment.

Critics of medicinal herbs, or nutraceuticals, or botanicals, or dietary supplements claim the industry is selling modern-day snake oil that has no proven

safety or efficacy. Loren D. Israelsen, president of the Utah Natural Products Alliance, said the dietary supplement industry wants to work with government regulators, physicians, and researchers to prove or disprove the safety and efficacy of medicinal herbs and to improve manufacturing practices. He also reminded naysayers opposed to herbal medicine that the debate has moved on.

"Consumers are voting with their feet, and that makes some in the medical profession unhappy," Israelsen said. "These medical professionals say, 'They should be coming to me instead of going to their pharmacists or health food store.' But patients say they would visit their physicians if the physicians knew something about these products."

"There's an awful lot of room to cooperate and improve the system. We're not going away, and modern medicine isn't going away, so some détente or rapprochement is needed."

Israelsen made these remarks following his talk in September at an international workshop to "Evaluate Research Needs on the Use and Safety of Medicinal Herbs" held in Raleigh, NC. The conference was sponsored by several member agencies of the National Institutes of Health (NIH) (especially the National Institute of Environmental Health Sciences), Department of Health and Human Services, Food and Drug Administration (FDA), and the Society for the Advancement of Women's Health Research. The workshop brought together

government leaders, researchers, and industry representatives to create an agenda for further study of dietary supplements.

Debatable DSHEA

Regardless of how the debate (or battle) unfolds, certain ground rules apply. Foremost is the Dietary Supplement Health and Education Act of 1994 (DSHEA). The act defines dietary supplements, places the responsibility for ensuring their safety on manufacturers, identifies how literature may be used in connection with sales, specifies types of statements of nutritional support that may be made on labels, specifies certain labeling requirements, and provides for the establishment of regulations for good manufacturing practices.

Many critics of medicinal herbs claim DSHEA deregulates the industry and places burdens of proof and enforcement on the FDA without providing the funding for such oversight. For example, DSHEA allows product labeling to list its nutritional benefits without preauthorization by FDA. In fact, a product can be manufactured for 30 days before its manufacturer is required to tell the government of such a labeling statement. In addition, the law does not require manufacturers to provide evidence supporting a statement for review by a regulatory agency prior to marketing of the product.

As for the safety of dietary supplements, the burden of proof falls on the FDA. In other words, the FDA can't say a product is unsafe and then leave it up to the manufacturer to prove otherwise.

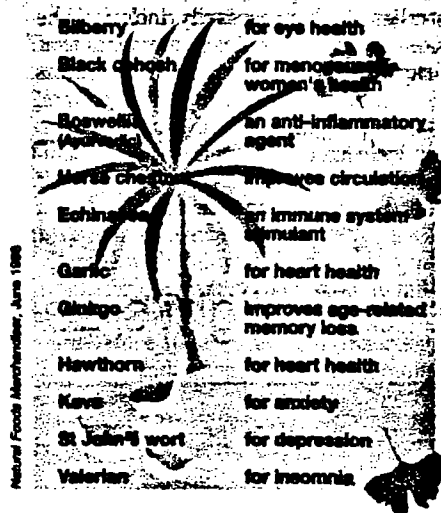
In the 4 years since enactment of DSHEA, the FDA has made several rulings and clarifications with regard to the law. The current proposed change centers on what a medicinal herb maker can say about its product.

What's a Claim? What's a Disease?

On April 29, the FDA issued a proposed rule, "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body."

Under the current interpretation of DSHEA, structure and/or function claims are allowed while disease claims are not. For example, a product can claim to "promote regularity," "help maintain cardiovascular health," or "support the immune system." It can't say it "alleviates constipation" or "lowers cholesterol."

Under the proposal, dietary supplements that expressly or implicitly claim to diagnose, treat, prevent, or cure a disease continue to be regarded as drugs and have to meet the safety and effectiveness standards for drugs under



These are some of the more popular medicinal herbs, with their structure/function claims.

the Food, Drug and Cosmetic Act," the FDA said.

What's causing problems with the new proposals is the FDA's definition of "disease." Herbal medicine advocates say the agency is widening the definition to limit structure/function claims and push botanicals under more stringent FDA oversight.

In the proposal, disease is defined as "any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms. For purposes of this definition, 'signs and symptoms' include laboratory or clinical measurements that are characteristic of a disease, such as elevated cholesterol fraction, uric acid, blood sugar, and glycosylated hemoglobin, and characteristic signs of disease, such as elevated blood pressure or intraocular pressure."

Mark Blumenthal, executive director of the American Botanical Council, said the FDA was stepping outside its mandate.

"We don't think the FDA should redefine disease and broaden its interpretation," he said. "Clearly, when Congress wrote the law, it codified disease to include damage to an organ, and the FDA is trying to expand it to nondamage. I don't think the FDA can do that legally—they can't change the law after the fact."

On the other hand, the American Medical Association (AMA) supports the FDA's definition and would like to expand it to include states of health leading to deviation, impairment, or interruption, as communicated in an August 26 comment letter on the proposed regulation.

In general, the AMA raises concerns about DSHEA.

"By allowing dietary supplement manufacturers to make 'structure/function claims' without FDA's pre-approval based on credible scientific evidence of safety and efficacy, the public must rely on the manufacturer's good faith assertion that they can substantiate their claim," the AMA letter states. "This is in contrast to drugs where FDA pre-approval of efficacy claims is necessary for marketing the product. Furthermore, some types of dietary supplements, such as botanicals, are not well characterized chemically. Thus, the AMA is concerned that the FDA lacks sufficient statutory and regulatory authority to adequately regulate dietary supplements to ensure their safe and appropriate use."

Since DSHEA went into effect, FDA has received about 2300 notifications from producers about structure/function claims, with the agency telling manufacturers that about 150 of these claims are problematic and about 60 more would not be permitted under the proposed criteria. An FDA spokeswoman said no timetable was in place for announcement of a final rule.

The other current area of FDA interest in clarification of DSHEA is "good manufacturing practices." A Food Advisory Committee Working Group is holding public meetings to "discuss and further develop a draft report on identity testing and record keeping." DSHEA allows the government to prescribe good manufacturing practices for dietary supplements that are modeled after current regulations for food and may not impose standards "for which there is no current and generally available analytical methodology."

Conference on Botanicals

So while DSHEA serves as the arena for discussion, other government agencies are also looking at botanicals. Good manufacturing practices and further research to improve dietary supplements were the focus of the NIH September workshop.

At times the meeting seemed to go in circles, with critics of medicinal herbs arguing that there wasn't enough research showing the efficacy and safety of these botanicals while advocates argued that the research was out there but in places that traditionally are overlooked.

"Do we need new drug approval standards for botanicals, even though they've been used safely for hundreds and thousands of years?" asked Blumenthal, who spoke at the workshop. He argued that the United States should use research produced in Germany, where herbal drugs are classified as conventional drugs and have to meet the same criteria of quality, efficacy, and safety.

that the country requires of synthetic drugs.

"Instead of reinventing the wheel, let's see what the Germans have done, so physicians and pharmacists can at least have access to positive and negative studies," Blumenthal said.

But others countered that European

studies don't necessarily look for the same safety and efficacy elements that drugs under study in the United States must meet.

Israelsen, although he said the industry welcomes US research into botanicals, cited several reasons why that isn't happening at the proper pace.

"There are no regulatory incentives—~~if anything~~, we've been given huge disincentives," he said. "The FDA says, 'If you bring us a new drug, these are the things you need to do.' It's a 29-foot pole vault. It won't happen. There is so much opaqueness in the FDA process."

by Mike Mitka

Dawn's Early Light to Twilight's Last Gleaming . . .

AT 8 AM, sun worshippers already lay prostrate on the shimmering oceanside beach at Amelia Island, Fla. In a dark, windowless room nearby, present-day priests at the temple of the sun, members of the Society for Light Treatment and Biological Rhythms (SLTBR), convened for rites of their own: a review of advances in their field.

Timed exposure to daylight-intensity light has become the treatment of choice for seasonal affective disorder (SAD), according to Anna Wirz-Justice, PhD, professor of psychiatry at the University of Basel in Switzerland. "Light is as effective as antidepressant medications are, perhaps more so," said Wirz-Justice, who cochaired a roundtable session at the SLTBR's annual meeting, held in conjunction with the Society for Research on Biological Rhythms (SRBR) in May.

Light therapy, she said, also is gaining acceptance as a treatment for circadian sleep disorders and circadian disruptions associated with jet lag and shift work. On the "up and coming" list of other possible indications, she said, are bulimia nervosa, premenstrual dysphoric disorder, and nonseasonal major depression. Lighting devices have become more powerful, more portable, and less expensive, Wirz-Justice said, prompting wider use in homes and workplaces. The devices typically use light with an intensity of 2500 to 10 000 lux, simulating outdoor light near dawn or dusk.

Result of Rhythm Research

"Light therapy is one of the most successful and practical results of basic research in biological rhythms," said Thomas Wehr, MD, chief of the Section on Biological Rhythms of the National Institute of Mental Health (NIMH).

Although the impact of changes in day length on animal behavior is well recognized, Wehr said, "everyone starts out thinking humans are unique." The landmark demonstration of the human biological response to light occurred in 1980, when Alfred Lewy, MD, with Wehr and other NIMH colleagues, showed that light suppresses secretion of the human



The Cafe Engel, in Helsinki, Finland, serves bright light with breakfast from October through March. Popular menu selections include Danish pastry, or traditional English, continental, or French breakfasts for about US\$7. A cup of coffee costs about US\$2. Use of one of the cafe's eight light boxes is free.

pineal hormone melatonin (*Science*. 1980;210:1267-1269). Lewy is now professor of psychiatry and director of the Sleep and Mood Disorders Laboratory at Oregon Health Sciences University in Portland.

Since the modern "discovery" of SAD came along after psychiatric methods had matured, Wehr said, its researchers from the start have used controlled trials and structured interviews that facilitate comparisons and have examined data with meta-analyses. The current buzz words at the NIMH, Wehr said, are "translational research—bench to bedside," and light therapy "is a classic example of that."

Michael Terman, PhD, of Columbia University College of Physicians and Surgeons and the New York State Psychiatric Institute, traced light therapy's path toward mainstream medicine. Media reports on SAD research in the 1980s, he said, prompted wide public interest, popular books, and a cottage industry in light boxes.

Researchers seeking to set standards for treatment formed the SLTBR in 1987. The group's initial priorities, Terman said, included liaison with the US Food and Drug Administration (FDA), consumer groups, lighting manufacturers, and third-party health insurers; development of consensus on the safety of light treatment and on supervised treatment vs self-treatment; and im-

provement and standardization of rating scales. All have been accomplished, Terman said, and all also remain on the SLTBR's ongoing agenda.

One milestone, he said, was the inclusion of SAD in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (Washington, DC: American Psychiatric Association; 1994). The criteria specify a regular temporal relationship between onset and offset of depression, with episodes occurring most often in winter, but occasionally in summer.

Symptoms of winter SAD, Terman said, include prominent anergy, hypersomnia, overeating, weight gain, and craving for carbohydrates, while summer SAD is characterized by loss of appetite and weight and by insomnia. SAD is most common in young adult women. Prevalence increases at higher latitudes, with about 1% to 5% of people in middle to northern latitudes reporting winter SAD symptoms. As much as 15% of the population of some countries report sub-syndromal SAD, sometimes characterized as "winter blues." Perhaps only one in 10 persons with SAD has the summer variety, for which treatment remains ill-defined.

Although ophthalmologists have expressed concern about the long-term safety of light treatment, Terman said, no evidence of retinal damage from the therapy has been reported (*Am J Ophthalmol*. 1995;119:202-210). The FDA considers light boxes to be Class III medical devices. Such devices may not be commercially distributed without premarket approval or an Investigational Device Exception, a measure that restricts medical claims made in advertising.

A joint task force of the SLTBR and the American Sleep Disorders Association (ASDA) reviewed experimental and clinical evidence for the potential efficacy of light treatment for sleep disorders. The group's recommendations (*J Biol Rhythms*. 1995;10:105-176), Terman said, are under review by the ASDA. Standards of practice are expected to be issued within the next year. More information about SLTBR

activities be found at the organization's Web site, <http://www.websciences.org/sltbr>.

Around the World

At the SLTBR roundtable session, an international panel of clinicians reviewed light treatment around the world. In Germany, said Wilfried Koehler, MD, PhD, head of the department for addictive diseases at Buerger-hospital in Frankfurt, where the general public makes extensive use of herbal remedies and other naturalistic treatments for depression, light therapy found early acceptance.

Every university hospital in Canada has a SAD clinic, said Raymond Lam, MD, chief of the Division of Mood Disorders at the University of British Columbia Faculty of Medicine in Vancouver. A Canadian consensus meeting on light treatment in May, he said, prompted a major educational initiative for primary care physicians to be launched this winter. It will include a SAD treatment manual and patient information brochures, covering both light and pharmacological therapy.

The prevalence of SAD in Australia is comparable with that reported elsewhere, said Stuart Armstrong, PhD, of the Brain Sciences Institute at Swinburne University of Technology in Hawthorn, Victoria, and Australians perceive SAD symptoms as a serious problem. But unlike in some other countries, he said, few seek treatment.

About 50% of US insurers now reimburse for light therapy for SAD, although often only after a battle, said Dan Oren, MD, associate professor of psychiatry at Yale University School of Medicine. One insurer told Oren, who is president of SLTBR, that "reimbursement is limited by light therapy's 'Vigra' problem": Insurers do not want to cover everyone who wants a light box. Some challenge the specificity and reliability of a SAD diagnosis, he said, and "some perceive light therapy as more akin to voodoo than to science."

Switzerland is the only country so far, Wirz-Justice said, to require mandatory medical insurance reimbursement for light therapy for SAD after the disorder is diagnosed by a physician or psychologist.

More Possible Applications

Speakers also described other potential applications of light therapy:

- **Circadian rhythm disorders.** These are not disorders of sleep per se, but of the timing of sleep, said Scott Campbell, PhD, director of the Laboratory of Human Chronobiology at New York Hospital-Cornell Medical Center. Patients may complain of sleep that starts too late, ends too early, is too fragile, or is irregular.

People with delayed sleep phase syndrome, for example, report trouble falling asleep until 3 AM and trouble getting going before 10 or 11 AM. This disorder, Campbell said, affects 7% of all persons seeking treatment for insomnia at sleep disorders centers. It is most common in adolescents. Light therapy in the early morning, he said, may help such people fall asleep earlier.

Advanced sleep phase syndrome affects mainly the elderly, causing trouble staying awake in the evening and fragile

Lam said, binge purge more in winter. Physicians, he suggested, should pay attention to seasonality in assessing treatment efficacy. Patients with bulimia, he said, often seek help in January when they are most ill. Their improvement in late spring may be the result of treatment, or it may just be seasonal. Worsening in the fall may be misinterpreted as a relapse caused by discontinuing treatment. Lam's research shows that light therapy acutely and rapidly improves both mood and eating symptoms in persons with bulimia (*Am J Psychiatry*. 1994;151:744-750).

- **Premenstrual depression.** Lam and colleagues also have found that patients with late luteal phase dysphoric disorder (LLPDD) often show substantial seasonal patterns, with winter worsening of mood and premenstrual symptoms. About one third of women with LLPDD also have SAD, he said, and report increased winter weight gain and need for sleep. While studies of light therapy for LLPDD to date have had inconsistent results, he said, the numbers of patients studied has been small. Light, given in winter, he said, theoretically would be beneficial (*Am J Psychiatry*. 1997;154:1436-1441).

- **Shift work.** Bright light improves sleep and alertness in night-shift workers, facilitating their adaptation to a new schedule, said Charmane Eastman, PhD, director of the

Biological Rhythms Research Laboratory at Rush-Presbyterian-St Luke's Medical Center in Chicago. Light may be presented at home to prepare for a shift change, she said, or in the workplace after the change or in both places.

Eastman's research shows that night workers benefit from protecting themselves from exposure to conflicting cues from sunlight by wearing dark goggles on their way home from work. They also should sleep at consistent times after the night shift, she said, and light-proof their bedrooms for day sleep. In a recent study of people adhering to these prescriptions, Stacia Martin, a student in Eastman's laboratory, and Eastman compared exposure to high-intensity (~5700 lux), medium-intensity (~1200 lux) and low-intensity light (<250 lux) on consecutive night shifts.

They found that high- and medium-intensity light, but not low-intensity light, enhanced circadian adaptation in nearly all subjects. Medium-intensity



A dawn-simulating alarm clock wakes travelers gently in the Hilton Hotel chain's "Sleep-Tight" rooms—available at present in fewer than a dozen hotels.

sleep in the second half of the night. Campbell and his colleagues treated older adults with trouble maintaining sleep with exposure to 4000 lux light for 2 hours in the evening, finding they awakened less frequently and slept nearly 1 hour longer (*J Am Geriatr Soc*. 1993;41:829-836). Other researchers have found that evening light exposure improves sleep and reduces nighttime wandering, or sundowning, in elderly nursing home residents with dementia.

Several factors, Campbell said, limit the use of light therapy for circadian sleep disorders. Proper timing of light requires circadian rhythm assessment; current techniques to record 24-hour body temperature continuously or to determine the onset of melatonin are not yet practical for general use. Compliance may be a problem; patients may not have the time or desire to sit in front of a light box for 30 to 120 minutes daily or several times a week.

- **Bulimia nervosa.** About one third of patients with this disorder have SAD,



Basel's soccer team, the Fussball Club Basel, put light boxes in its locker room in hopes of improving player performance. No effect was apparent.

light, while brighter than most ordinary room light, they said, is less offensive to the eye and causes less glare on computer monitors than high-intensity light (*Sleep*. 1998;21:154-165).

• **Nonseasonal depression.** Light may produce antidepressant benefits within 1 week, in contrast to psychopharmacological treatments, which typically take several weeks, said Daniel Kripke, MD, director of the Circadian Pacemaker Laboratory at the University of California, San Diego.

In a recent review of clinical trials, Kripke found that bright light therapy for nonseasonal major depression produced statistically significant net reductions in mood symptoms of about 12% to 35% on the Hamilton Depression Rating Scale. These results, he said, are comparable with those obtained in major trials of antidepressant medications.

Light and medications appear to work best in combination, he said, suggesting it would be advantageous to offer depressed patients speedy relief with light

therapy while also starting them on medications that have more extensively verified efficacy. Combined treatment should lower costs, he said, because faster improvement means less disability and morbidity (*J Affective Disord*. 1998;49:109-117).

• **Jet lag.** Bright light, at least theoretically, can ease jet lag by speeding adaptation to new time zones, according to the SLTBR/ASDA joint task force report. While the few field trials conducted to date are encouraging, the task force concluded, the studies' applicability to the population at large and optimal timing after travel are still unresolved (*J Biol Rhythms*. 1995;10:167-176).

Some hotels offer lighting devices to jet-lagged guests. In 35 "Sleep-Tight" rooms available in seven Hilton Hotels in the United States, for example, travelers will find a dawn-simulating alarm clock. Its light comes on gradually, starting 30 minutes before a desired wake-up time, allegedly providing a gentle way to start the day. The rooms also contain a standard light box, with a note inviting travelers to use it to "jump-start" their day.

As often occurs with new treatments that eventually may serve as alternatives or adjuncts to traditional medicine, the public's enthusiasm for light therapy outpaces scientific demonstrations of efficacy. SLTBR program organizer Wirz-Justice reported that Basel's soccer team, the Fussball Club Basel, put light boxes in its locker room in 1996 in hopes of improving player performance. But light evidently is not a panacea. The team, Wirz-Justice said, fell in league standings.

—by Lynne Lamberg,
JAMA contributor

Miscellanea Medica

Richard Axel, MD, Columbia University College of Physicians and Surgeons, New York, a researcher who outlined fundamental principles of how key cells involved in perception are organized in the brain, has received the Bristol-Myers Squibb Award for Distinguished Achievement in Neuroscience Research.

W. Westley Clark, MD, JD, MPH, has been named director of the Center for Substance Abuse Treatment at the Substance Abuse and Mental Health Services Administration.

Sue Bailey, DO, in June became assistant secretary of defense for health af-

fairs, the highest-ranking health position in the US Department of Defense.

Dale E. Bredesen, MD, has been named founding president of the Buck Center for Research in Aging in Novato, Calif.

The following physicians and programs are recipients of the 1998 Primary Care Achievement Awards funded by the Pew Charitable Trusts: **Joel J. Alpert, MD**, Boston University School of Medicine, a leader in primary health care education and president-elect of the American Academy of Pediatrics; **University of New Mexico School of Medicine Primary Care Curriculum**, which was cre-

ated particularly to serve the state's rural areas; **John W. Runyan, Jr, MD**, founder of the Department of Family Medicine at the University of Tennessee, Memphis; **Bernard Ewigman, MD, MSPH**, University of Maryland-Columbia, translator of research into effective care for underserved populations; and **Pediatric Research in Office Settings**, a network of 1400 clinicians who study primary care in pediatric practice.

Editor's Note: Miscellanea Medica normally appears in the Medical News & Perspectives section several times each month. Items submitted for consideration should be sent to Marsha F. Goldsmith, editor, Medical Perspectives.

Trends in Alternative Medicine Use in the United States, 1990-1997

Results of a Follow-up National Survey

David M. Eisenberg, MD; Roger B. Davis, ScD; Susan L. Ettner, PhD; Scott Appel, MS; Sonja Wilkey; Maria Van Rompay; Ronald C. Kessler, PhD

Context.—A prior national survey documented the high prevalence and costs of alternative medicine use in the United States in 1990.

Objective.—To document trends in alternative medicine use in the United States between 1990 and 1997.

Design.—Nationally representative random household telephone surveys using comparable key questions were conducted in 1991 and 1997 measuring utilization in 1990 and 1997, respectively.

Participants.—A total of 1539 adults in 1991 and 2055 in 1997.

Main Outcomes Measures.—Prevalence, estimated costs, and disclosure of alternative therapies to physicians.

Results.—Use of at least 1 of 16 alternative therapies during the previous year increased from 33.8% in 1990 to 42.1% in 1997 ($P \leq .001$). The therapies increasing the most included herbal medicine, massage, megavitamins, self-help groups, folk remedies, energy healing, and homeopathy. The probability of users visiting an alternative medicine practitioner increased from 36.3% to 46.3% ($P = .002$). In both surveys alternative therapies were used most frequently for chronic conditions, including back problems, anxiety, depression, and headaches. There was no significant change in disclosure rates between the 2 survey years; 39.8% of alternative therapies were disclosed to physicians in 1990 vs 38.5% in 1997. The percentage of users paying entirely out-of-pocket for services provided by alternative medicine practitioners did not change significantly between 1990 (64.0%) and 1997 (58.3%) ($P = .36$). Extrapolations to the US population suggest a 47.3% increase in total visits to alternative medicine practitioners, from 427 million in 1990 to 629 million in 1997, thereby exceeding total visits to all US primary care physicians. An estimated 15 million adults in 1997 took prescription medications concurrently with herbal remedies and/or high-dose vitamins (18.4% of all prescription users). Estimated expenditures for alternative medicine professional services increased 45.2% between 1990 and 1997 and were conservatively estimated at \$21.2 billion in 1997, at \$12.2 billion paid out-of-pocket. This exceeds the 1997 out-of-pocket expenditures for all US hospitalizations. Total 1997 out-of-pocket expenditures relating to alternative therapies were conservatively estimated at \$27.0 billion, which is comparable with the projected 1997 out-of-pocket expenditures for all US physician services.

Conclusions.—Alternative medicine use and expenditures increased substantially between 1990 and 1997, attributable primarily to an increase in the proportion of the population seeking alternative therapies, rather than increased visits per patient.

native medicine prevalence, costs, and patterns of use¹ demonstrated that alternative medicine has a substantial presence in the US health care system. Data from a survey in 1994² and a public opinion poll in 1997³ confirmed the extensive use of alternative medical therapies in the United States. An increasing number of US insurers and managed care organizations now offer alternative medicine programs and benefits.⁴ The majority of US medical schools now offer courses on alternative medicine.⁵

National surveys performed outside the United States suggest that alternative medicine is popular throughout the industrialized world.⁶ The percentage of the population who used alternative therapies during the prior 12 months has been estimated to be 10% in Denmark (1987),⁷ 33% in Finland (1982),⁸ and 49% in Australia (1993).⁹ Public opinion polls and consumers' association surveys suggest high prevalence rates throughout Europe and the United Kingdom.¹⁰⁻¹³ The percentage of the Canadian population who saw an alternative therapy practitioner during the previous 12 months has been estimated at 15% (1995).¹⁴ The wide range of utilization rates can be explained, in part, by the disparity in definitions of alternative therapy and the selection of therapies assessed.

The presumption is that alternative medicine use in the United States has increased at a considerable pace in recent years. The purpose of this follow-up national survey was to investigate this presumption and document trends in alternative medicine prevalence, costs, disclosure of use to physicians, and correlates of use since 1990.

METHODS

Sample

We conducted parallel nationally representative telephone surveys in 1991 and 1997. Survey methods were approved by the Beth Israel Deaconess Institutional Review Board, Boston, Mass.

ALTERNATIVE medical therapies, functionally defined as interventions neither taught widely in medical schools nor generally available in US hospitals, have attracted increased national attention from the media, the medical community, governmental agencies, and the public. A 1990 national survey of alter-

on the Center for Alternative Medicine Research, Education, Department of Medicine, Beth Israel Medical Center (Drs Eisenberg and Davis, Appel, and Miss Wilkey and Van Rompay), and the Department of Health Care Policy, Harvard Medical School (Drs Ettner and Kessler), Boston, Mass. Grants: David M. Eisenberg, MD, Center for Alternative Medicine Research and Education, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Boston, 02115.

JAMA. 1998;280:1569-1576.

Both surveys used random-digit dialing to select households and random selection of 1 household resident, aged 18 years or older, as the respondent. Eligibility was limited to English speakers in whom cognitive or physical impairment did not prevent completion of the interview. We asked respondents about their use of alternative therapies during the prior 12 months. We consider the results of the 1991 survey, fielded between January and March of that year, representative of 1990, and the results of the 1997 survey, fielded between November 1997 and February 1998, representative of 1997.

The sampling scheme was designed with a target sample of 1500 in 1990 and 2000 in 1997. The latter sample size was chosen to provide power in excess of 80% to detect an increase from 34% to 39% in the proportion of adults who used at least 1 form of alternative therapy during the prior 12 months. The actual numbers of completed interviews were 1539 in 1990 (67% response rate) and 2055 in 1997 (60% weighted response rate). A secular trend in lower survey response required us to offer a \$20 financial incentive for participation in the 1997 survey to maintain a response rate near the one achieved in 1990. No financial incentive was used in the 1990 survey.

The data in each survey were separately weighted to adjust for geographic variation in cooperation (eg, by region of country and urbanicity) and for household variation in probability of selection (ie, the inverse relationship between size of household and probability of selection because only 1 interview was completed in each sample household). The data were then weighted in parallel on sociodemographic variables to adjust for aggregate discrepancies between the sample distributions and population distributions provided by the US Census Bureau. This last stage of weighting was based on the 1997 Current Population Survey data¹⁵ and was done in parallel across the 2 surveys to remove any between-survey discrepancies of weighted sociodemographic distributions.

Of the initial sample of 9750 telephone numbers in 1997, 26% were nonworking, 17% were not assigned to households, and 9% were unavailable (ie, despite 6 attempted follow-up contacts). We declared 481 households ineligible because respondents did not speak English or because of cognitive or physical incapacity. Among the remaining 4167 eligible respondents, 1720 (41.3%) completed the interview on initial request. Attempts were then made to convert a random subsample of 1066 refusals by offering them an increased stipend (\$50). A total of 335 (31.4%) of the 1066 contacted were converted in this manner. Extrapolating this

conversion rate to all of the refusals and weighting the data for the undersampling of initial refusals, we obtained a 60% $(41.3\% + [31.4\% \times (100\% - 41.3\%)])$ weighted overall response rate among eligible respondents.

Interview

In both years, the interview was presented as a survey conducted about the health care practices of Americans by investigators from Harvard Medical School. No mention was made of alternative or complementary therapies. The substantive questions began by asking about perceived health, health worries, days spent in bed, and functional impairment due to health problems. We then asked respondents about their interactions with a *medical doctor*, defined as "a medical doctor (MD) or a doctor of osteopathic medicine (DO), not a chiropractor or other nonmedical doctor." The term *medical doctor* was used throughout the remainder of the interview.

To document trends we explored the following: (1) Respondents in both surveys were presented with a list of common medical conditions and asked if they had experienced each of these conditions during the previous 12 months. (2) Respondents who reported more than 3 conditions were asked to identify their 3 most bothersome or serious medical conditions and were then asked about seeing a medical doctor for these principal medical conditions and about the perceived quality of these interactions. (3) Respondents were asked about their lifetime and past 12-month use of 16 alternative therapies and whether each of these therapies was used for each of the principal medical conditions. The 1997 survey also asked about use for a representative sample of other medical conditions and expanded the list of therapies beyond the original 16 assessed in 1990. (4) We distinguished between use under the supervision of a practitioner of alternative therapy and use without such supervision. Respondents who reported supervised use were asked about their number of visits in the past 12 months to practitioners of each therapy. (5) All users of alternative therapies in 1997 who acknowledged seeing a medical doctor during the past year were then asked if they had discussed their use of each therapy with a medical doctor and, if not, why not.

Prior use of 16 targeted therapies was explored using a computer-assisted interview transcript, which included the following clarifications in both 1990 and 1997: When asking about high-dose vitamin or megavitamin therapies, interviewers made clear that the survey sought information on vitamins not including a daily vitamin or vitamin pre-

scribed by a doctor. Prayer or spiritual healing by others was asked about separately from prayer or spiritual practice for individual health concern. Commercial diet programs were described as "the kind you have to pay for, but not including trying to lose or gain weight on your own." A lifestyle diet included examples like vegetarianism or macrobiotics. Questions regarding energy healing included examples of magnets, energy-emitting machines, or the "laying on of hands," and use of relaxation techniques was explained using the examples of meditation or the relaxation response. The remaining 9 therapies were asked about without interviewer clarification.

The 1997 survey was longer (average, 30 minutes) than the 1990 survey (average, 25 minutes) because we sought to explore a number of areas in more depth. All the important questions in the 1990 survey were repeated in 1997. These replicated questions are the focus of the current report. One major change in the 1997 survey involved replicated questions: respondents who reported using more than 3 alternative therapies were asked in-depth questions (eg, use of a practitioner of alternative therapies, number of visits, out-of-pocket expenses, reasons for use) for all such therapies in 1990 but only for a random sample of 3 such therapies in 1997. This was required because of expansion in both the number of alternative therapies we assessed in 1997 and questions about each therapy. The 1997 data were weighted to adjust for this sampling in making comparisons with the 1990 data.

Insurance Coverage

For each therapy for which respondents said they used services of an alternative medicine practitioner, we asked whether insurance helped pay for any of the costs of the therapy and whether the respondent paid any of the costs out-of-pocket. Based on the answers to these questions, we calculated the proportion of users of each therapy who had complete, partial, or no insurance coverage for that therapy. We also calculated the overall frequency of insurance coverage by weighting the insurance frequencies within each therapy by the proportion of all user therapies accounted for by that therapy.

Construction of Cost Measures

The total cost of visits to alternative medicine practitioners was calculated by multiplying the number of visits for each therapy by a per-visit price and adding the prices of the following therapies: relaxation techniques, herbal medicine, massage therapy, chiropractic care, megavitamins, self-help groups, imagery techniques, commercial diet, folk rem-

edies, lifestyle diet, energy healing, homeopathy, hypnosis, biofeedback, and acupuncture. Out-of-pocket costs were constructed for each therapy by multiplying each user's visits by the full price of the visit if the user had no insurance coverage, by 0.2 if the user had partial insurance coverage, and by zero if insurance paid the full price of the visit. The assumption of a 20% coinsurance rate among users with partial insurance coverage should yield a conservative estimate of out-of-pocket costs, because it ignores deductibles and benefit caps and assumes that insurance benefits for alternative therapy are similar to medical coverage.

We calculated costs based on per-visit prices chosen from typical prices paid for such services by private insurers using a Resource-Based Relative Value Scale (RBRVS)¹⁶ system in selected states. We then recalculated costs using a second set of prices chosen partly to reflect empirical data on the out-of-pocket costs paid by the respondents, but primarily to represent conservative estimates of the per-visit cost of alternative therapies. Total costs based on this second set of prices should represent a lower bound on true expenditures.

Out-of-pocket costs of herbs, megavitamin supplements, and commercial diet products were calculated by multiplying the total population of users by the average out-of-pocket expenditures reported by respondents who used each of these products. In 1997, each respondent who used an alternative therapy was also asked, "Did you spend any additional money on things like books, classes, equipment, or any other items related to [the alternative therapy] in the past 12 months?" Out-of-pocket expenditures on these other items were calculated following the same procedures used for herbs, megavitamins, and commercial diet products. Out-of-pocket expenditures on herbs, megavitamins, commercial diet products, and related items were based on actual dollar amounts reported, so changes between 1990 and 1997 include inflation. To isolate the increase in the cost of practitioner visits between 1990 and 1997 solely because of the increase in the use of alternative therapies, we calculated 1990 practitioner costs using 1997 prices. The differences between the 1990 and 1997 costs of practitioner services reported are understated because they do not take into account inflation, estimated at 44% by the medical component of the Consumer Price Index.¹⁷

Statistical Analysis

Analyses reported herein consist of computation of prevalence and mean estimates and comparisons of these estimates

through the Taylor series method was used to compute significance tests using SUDAAN software.¹⁸ χ^2 Tests of independence were used for comparing proportions, while t tests were used for continuous measures. Extrapolations of survey estimates to the total population were based on the assumption that there were 180 million adults living in the US household population in 1990 and 198 million in 1997.¹⁵

RESULTS

Characteristics of Respondents

The characteristics of the subjects we interviewed are shown in Table 1. The sociodemographic characteristics of the survey sample are similar to the population distributions published by the US Bureau of the Census.¹⁵

Patterns of Use

Use of alternative therapies in 1997 was not confined to any narrow segment of society. Rates of use ranged from 32% to 54% in the wide range of sociodemographic groups examined. Use was more common among women (48.9%) than men (37.8%) ($P = .001$) and less common among African Americans (33.1%) than members of other racial groups (44.5%) ($P = .004$). People aged 35 to 49 years reported higher rates of use (50.1%) than people either older (39.1%) ($P = .001$) or younger (41.8%) ($P = .003$). Use was higher among those who had some college education (50.6%) than with no college education (36.4%) ($P = .001$) and more common among people with annual incomes above \$50 000 (48.1%) than with lower incomes (42.6%) ($P = .03$). Use was more common among those in the West (50.1%) than elsewhere in the United States (42.1%) ($P = .004$). With the exception of observed sex differences in 1997, these patterns are consistent with those identified in 1990.

Population prevalence estimates of alternative medicine use in 1990 and 1997 are shown in Table 2. The 1990 survey estimated that 33.8% of the US adult population (60 million people) used at least 1 of the 16 alternative therapies listed, while the 1997 survey estimated that this proportion increased significantly to 42.1% (83 million people). A comparison of specific therapies in the first column shows increases in 15 of the 16 therapies; 10 of these were statistically significant ($P \leq .05$). The largest increases were in the use of herbal medicine, massage, megavitamins, self-help groups, folk remedies, energy healing, and homeopathy. Summing Table 2 (first column) data shows a 65% increase in

Table 1.—Characteristics of the 1997 US and 1990 (N = 1539) Subjects Interviewed Compared With the US Population*

Characteristic	1997 Survey, %	1997 US Bureau of the Census, %	1990 Survey, %
Sex			
Female	52	52	48
Male	48	48	52
Age, y			
18-24	10	13	16
25-34	22	20	23
35-49	33	32	27
≥50	35	35	34
Race/ethnicity			
White	77	73	82
African American	8	12	9
Hispanic	10	11	8
Asian	1	4	1
Other	4	1	2
Education			
<High school	14	18	24
High school graduate	37	34	35
College or more	49	48	40
Annual income, \$			
<20 000	27	33	30
20 000-49 999	45	41	53
≥50 000	27	26	18
Region			
Northeast	21	19	22
North central	24	24	32
South	35	35	26
West	20	22	19

*Due to rounding, percentages do not always total 100.

total number of therapies used, from 577 therapies per 1000 population in 1990 to 953 per 1000 in 1997.

Several categories of alternative therapy warrant clarification about the actual modalities used. Three quarters of respondents who acknowledged use of relaxation techniques said they used meditation. Among those who reported using energy healing, the most frequently cited technique involved the use of magnets. Other modalities common to this category included Therapeutic Touch, Reiki, and energy healing by religious groups. The use of self-prayer, in contrast to spiritual or energy healing performed by others, was investigated in terms of prevalence of use but not in terms of costs, referral patterns, or insurance reimbursement. All analyses in this article exclude data involving self-prayer.

Table 2 (second column) shows that a significantly higher proportion of alternative therapy users saw an alternative medicine practitioner in 1997 (46.3%, equivalent to 39 million people) than in 1990 (36.3%, equivalent to 22 million people). Of the 15 therapies for which the question was asked, the proportion of users who saw a practitioner increased for 11. However, even in 1997 there were only 5 therapies in which a majority of users consulted a practitioner.

Table 2.—Comparison of Prevalence and Frequency of Use of Alternative Therapies Among Adult Respondents, 1997 vs 1990*

Type of Therapy	Used in Past 12 mo, %		Saw a Practitioner in Past 12 mo, %		Mean No. of Visits per Year in Past 12 mo		No. of Visits per 1000 Population		Estimated Total No. of Visits in 1997 (in Thousands)†	Total Visits, %‡
	1997	1990	1997	1990	1997	1990	1997	1990		
Relaxation techniques	35.3*	33.1	35.3	30.0	20.9	18.6	321.2	219.3	6203203	16.4
Herbal medicine	12.1**	2.5	15.1	40.2	2.9	8.1	33.0	20.7	40481	1.7
Massage	11.1**	6.9	31.6*	41.4	4.4	14.8	574.4	422.8	15723	48.1
Chiropractic	11.0	40.1	39.9**	71.1	8.8	12.6	389.1†	304.8	1091886	30.5
Spiritual healing by others	7.0#	4.2	...	9.2	...	14.2	...	54.9	...	...
Megavitamins	5.5**	2.4	23.7	11.8	6.6	12.6	412.1	186.7	22196	3.5
Self-help group	4.8**	2.3	44.4	38.3	18.9	20.5	402.8	180.6	79754	12.7
Imagery	4.5	4.2	23.1	15.1	11.0	14.2	114.3	90.1	22640	3.6
Commercial diet	4.4	3.9	43.2	24.0	7.3	20.7	138.8	193.8	27474	4.4
Folk remedies	4.2**	0.2	6.2	0.0	1.0	...	2.6	...	616	0.1
Lifestyle diet	4.0	3.6	8.0	12.5	2.8	8.1	9.0	36.5	1774	0.3
Energy healing	3.8**	1.3	26.3	32.2	20.2#	8.3	201.9†	34.7	39972	6.4
Homeopathy	3.4**	0.7	16.5	31.7	1.6	6.1	9.0	13.5	1777	0.3
Hypnosis	1.2	0.9	62.7	51.8	2.8	2.6	21.1	12.1	4171	0.7
Biofeedback	1.0	1.0	54.3	20.8	3.6	6.4	19.5	13.3	3871	0.6
Acupuncture	1.0†	0.4	87.6	91.3	3.1	38.4	27.2	140.2	5377	0.9
≥1 of 16 alternative therapies	42.1**	33.8	46.3#	36.3	16.3	19.2	3176.0	2373.0	628825	...
SE	1.2	1.4	1.8	2.5	1.8	4.5	378.7	599.7	74997	...
Self-prayer	35.1**	25.2	...	...	...	...	...	...	...	...

*Percentages are of those who used that type of therapy. Ellipses indicate data not applicable.

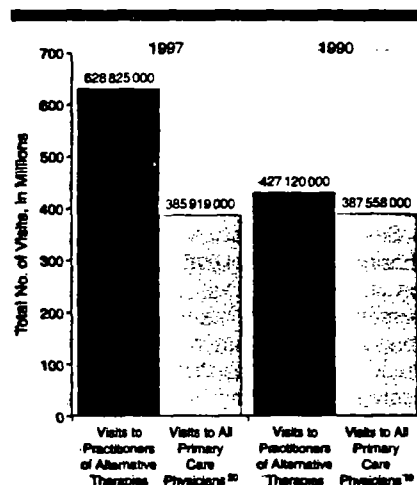
†Estimate based on 1997 population estimate of 198 million.

‡Percentage of total visits of the 16 therapies (ie, excluding self-prayer).

§Because of rounding, percentages do not total 100.

||Respondents who received spiritual healing by others were not asked for details of visits in 1997, nor were those who used self-prayer in either year.

†P≤.05; #P≤.01; **P≤.001.

Figure 1.—Trends in annual visits to practitioners of alternative therapies vs visits to primary care physicians, United States, 1997 vs 1990. Data are from the National Ambulatory Medical Care Survey from 1996²⁰ and 1990.¹⁹

tioner: massage, chiropractic, hypnosis, biofeedback, and acupuncture. Unsupervised use (ie, a form of expanded self-care) remains the usual method of use for all other alternative therapies.

Table 2 (third column) reveals no consistent change in the average number of visits among respondents who consulted practitioners of alternative therapy between 1990 (19.2%) and 1997 (16.3%). However, because of the increase in the proportion of people using these therapies, the total number of visits increased substantially from 1990 to 1997. This

47.3% increase in total visits is largely because of increases in visits for relaxation therapy, massage, chiropractic, self-help, and energy healing. The visits to practitioners of alternative therapy in 1997 exceeded the projected number of visits to all primary care physicians in the United States by an estimated 243 million (Figure 1).^{19,20} Visits to chiropractors and massage therapists accounted for nearly half of all visits to practitioners of alternative therapies.

Prevalence estimates for selected additional therapies assessed in 1997 but not 1990 include: aromatherapy (5.6%), neural therapy (1.7%), naturopathy (0.7%), and chelation therapy (0.13%) (data not shown). Comparisons of total visits and costs for 1990 and 1997 were performed without inclusion of these data. Prevalence estimates for the simultaneous use of prescription medications with herbs, with high-dose vitamins, or with both were obtained. Among the 44% of adults who said they regularly take prescription medications, nearly 1 (18.4%) in 5 reported the concurrent use of at least 1 herbal product, a high-dose vitamin, or both.

Table 3 summarizes results regarding use of alternative therapies for the most commonly reported principal medical conditions in either survey. In each year, a majority of respondents reported 1 or more principal medical conditions. The list of conditions was expanded in 1997 (87 conditions) compared with 1990 (24 conditions). Significant increases in the proportion using alternative therapies

for principal condition(s) (second column) occurred for back problems, allergies, arthritis, and digestive problems. The highest condition-specific rates of alternative therapy use in 1997 were for neck (57.0%) and back (47.6%) problems. The proportion of respondents with 1 or more medical conditions who reported use of an alternative therapy for at least 1 of those conditions increased significantly from 22.9% in 1990 to 33.7% in 1997 ($P\leq.001$). The weighted condition-specific proportion who saw an alternative medicine practitioner for a given condition also increased significantly from 6.8% in 1990 to 11.4% in 1997 ($P\leq.001$).

Table 3 also summarizes the probability that individuals who saw a medical doctor for a particular condition also saw an alternative therapy (fourth column) or also saw a practitioner of alternative therapy (fifth column) for that same condition during the same year. A generally increasing pattern of alternative medicine use can be seen across the range of conditions studied. In 1990, an estimated 1 (19.9%) in 5 individuals seeing a medical doctor for a principal condition also saw an alternative therapy. This percentage increased to nearly 1 (31.8%) in 3 in 1997 ($P\leq.001$). The percentage who saw a medical doctor and also sought the services of an alternative practitioner increased significantly from 8.8% in 1990 to 18.7% in 1997 ($P\leq.01$). In both 1990 and 1997, chiropractic, relaxation techniques, and massage therapy were among the al-

Table 3.—Comparison of Use of Alternative Therapies for the Frequently Reported Principal Medical Conditions, 1997 vs 1990

Condition	Percentage Reporting Condition		Used Alternative Therapy for Condition in Past 12 mo, %		Saw Alternative Practitioner for Condition in Past 12 mo, %		Saw Medical Doctor and Used Alternative Therapy for Condition in Past 12 mo, %		Saw Medical Doctor and Alternative Practitioner for Condition in Past 12 mo, %		Therapies Most Commonly Used in 1997
	1997	1990	1997	1990	1997	1990	1997	1990	1997	1990	
problems	24.0#	19.9	47.6#	35.9	30.1#	19.5	58.8**	36.1	39.1#	23.0	Chiropractic, massage
Allergies	20.7#	16.0	16.6#	8.7	4.2	3.3	28.0#	15.7	6.4	5.0	Herbal, relaxation
Fatigue*	16.7	...	27.0	...	6.3	...	51.6	...	13.1	...	Relaxation, massage
Arthritis	16.6	15.9	26.7#	17.5	10.0	7.6	38.5#	23.8	15.9	13.8	Relaxation, chiropractic
Headaches	12.9	13.2	32.2	26.5	13.3#	6.3	42.0	31.8	20.0	12.1	Relaxation, chiropractic
Neck problems*	12.1	...	57.0	...	37.5	...	66.6	...	47.5	...	Chiropractic, massage
High blood pressure	10.9	11.0	11.7	11.0	0.9	2.9	11.9	11.6	1.1	3.5	Megavitamins, relaxation
Sprains or strains	10.8	13.4	23.6	22.3	10.3	9.6	29.4	24.7	15.9	13.6	Chiropractic, relaxation
Insomnia	9.3#	13.6	26.4	20.4	7.6	4.0	48.4	19.8	13.3	10.9	Relaxation, herbal
Lung problems	8.7	7.3	13.2	8.8	2.5	0.5	17.9	11.1	3.4	0.6	Relaxation, spiritual healing, herbal
Skin problems	8.6	8.0	6.7	6.0	2.2	1.6	6.8	6.9	0.0	2.5	Imagery, energy healing
Digestive problems	8.2	10.1	27.3#	13.2	9.7#	3.6	34.1#	15.3	10.7	5.8	Relaxation, herbal
Depression†	5.6	8.4	40.9	20.2	15.6	7.0	40.9	35.2	26.9	14.0	Relaxation, spiritual healing
Anxiety‡	5.5	9.5	42.7	27.9	11.6	6.5	42.7	45.4	21.0	10.4	Relaxation, spiritual healing
Weighted average across all conditions§	...	...	28.2**	19.1	11.4**	6.8	31.6**	19.9	13.7#	8.3	...
People with ≥1 condition	77.8#	81.5	33.7**	22.9	15.3**	6.9	...	...	...	...	...

*Not included as a separate question in 1990 survey. Ellipses indicate data not applicable.

†The 1997 question asked about severe depression, which is not directly comparable with the 1990 question that asked about depression.

‡The 1997 question asked about anxiety attacks, which is not directly comparable with the 1990 question that asked about anxiety.

§The weighted averages are calculated based on all 37 conditions studied in 1997 and all 24 conditions studied in 1990, ie, condition is unit of analysis.

||This row shows percentage of respondents who reported 1 or more principal medical conditions, along with the percentage of these respondents who reported use of therapy or practitioners for at least 1 of these conditions, ie, person is the unit of analysis.

#P≤.05; #P≤.01; **P<.001.

ternative therapies used most commonly to treat principal medical conditions.

As in 1990, 96% of 1997 respondents who saw a practitioner of alternative therapy for a principal condition also saw a medical doctor during the prior 12 months, and only a minority of alternative therapies used were discussed with a medical doctor. Among the 618 respondents in 1997 who used 1 or more alternative therapies and had a medical doctor, only 377 (38.5%) of the 979 therapies used were discussed with the respondent's medical doctor. This is not significantly different from the 353 (39.8%) of the 886 therapies discussed by the comparable group of respondents (n=501) in the 1990 survey. Given that most alternative therapy is used without the supervision of an alternative practitioner, a substantial portion of alternative therapy use for principal medical conditions (46.0% in 1997 and 51.3% in 1990) was done without input from either a medical doctor or practitioner of alternative therapy.

Payment for Alternative Therapy

Data on insurance coverage of expenditures for alternative therapy services are shown in Table 4. The majority of people who saw alternative therapy practitioners paid all the costs out-of-pocket in both 1990 (64.0%) and 1997 (58.3%). None of the changes in insurance coverage between 1990 and 1997 were statistically significant, probably due in part to small sample sizes.

Using conservative assumptions about the fees charged by practitioners of alternative therapies and assuming no changes in visit prices, Americans spent an estimated \$14.6 billion on visits to these practitioners in 1990 and \$21.2 billion in 1997 (Table 5). Using less conservative (RVRBS) price figures, the amount spent on services of practitioners of alternative therapies was estimated at \$22.6 billion in 1990 and \$32.7 billion in 1997. Regardless of which set of prices is used, total expenditures for practitioners of alternative therapies are estimated to have increased by approximately 45% between 1990 and 1997 exclusive of inflation.

Estimated out-of-pocket expenditures for high-dose vitamins increased from \$0.9 billion in 1990 to \$3.3 billion in 1997. Smaller increases were observed for commercial diet products (\$1.3 billion vs \$1.7 billion). Unlike the 1990 survey, the 1997 survey included questions about expenditures for herbal products (\$5.1 billion) and respondents' alternative therapy-specific books, classes, or equipment (\$4.7 billion).

The estimated total out-of-pocket component of the alternative medicine market in 1997 is shown in Figure 2. Projected out-of-pocket expenditures for all hospitalizations in 1997 in the United States totaled \$9.1 billion, while projected out-of-pocket expenses for all US physician services in the same year were \$29.8 billion.²¹ This compares to a conservatively estimated \$12.2 billion in out-of-

pocket payments to alternative medicine practitioners for the 15 therapies studied. Adding the estimates of \$5.1 billion for herbal therapies, \$3.3 billion for megavitamins, \$1.7 billion for diet products, and \$4.7 billion on alternative therapy-specific books, classes, and equipment, the total out-of-pocket expenditures for alternative medicine are conservatively estimated to be \$27.0 billion. Using the average per-visit prices derived from an RBRVS system¹⁶ rather than our conservative estimates (Table 5), the estimated total out-of-pocket expense is approximately \$34.4 billion, which is comparable with the projected 1997 out-of-pocket expenditures for all physician services.²¹ These estimates exclude out-of-pocket expenditures associated with therapies unique to the 1997 survey (eg, naturopathy, aromatherapy, neural therapy, and chelation therapy).

COMMENT

The results of our study are limited by the restriction of the sampling frame to people who speak English and have telephones and by the low response rate. The decrease in overall response rate from 67% in 1990 to 60% in 1997 is consistent with secular trends for US telephone interviews in recent years.²² It is difficult to know what, if any, bias was introduced or whether trend estimates are biased by the fact that financial incentives were used in 1997 but not 1990. Furthermore, we have no data on the accuracy of self-

Table 4.—Insurance Coverage of Alternative Medicine Services in the United States, 1997 vs 1990*

Type of Therapy	Percentage of Users of Services					
	Coverage, 1997			Coverage, 1990		
	Complete	Partial	None	Complete	Partial	None
Relaxation techniques	28.8	6.6	64.7	5.3	25.9	68.7
Herbal medicine	8.6	11.2	80.2	30.7	15.5	53.8
Massage	11.8	16.7	71.5	49.1	18.3	32.6
Chiropractic	17.6	18.1	64.3	41.5	22.8	35.9
Spiritual healing by others†	...	...	...	0.0	0.0	100.0
Megavitamins	2.7	53.3	44.0	0.0	100.0	0.0
Self-help group	11.7	36.9	51.5	2.8	17.4	79.8
Imagery	51.5	3.5	45.0	16.1	0.0	83.9
Commercial diet	5.0	40.1	54.9	0.0	5.1	94.9
Folk remedies	0.0	0.0	100.0	...	...	...
Lifestyle diet	0.0	44.9	55.1	62.3	0.0	37.7
Energy healing	30.8	8.2	61.1	0.0	19.1	80.9
Homeopathy	0.0	0.0	100.0	0.0	24.7	75.3
Hypnosis	5.1	0.0	94.9	7.0	0.0	93.0
Biofeedback	30.5	43.7	26.0	14.1	19.9	66.0
Acupuncture	0.0	40.7	59.3	21.6	23.0	55.4
Weighted average across all therapies	15.3	26.4	58.3	12.3	23.7	64.0

*Data are percentage of users of alternative therapies provided by practitioners. Ellipses indicate data not applicable.
†Reimbursement patterns not explored in 1997.

Table 5.—National Projections of Expenditures for Alternative Therapies in the United States, 1997 vs 1990*

Category of Expenditure	1997 (Billions of Dollars)		1990 (Billions of Dollars)		Change (%), 1997 vs 1990 (Billions of Dollars)	
	Conservative (SE)	RBRVS (SE)	Conservative (SE)	RBRVS (SE)	Conservative	RBRVS
Total expenditures on professional services for 15 alternative therapies†	21.2 (2.4)	32.7 (3.8)	14.6 (4.0)	22.6 (6.1)	6.6 (45.2)	10.1 (44.7)
Out-of-pocket expenditures						
Professional services, 15 therapies†‡	12.2 (1.7)	19.6 (3.3)	7.2 (1.3)	11.0 (2.1)	5.0 (69.4)§	8.6 (78.2)§
Megavitamins	3.3 (0.4)	...	0.9 (0.3)	...	2.4 (266.7)¶	...
Commercial diet products	1.7 (0.3)	...	1.3 (0.3)	...	0.4 (30.8)	...
Subtotal of out-of-pocket expenditures assessed in 1997 and 1990†	17.2	24.6	9.4	13.2	7.8 (83.0)	11.4 (86.4)
Out-of-pocket expenditures assessed only in 1997						
Herbal medicine	5.1 (0.5)	...	...	...	...	...
Therapy-specific books, classes, and equipment	4.7 (0.8)	...	...	...	...	...
Total out-of-pocket expenditures for alternative therapies in 1997†	27.0	34.4	...	...	...	...

*The 1990 and 1997 cost measures are based on 1990 and 1997 population estimates, respectively (180 million vs 196 million). Both used 1997 per-visit price estimates as follows (conservative price estimate is followed by Resource-Based Relative Value Scale [RBRVS] estimate for each therapy): relaxation techniques (\$20, \$50), herbal medicine (\$40, \$60), massage therapy (\$40, \$60), chiropractic care (\$40, \$65), megavitamins (\$40, \$50), self-help groups (\$20, \$20), imagery techniques (\$45, \$50), commercial diet (\$20, \$20), folk remedies (\$20, \$50), lifestyle diet (\$20, \$60), energy healing (\$40, \$50), homeopathy (\$45, \$60), hypnosis (\$60, \$80), biofeedback (\$60, \$80), and acupuncture (\$40, \$80). (Price estimates for spiritual healing by others were not included because respondents reporting use were not asked for details of professional visits). Ellipses indicate data not applicable.

†These figures reflect the range in out-of-pocket expenditures for conservative vs RBRVS-derived visit prices.

‡Assumes a 20% copayment for users with partial insurance coverage.

§P<.05; ¶P<.001.

reports concerning recollections of number of visits and amounts spent on books, classes, relevant equipment, herbs, or supplements. To the extent possible, we adjusted by weighting data on sociodemographic variables associated with alternative therapy use (eg, income, education, age, region). It is conceivable that the estimated prevalence and costs of alternative therapy use would have been lower if it were possible to correct for those limitations.

Within the context of these limitations, the results of these 2 surveys suggest that the prevalence and expenditures associated with alternative medical therapies in the United States have increased substantially from 1990 to 1997. This increase appears to be primarily due to increases in the prevalence of use and in the frequency with which users of alternative therapy sought professional services. In 1997, an estimated 4 in 10 Americans used at least 1 alternative therapy as com-

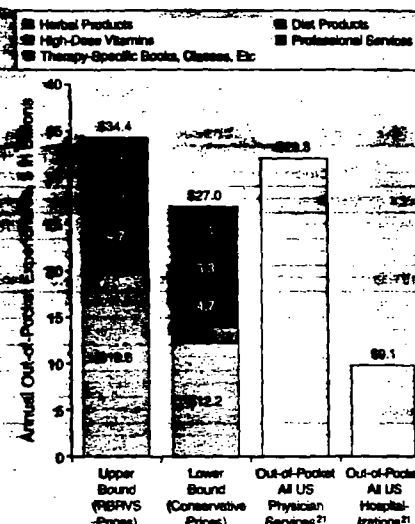


Figure 2.—Estimated annual out-of-pocket expenditures for alternative therapies vs conventional medical services, United States, 1997. Data are from the Health Care Financing Administration, United States.* RBRVS indicates Resource Relative Value Scale.

pared with 3 in 10 in 1990. For adults aged 35 to 49 years in 1997, it is estimated that 1 of every 2 persons used at least 1 alternative therapy. Overall prevalence of increased by 25%, total visits by an estimated 47%, and expenditures on services provided by practitioners of alternative therapies by an estimated 45% exclusive of inflation. Moreover, the use of alternative therapies is distributed widely across all sociodemographic groups.

It is possible to arrange the 16 principal therapies common to the 1990 and 1997 surveys along a spectrum that varies from "more alternative" to "less alternative" in relationship to existing medical school curricula, clinical training, and practice. Arguably, therapies such as biofeedback, hypnosis, guided imagery, relaxation techniques that involve elicitation of the relaxation response (<1% of the sample), lifestyle diet, and (possibly) vitamin therapy can be considered as representative of the more conventional (ie, less alternative) side of the spectrum. Visits associated with these 6 categories accounted for less than 10% of total visits to alternative medicine practitioners; the remainder were associated with the more alternative therapies.

In light of the observed 380% increase in the use of herbal remedies and the 190% increase in high-dose vitamin use, it is not surprising to find that nearly 1 in 5 individuals taking prescription medications also was taking herbs, high-dose vitamin supplements, or both. Extrapolations to the total US population suggest that an estimated 15 million adults are at risk for potential adverse interac-

tions involving prescription medications and herbs or high-dose vitamin supplements. This figure includes nearly 3 million adults aged 65 years or older. Adverse interactions of this nature, including alterations of drug bioavailability or efficacy, are known to occur²³⁻²⁷ and are more likely among individuals with chronic medical illness, especially those with liver or kidney abnormalities. No adequate mechanism currently is in place to collect relevant surveillance data to document the extent to which the potential for drug-herb and drug-vitamin interaction is real or imaginary.

The magnitude of the demand for alternative therapy is noteworthy, in light of the relatively low rates of insurance coverage for these services. Unlike hospitalizations and physician services, alternative therapies are only infrequently included in insurance benefits. Even when alternative therapies are covered, they tend to have high deductibles and co-payments and tend to be subject to stringent limits on the number of visits or total dollar coverage. Because the demand for health care (and presumably alternative therapies) is sensitive to how much patients must pay out-of-pocket,²⁸ current use is likely to underrepresent utilization patterns if insurance coverage for alternative therapies increases in the future.

In 1990, a full third of respondents who used alternative therapy did not use it for any principal medical condition.¹ From these data, we inferred that a substantial amount of alternative therapy was used for health promotion or disease prevention. In 1997, 42% of all alternative therapies used were exclusively attributed to treatment of existing illness, whereas 58% were used, at least in part, to "prevent future illness from occurring or to maintain health and vitality."

Despite the dramatic increases in use and expenditures associated with alternative medical care, the extent to which patients disclose their use of alternative therapies to their physicians remains low. Less than 40% of the alternative therapies used were disclosed to a physician in both 1990 and 1997. It would be overly simplistic to blame either the patient or their physician for this inadequacy in patient-physician communication. The current status quo, which can be described as "don't ask and don't tell," needs to be abandoned.²⁹ Professional strategies for responsible dialogue in this area need to be further developed and refined.

Data from this survey, reflective of the US population, are representative of a predominantly white population. Even if we were to combine data sets from the 1990 and 1997 surveys, we would not

have sufficiently large data to provide precise estimates of the patterns of alternative therapy use among African Americans, Hispanic Americans, Asian Americans, or other minority groups. Parallel surveys, modified to include therapies unique to minority populations and translated when appropriate, should be conducted using necessary sampling strategies. Only then can we compare patterns across ethnic groups and prioritize research agendas for individual populations. As alternative medicine is introduced by third-party payers as an attractive insurance product, it would be unfair for individuals without health insurance and those with less expendable income to be excluded from useful alternative medical services or consultation (eg, professional advice on use or avoidance of alternative therapies).

In conclusion, our survey confirms that alternative medicine use and expenditures have increased dramatically from 1990 to 1997. In light of these observations, we suggest that federal agencies, private corporations, foundations, and academic institutions adopt a more proactive posture concerning the implementation of clinical and basic science research, the development of relevant educational curricula, credentialing and referral guidelines, improved quality control of dietary supplements, and the establishment of postmarket surveillance of drug-herb (and drug-supplement) interactions.

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Spinal Manipulation in the Treatment of Episodic Tension-Type Headache

A Randomized Controlled Trial

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Context.—Episodic tension-type headache is common and is often treated using manual therapies. Few data exist for the efficacy of these interventions.

Objective.—To determine the effects of spinal manipulation therapy on adults with episodic tension-type headache.

Design.—Randomized controlled trial lasting 19 weeks.

Setting.—Outpatient facility of a National Health Service-funded chiropractic research institution in Denmark.

Participants.—Volunteer sample of 26 men and 49 women aged 20 to 59 years who met the diagnostic criteria for episodic tension-type headache as defined by the International Headache Society.

Intervention.—Participants were randomized into 2 groups, 1 receiving soft tissue therapy and spinal manipulation (the manipulation group), and the other receiving soft tissue therapy and a placebo laser treatment (the control group). All participants received 8 treatments over 4 weeks; all treatments were performed by the same chiropractor.

Main Outcome Measures.—Daily hours of headache, pain intensity per episode, and daily analgesic use, as recorded in diaries.

Results.—Based on intent-to-treat analysis, no significant differences between the manipulation and control groups were observed in any of the 3 outcome measures. However, by week 7, each group experienced significant reductions in mean daily headache hours (manipulation group, reduction from 2.8 to 1.5 hours; control group, reduction from 3.4 to 1.9 hours) and mean number of analgesics per day (manipulation group, reduction from 0.66 to 0.38; control group, reduction from 0.82 to 0.59). These changes were maintained through the observation period. Headache pain intensity was unchanged for the duration of the trial.

Conclusion.—As an isolated intervention, spinal manipulation does not seem to have a positive effect on episodic tension-type headache.

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TENSION-TYPE headaches (TTHs) are extremely common, affecting more than one third of the population¹ and accounting for more than two thirds of all headache episodes.² The pain of TTHs is usually mild to moderate and typically bilateral. Symptoms are usually described as pressing or tightening with a

nonpulsating quality, and symptoms characteristic of migraine (nausea, vomiting, photophobia, and phonophobia) are absent. The International Headache Society (IHS) classifies persons with 1 to 15 and 16 or more occurrences of TTH per month as having episodic TTH (ETTH) and chronic TTH, respectively.³ Episodic tension-type headache is by far the more common form, with a 1-3 prevalence of more than 38%.¹ Because many sufferers report interference with their lifestyle, ETTH has a significant socioeconomic impact.¹

Although ETTH is typically medically treated with nonprescription analgesics, many people with ETTH seek hands-on therapy, delivered by various groups of practitioners. Several uncontrolled studies have suggested that a combination of physical treatment methods can relieve the symptoms of TTH,⁴⁻⁶ and the single randomized controlled study using IHS criteria suggested a positive treatment effect of a combination of therapies (including manipulation, heat, massage, and trigger-point therapy) for chronic TTH,⁹ compared with a hands-off pharmaceutical treatment protocol. In all these studies, however, it is unclear whether the effects were due to one, all, or a combination of the treatment elements. The common element in these studies was joint manipulation, recently demonstrated to be effective in the treatment of cervicogenic headache.¹⁰ The sole report of manipulation as an isolated treatment for TTH found a reduction in pain intensity immediately after the treatment, but the subjects were not further evaluated.¹¹

The goal of this randomized controlled trial was to evaluate the long-term effect of joint manipulation as an isolated intervention for ETTH.

METHODS

Experimental Design

This was a randomized, controlled clinical trial with a blinded observer designed to evaluate the effect of spinal manipulative therapy in the treatment of ETTH. The trial was carried out in the outpatient facility of a National Health Service-funded independent chiropractic research institution (Nordisk Institut for Kiropraktik, Odense, Denmark). Data were interpreted by a blinded observer and analyzed at the Center for Biomechanics, Faculty of Health Science, Odense University, Odense, Denmark. All procedures were approved by the regional ethics committee (permit No. 97/12), and all subjects gave verbal and written informed consent prior to participation.

Participants

Participants were recruited from the general community by advertisements in the local newspapers. Initial eligibility screening was done over the telephone, followed by a personal interview and physical examination. Eligibility criteria for participation in this study were as follows: (1) fulfillment of IHS criteria for ETTH,³ with more than 5 but fewer than 15 headache episodes per month; (2) age 20 to 60 years; (3) score for typical headache intensity between 25 and 85 on a visual analog scale from 0 to 100; and (4) no relative or absolute contraindications to manipulation. The selection refinements of criteria 1 and 3 were designed to better allow the possibility of seeing a change by using more typical rather than very mild or severe cases. After acceptance, a participant could be excluded for any adverse reaction to treatment or any event triggering or potentially triggering a change in headache status (eg, vehicular crash with neck injury).

Participants were informed that the purpose of the trial was to compare the relative efficacy of 2 physical treatments commonly used for ETTH. Participants were instructed to continue their normal lifestyle during the trial, including their usual pattern of medication.

Interventions

After baseline data collection and randomization (see below), participants underwent 1 of 2 treatment protocols. All participants received 8 treatments over 4 weeks, all performed by one chiropractor (Birthe Hove Madsen, DC) and each

lasting approximately 15 minutes. The chiropractor routinely uses both treatment protocols in daily practice and was confident in performing both techniques. The manipulation group received joint manipulation of the cervical spine as determined by the chiropractor based on palpatory examinations and also deep friction massage (including trigger-point therapy, if indicated) of the trapezius and muscles deep to it. Specific manipulation maneuvers consisted of diversified and/or toggle-recoil techniques, depending on the level of the palpated segmental dysfunction.¹² These techniques use a high-velocity, low-amplitude thrust delivered in a specific line of drive at the palpated end point of the normal passive range of motion and are often accompanied by a clicking or crackling noise.

The control group also received deep friction massage. In addition, this group underwent the application of low-power laser light (Omega Biotherapy, London, England) to the upper cervical region. No effect, apart from placebo, can be expected from low-power laser therapy.¹³

The control group was designed to be an active control group for spinal manipulation, with the added goal of making the 2 groups more similar. A control group that receives no treatment is not ideal in procedures that use physical contact; in this study, every active intervention parameter was identical in the 2 groups except for the actual manipulation procedure. Our design allowed evaluation of the contribution of spinal manipulation, as it was the only difference between the 2 groups.

Measurements and Procedures

The trial lasted 19 weeks. In weeks 1 and 2, data were collected to determine a baseline for the outcome variables. Before starting week 3, participants were randomized to either the manipulation group or the control group by a blinded drawing of a ticket by a secretary. In weeks 3 through 6, subjects were treated 8 times, usually twice a week. Posttreatment data were collected from headache diaries completed during weeks 7, 11, 15, and 19.

All participants were required to fill out a headache diary¹⁴ for each of weeks 1, 2, 7, 11, 15, and 19. Recorded information included hours per day that headache was present, the intensity of the headache, and daily analgesic consumption. Additionally, to reveal any difference between the 2 physical treatment regimens in their ability to generate a placebo effect, participants scored their expected treatment outcome on a visual analog scale immediately before randomization and again immediately after

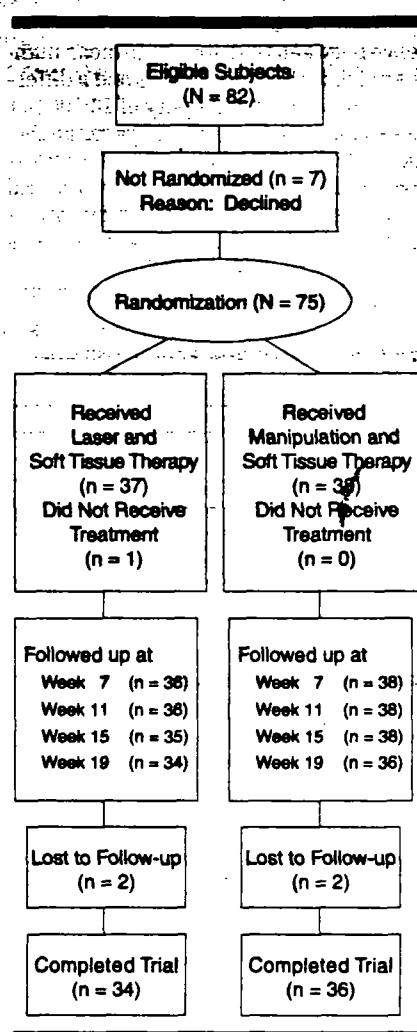


Figure 1.—Progression of subjects through the trial, including withdrawal and follow-up losses.

the first treatment session, before a new treatment effect could have been noted.¹⁵

Outcome Measures

The primary outcome measures were the number of headache hours per day, mean headache intensity per headache episode, and consumption of analgesics per day. From a previous study on a similar headache population,¹⁰ we expected most patients to stay with their preferred analgesic regimen throughout the trial period. In case of medication change, 500 mg of acetylsalicylic acid, 500 mg of paracetamol, and 200 mg of ibuprofen were regarded as equivalent doses. All data were retrieved from the diaries by assistants unaware of the treatment group assignment.

Statistical Analysis

The outcome measures were compared between pretreatment and each posttreatment period within and between the 2 treatment groups. A sample size of 84 was projected to provide a

power of 90% to detect a 1-hour difference between the 2 groups in mean number of daily headache hours and a difference in headache intensity of 13/100 per episode, as scored on the visual analog scale. All tests of hypotheses and reported *P* values are 2-tailed. Statistical analysis was conducted on an intention-to-treat basis, using StatView (Abacus Concepts, Berkeley, Calif).

RESULTS

Subjects

Participant flow and retention is summarized in Figure 1. Recruitment was conducted over a 9-month period from February through October 1997. Of the persons who responded to the advertisements and completed telephone and personal interviews, 82 fulfilled the inclu-

criteria; of 1, 7 did not wish to take part in the study, leaving 75 participants to enter the trial. The characteristics of the randomized participants are shown in Table 1. There were no statistically significant differences between the 2 groups with respect to age, mean headache hours per day, headache intensity per episode, or analgesics. No side effects were experienced by any participant in either group.

One participant was excluded in 5 following a neck injury due to a car crash. One participant from the placebo group was lost to follow-up at week 15 and a further 3 (manipulation group, 2; control group, 1) were lost to follow-up in week 19.

Outcomes

There was no significant difference between the 2 groups for any outcome variable before or following treatment (Table 1 and Table 2, Figure 2). However, mean headache hours per day and analgesic use within both groups showed improvement from pretreatment to week 7. The mean headache hours per day was reduced by approximately 1.5 hours by week 7 (95% confidence interval [CI], -2.4 to -0.6; Figure 2, B), and this change did not lessen significantly by the end of the trial. Headache intensity was unchanged for the duration of the trial (95% CI, -12 to 11; Figure 2, C). Analgesic consumption also lessened in both groups by week 7 (95% CI, -0.5 to -0.1; Figure 2, B). Of the 74 participants, 48 stayed with the same medication throughout the trial and 25 switched between 2 of the following: 500 mg of acetylsalicylic acid, 500 mg of paracetamol, or 200 mg of ibuprofen. One participant switched between acetylsalicylic acid and a morphine preparation; analgesic data for this person were not included in the results. Analysis of the 48

Table 1.—Pretreatment Characteristics of the Study Population*

Variable	Whole Group	Control Group	Manipulation Group	P Value for Difference†
No. of subjects	75	37	38	
Sex				
Male	26	11	15	.52 (Fisher exact)
Female	49	26	23	
Age, mean (range), y	38 (20-59)	38 (20-58)	37 (22-59)	.86
Mean headache hours per day (95% CI)	3.1 (2.5-3.7)	3.4 (2.4-4.4)	2.8 (2.1-3.5)	.29
Mean headache intensity, VAS, per episode (95% CI)	38/100 (35-41/100)	37/100 (33-41/100)	37/100 (33-41/100)	.69
Mean No. of analgesics per day (95% CI)	0.74 (0.56-0.92)	0.82 (0.50-1.14)	0.66 (0.49-0.83)	.38

*CI indicates confidence interval; VAS, visual analog scale. Ellipses indicate data not applicable.
†Reported as *t* test, unless otherwise noted.

Table 2.—Results of Outcome Variables During the 13-Week Follow-up Period*

Outcome Variable	Control Group	Manipulation Group	P Value for Difference (<i>t</i> Test)
Mean analgesics per day (95% CI)			
Week 7 (n = 73)	0.59 (0.00-1.49)	0.38 (0.00-0.76)	.14
Week 11 (n = 73)	0.54 (0.30-0.78)	0.41 (0.27-0.55)	.35
Week 15 (n = 72)	0.60 (0.26-0.94)	0.48 (0.34-0.62)	.51
Week 19 (n = 69)	0.56 (0.22-0.90)	0.48 (0.34-0.62)	.66
Mean headache hours per day (95% CI)			
Week 7 (n = 74)	1.9 (0.9-2.9)	1.5 (1.1-1.9)	.33
Week 11 (n = 74)	1.7 (0.9-2.5)	1.6 (1.2-2.0)	.77
Week 15 (n = 73)	2.1 (1.1-3.1)	1.6 (1.2-2.0)	.30
Week 19 (n = 70)	2.2 (1.2-3.2)	2.1 (1.3-2.9)	.87
Mean headache intensity (95% CI)			
Week 7 (n = 74)	34 (26-38)/100	38 (30-46)/100	.43
Week 11 (n = 74)	30 (26-38)/100	36 (28-44)/100	.28
Week 15 (n = 73)	33 (25-41)/100	29 (23-35)/100	.41
Week 19 (n = 70)	26 (20-32)/100	35 (27-43)/100	.13

*CI indicates confidence interval.

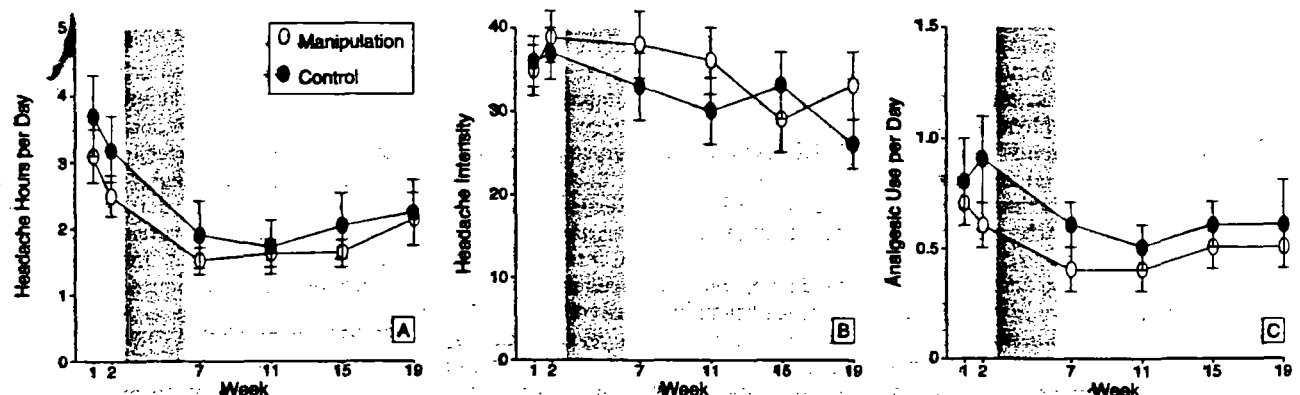


Figure 2.—Results of primary outcome measures. No difference was observed between groups for any measure. Intervention in weeks 3 to 6 indicated by shaded areas. Error bars equal 1 SE.

tics who continued the same medication yielded similar results (data not shown).

The expected treatment outcome was similar in both the manipulation group and the control group before (95% CI, 69-83/100 vs 68-80/100) and after (95% CI, 64-80/100 vs 69-81/100) the initial treatment. The treatment expectation did not change following the first treatment (95% CI, -2 to 10/100 vs -5 to 7/100), indicating that the 2 treatment methods had no major placeboogenic differences.

COMMENT

This study showed that spinal manipulation did not significantly improve the outcome for ETTH. We point out that our study population was carefully selected based on accepted criteria for ETTH. In practice, ETTH and cervicogenic headache can be difficult to differentiate,¹⁶ and often occur together.¹⁷ Our conclusions are in stark contrast to those

of an earlier and very similar study of cervicogenic headache, in which the effect of spinal manipulation was quite dramatic.¹⁰ These data thus underline the importance of accurate diagnosis in the selection of headache patients for spinal manipulation.

The only other randomized controlled study including manipulation as a treatment for ETTH compared a hands-off pharmaceutical treatment (6 weeks of amitriptyline) with a chiropractic treatment that included personal contact, heat, massage, ergonomic advice, and spinal manipulation.⁹ There was a significant decrease in overall symptoms in the chiropractic treatment group, but this effect could have been due to the higher level of personal attention given to that treatment group. Our manipulation group was comparable to that chiropractic group, and we controlled for the treatment elements of personal attention and hands-on treatment.

As always, when a controlled clinical trial fails to demonstrate a treatment effect, the question of a possible type II error (ie, overlooking a real difference) is an issue. In this trial, the number of participants was relatively small, and it is possible that a larger trial might have identified an effect in 1 or more of the outcome variables. However, the data in Table 2 and Figure 2 suggest that any such effect, statistically significant or not, would be of little clinical significance.

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Moxibustion for Correction of Breech Presentation

A Randomized Controlled Trial

Francesco Cardini, MD; Huang Weixin, MD

Context.—Traditional Chinese medicine uses moxibustion (burning herbs to stimulate acupuncture points) of acupoint BL 67 (Zhiyin, located beside the outer corner of the fifth toenail), to promote version of fetuses in breech presentation. Its effect may be through increasing fetal activity. However, no randomized controlled trial has evaluated the efficacy of this therapy.

Objective.—To evaluate the efficacy and safety of moxibustion on acupoint BL 67 to increase fetal activity and correct breech presentation.

Design.—Randomized, controlled, open clinical trial.

Setting.—Outpatient departments of the Women's Hospital of Jiangxi Province, Nanchang, and Jiujiang Women's and Children's Hospital in the People's Republic of China.

Patients.—Primigravidas in the 33rd week of gestation with normal pregnancy and an ultrasound diagnosis of breech presentation.

Interventions.—The 130 subjects randomized to the intervention group received stimulation of acupoint BL 67 by *moxa* (Japanese term for *Artemisia vulgaris*) rolls for 7 days, with treatment for an additional 7 days if the fetus persisted in the breech presentation. The 130 subjects randomized to the control group received routine care but no interventions for breech presentation. Subjects with persistent breech presentation after 2 weeks of treatment could undergo external cephalic version anytime between 35 weeks' gestation and delivery.

Main Outcome Measures.—Fetal movements counted by the mother during 1 hour each day for 1 week; number of cephalic presentations during the 35th week and at delivery.

Results.—The intervention group experienced a mean of 48.45 fetal movements vs 35.35 in the control group ($P < .001$; 95% confidence interval [CI] for difference, 10.56-15.60). During the 35th week of gestation, 98 (75.4%) of 130 fetuses in the intervention group were cephalic vs 62 (47.7%) of 130 fetuses in the control group ($P < .001$; relative risk [RR], 1.58; 95% CI, 1.29-1.94). Despite the fact that 24 subjects in the control group and 1 subject in the intervention group underwent external cephalic version, 98 (75.4%) of the 130 fetuses in the intervention group were cephalic at birth vs 81 (62.3%) of the 130 fetuses in the control group ($P = .02$; RR, 1.21; 95% CI, 1.02-1.43).

Conclusion.—Among primigravidas with breech presentation during the 33rd week of gestation, moxibustion for 1 to 2 weeks increased fetal activity during the treatment period and cephalic presentation after the treatment period and at delivery.

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IN CASES OF BREECH presentation at the onset of labor, delivery is associated with additional risks: for the mother, cesarean delivery and for the neonate, physical injury. Breech presentation is common in the midtrimester

pregnancy and the incidence decreases as the pregnancy approaches term because of spontaneous version.¹⁻⁴ It is reasonable to assume (although not firmly established) that fetal activity plays an important role in spontaneous version.⁵⁻⁹ The incidence of breech presentation at delivery can be reduced, but not eliminated, by the use of external cephalic version (ECV).¹⁰

Since ancient times, traditional Chinese medicine has proposed moxibustion of acupoint BL 67 (Zhiyin) to promote

version of fetuses in breech presentation. Moxibustion is a traditional Chinese method that uses the heat generated by burning herbal preparations containing *Artemisia vulgaris* (mugwort) (the Japanese name is *moxa*) to stimulate acupuncture points. Acupoint BL 67 is beside the outer corner of the fifth toenail.

At present, there are no randomized, controlled clinical trials to evaluate the efficacy of this therapy. The 2 published Chinese studies^{11,12} are not randomized and are based on a mixed population of primipara and multipara subjects stimulated at varying times between the 28th and 38th weeks of pregnancy. Although both studies give encouraging results and stimulate reflection regarding possible mechanisms of action, they do not allow definitive conclusions regarding efficacy because they are not randomized, little information is provided about the population sample, and the times at which stimulation is applied are wide ranging.

Cardini et al¹³ identified the stage of pregnancy at which stimulation should commence and the parity status of the groups studied as primary factors to ensure the reliability of a clinical trial concerning spontaneous or induced correction of breech presentation.

Data in the literature concerning the probability of spontaneous correction indicate that correcting breech presentation before the 32nd week is useless.¹⁴⁻¹⁶ There is also a sharp differentiation between multigravidas (high likelihood of spontaneous correction of breech presentation, even between the 32nd and 35th weeks) and primigravidas or multigravidas with a previous breech presentation at term (low probability of spontaneous version after the 32nd week).¹⁵⁻¹⁷

Gottlicher and Madjaric,^{15,16} by ultrasound examination of 4066 pregnant women, defined the likelihood of spontaneous correction of breech presentation from the 33rd week of pregnancy as 15.5% (95% confidence interval [CI], 2.8%-28.2%) for primigravidas and 57.5% (95% CI, 36.3%-78.7%) for multigravidas.

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Reprints not available from the author.

Westgren et al,¹⁷ by ultrasound screening of 4600 women in the 32nd week of pregnancy, identified 310 cases (6.7%) of breech presentation, which were prospectively studied until birth. Rates of spontaneous cephalic version varied, according to whether subjects were primigravida (46%), multigravida with a previous breech presentation (32%), or multigravida with no previous breech presentation (78%). All the studies available report data relating to Western populations and we have been unable to retrieve any information regarding the spontaneous version rate from the 33rd week to term among Chinese pregnant women.

Given this background, Cardini and Marcolongo,¹⁸ in a retrospectively controlled clinical trial, compared 23 primigravidas treated for breech presentation by moxibustion in the 32nd and 33rd week with a retrospective, untreated group at the same stage of pregnancy. The difference in prevalence of breech presentation showed borderline statistical significance ($P = .05$). Thus, the subgroup of primigravidas with breech presentation at the 33rd week of pregnancy seemed to be the ideal population for a randomized, controlled clinical trial.

We undertook this study to evaluate the efficacy and safety of moxibustion on acupoint BL 67 in correcting breech presentation in a population of primigravidas treated since the 33rd week of pregnancy and to evaluate the efficacy of this technique in increasing active fetal movements (AFMs).

These 2 main objectives are consistent with the hypothesis that the use of moxibustion in women whose fetuses are breech in the 33rd week of pregnancy will (1) increase fetal activity; (2) reduce the proportion of fetuses that remain in a nonvertex presentation and, hence, decrease the need for ECV; and (3) decrease the incidence of breech presentation at birth. A secondary aim of the study was to assess the efficacy of 2 different dosages of moxibustion.

METHODS

This was a randomized, controlled, open clinical trial of subjects treated by moxibustion since the 33rd week of pregnancy (intervention group) vs untreated subjects (control group). Subjects with persistent breech presentation after 2 weeks' treatment (intervention group) or observation (control group) could undergo ECV. Moxibustion in the early third trimester and ECV in late pregnancy are the standard care for breech presentation in both the centers involved in the trial. Thus (and also for ethical reasons), the availability of ECV was maintained for all subjects recruited.

Subjects were included if they were primigravidas, in the 33rd week of gestation (from 32 weeks + 1 day to 33 complete weeks, based on the last menstruation date and ultrasound data), with breech presentation diagnosed by ultrasound within 24 hours of randomization, and with normal fetal biometry (biparietal diameter and abdominal circumference between the 10th and 90th percentiles). Subjects were excluded if they had pelvic defects, previous uterine surgery, uterine malformation or fibromyoma of diameter greater than 4 cm, fetal malformation, twin gestation, tocolytic therapy during pregnancy, risk of premature birth (uterine hypercontractility and/or initial shortening or dilatation of the neck, with a Bishop score ≥ 4), or pathological pregnancy (eg, intrauterine growth retardation, gestosis, serious infections, placenta previa, polyhydramnios, oligohydramnios) judged by the investigator to contraindicate inclusion in the study. Subjects refusing to undergo treatment were also excluded.

Study Procedures

The trial was conducted from April 1995 through August 1996 in the Women's Hospital of Jiangxi Province, Nanchang, People's Republic of China. A few subjects (23) were recruited in the nearby Jiujiang Women's and Children's Hospital, also in Jiangxi Province. The subjects were recruited during the routine management of normal pregnancies in the outpatient department. All procedures were executed by midwives (with the supervision of physicians) except ultrasound examinations and ECVs. The protocol followed the ethical standards of the Declaration of Helsinki.

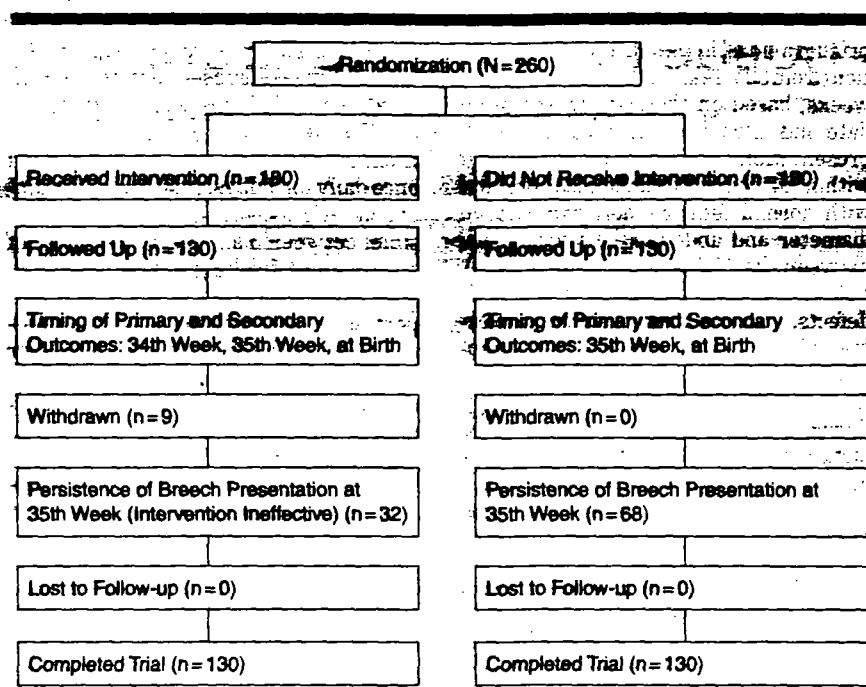
Pregnant women fulfilling all criteria of the study were asked to participate. Interested subjects gave oral informed consent. Subjects had an ultrasound scan at the 33rd week. On the day of the ultrasound scan by which breech presentation was confirmed, the selected subject was randomly assigned to 1 of the 2 groups. The sample was randomly allocated by numbered envelopes (randomized in groups of 10 by the computer program PACT, Version 2.0 [Glaxo-Wellcome, London, England], in Italy). Once randomized, subjects and investigators were aware of group assignment. All subjects recruited were advised to avoid or, at least, to ask the investigators about other interventions or therapies that could contaminate the results of the trial. All subjects were asked to return after 2 weeks for an ultrasound check on presentation. If breech presentation persisted at this time, the subject (after giving informed consent) could undergo ECV in the following weeks.

All subjects were also asked to complete 2 record forms for AFMs, 1 for each of the 2 weeks subsequent to recruitment. These 2 forms were returned at the time of the ultrasound examination. Each record form had to be completed once daily for 7 days, reporting the number of AFMs counted in 1 hour (if possible, between 5 and 8 PM) and times of starting and finishing the count.

Finally, each subject was asked to report all significant details of her pregnancy and delivery during a personal or telephone appointment after she had given birth. The following specific information was collected: date of birth, place of birth, name and address of the obstetrician normally consulted, and name and address of the obstetrician present at birth. In this way, it was possible to consult other sources of information (obstetrician normally consulted, obstetrician present at birth, patient record forms) if the subject provided incomplete or unreliable information. Because almost all the enrolled subjects gave birth in the same hospital where they had been studied, information about delivery was reliable and easy to check.

If the subject belonged to the intervention group, she was admitted to the hospital to attend an instruction session within 24 hours of randomization, alone or with her partner or the person who was actually going to help administer the treatment. Teaching the technique for applying moxibustion at home included presenting the moxibustion material (cigar-shaped rolls containing *Artemisia*), locating of acupoint BL 67, and explaining the technique for stimulation of acupoint BL 67. During the therapy the subject relaxed in the sitting or semisupine position, with the partner sitting comfortably. The therapy was executed for 30 minutes (15 minutes per side) daily for 7 days in the first 87 subjects, and twice daily in the last 43 subjects. The subjects were allowed to choose the time, ensuring no interruptions in the therapy (if possible, between 5 and 8 PM). The intensity of moxibustion was just below the individual tolerability threshold, causing hyperemia from local vasodilatation but not burn blisters.

Reasons for discontinuing stimulation and consulting the investigator (abdominal pain, other suspected adverse effects, sensation that version had occurred before completion of 7 days' treatment) were explained to the subject, together with symptoms suggesting that version had occurred (decreased pressure in the epigastrium or hypochondrium, increased pressure in the hypogastrium, pollakiuria, a "different feeling" in the abdomen). The first stimulation session was executed in the hospital and the neces-



Profile of the randomized controlled trial.

sary materials for the following 6 days' stimulation were dispensed, together with the AFM record forms.

Last, an examination after 1 week's treatment (visit 2) was scheduled. Visit 2 included a check on presentation and collection of the AFM record form. The presentation check was by localization of fetal heartbeats and abdominal palpation (Leopold maneuvers). Ultrasound examination was performed only in the event that the techniques described herein failed or yielded uncertain findings.¹⁹ This was to avoid an excess of ultrasound examinations, given that an ultrasound examination was scheduled for the 35th week in all subjects. If cephalic version had not occurred, another week's treatment was advised if there were no adverse effects and the subject agreed to continue. Further *moxa* rolls were therefore dispensed to the subject with a second AFM record form. The frequency of the treatment was the same as in the first week. Visit 3 was scheduled and executed after a further week; the procedure was the same for all treated and untreated subjects as described herein (Figure).

Outcomes Measured

The primary outcomes were number of cephalic presentations at the 35th week and at birth and fetal motor activity. Secondary outcomes were compliance with treatment, observation of possible adverse effects in the intervention group and adverse events in both groups, number of cephalic versions after 1 and 2 weeks of treatment (ie, 34th and 35th weeks' gestation), number of

cephalic versions with 2 different dosages of moxibustion (once or twice daily), number and causes of cesarean deliveries, spontaneous and induced vaginal deliveries, and Apgar score at 5 minutes.

Statistical Analysis

On the basis of the study by Cardini and Marcolongo,¹⁸ for primigravidas it seemed possible to identify a 30% difference in the number of cephalic presentations at the 35th week and at term between the intervention and control groups, with an α significance level of .05 and greater than 90% power if 60 subjects per group completed the study. Given that the reliability of the preliminary study was limited because it was based on retrospective data and that we decided to assess the efficacy of 2 different dosages of moxibustion, the number of enrolled subjects was increased to 130 per group.

Even if not attributable to 1 of the causes specified in the research protocol, discontinuation of treatment did not entail the subject's exclusion from the study. Outcomes of all subjects recruited were analyzed on the basis of intention to treat. Every possible effort was made to ascertain the reason for withdrawal.

The statistical processing was performed using Epi Info, Version 6.04 (Centers for Disease Control and Prevention, Atlanta, Ga). The χ^2 test (supplemented, where necessary, by the Fisher exact test) and the *t* test were used for comparing qualitative and continuous variables, respectively. The measurement of effects was also described in terms of relative risk (RR) with 95% confidence intervals (CI).

Table 1.—Comparability of Control Groups*

	Intervention Group (n = 130)	Control Group (n = 130)
Maternal age, y	25.5 (2.5)	25.2 (3.0)
Maternal height, cm	159.8 (3.9)	158.8 (3.8)
Maternal weight, kg	62.4 (11.8)	62.5 (11.8)
Maternal parity, No. (%)	82 (47.7)	56 (43.1)
Legs straight at 33rd week, No. (%)	79 (60.8)	68 (52.3)

*Unless noted otherwise, values are expressed as mean (SD).

RESULTS

The total number of subjects was 260 (130 subjects per group), recruited, randomized, observed, or treated and followed up to delivery. No significant differences emerged between the intervention group and the control group (Table 1). Neither the placental localization and grading nor the amount of amniotic fluid at the 33rd week showed significant differences between the 2 groups.

The main results of the trial are summarized in Table 2. At the ultrasound check at the 35th week of gestation (2 weeks after the first visit), 98 (75.4%) of 130 fetuses in the intervention group were cephalic compared with 62 (47.7%) of 130 in the control group ($P < .001$; RR, 1.58; 95% CI, 1.29-1.94).

After 35 weeks of pregnancy, only 1 subject in the intervention group agreed to undergo ECV, but version was not obtained. Twenty-four subjects in the control group agreed to undergo ECV and in 19 subjects cephalic version was obtained. Despite this, the number of cephalic presentations at birth was still significantly different in the 2 groups: 98 (75.4%) of 130 in the intervention group compared with 81 (62.3%) of 130 in the control group ($P = .02$; RR, 1.21; 95% CI, 1.02-1.43). The results obtained excluding subjects treated with ECV are shown in Table 2.

Of the 98 cephalic versions obtained in the intervention group, 82 occurred during the first week and 16 during the second week of treatment. The cephalic or breech presentations observed at the second visit (35th week of pregnancy) remained unchanged up to term in all subjects treated and observed, except for those successfully treated with ECV.

Compliance and Adverse Effects and Events

The only intervention allowed for the subjects in the control group was ECV during the last 5 weeks of pregnancy. They were specifically questioned at the 35th week and after delivery and none reported having been treated with moxibustion or other therapies.

Among the intervention group only 1 subject failed to comply with the treatment schedule prescribed and discontinued the therapy. At the end of the first week of treatment 8 subjects withdrew from therapy, 3 on the advice of the obstetrician (for Braxton Hicks contractions, breech engagement, and maternal tachycardia and atrial sinus arrhythmia, respectively) and 5 subjects for unspecified reasons. All 9 subjects maintained the breech presentations of their fetuses to term and none of them were excluded from the statistical analysis.

The form of discomfort most frequently reported by both groups was a sense of tenderness and pressure in the epigastric region or in one of the hypochondria (epigastric crushing) attributable to the head of the breech fetus pressing against the maternal organs.

No adverse events occurred in the intervention group during treatment. After treatment, 2 premature births occurred (both at 37 weeks), 1 of which was preceded by premature rupture of the membranes (PROM). There were 4 PROMs in the intervention group.

Adverse events occurring in the control group included 3 premature births at 34, 35, and 37 weeks (the third was preceded by placental detachment with fetal distress) and 1 intrauterine fetal death (intrauterine growth retardation and oligohydramnios, spontaneous delivery at 38 weeks; growth was within normal limits at ultrasound examination at 35 weeks). The total number of PROMs in the control group was 12.

Active Fetal Movements

Regarding the efficacy of the moxibustion treatment in producing an increase in fetal motility, comparison between the 2 groups proved possible for only the first week of treatment (or observation) because all the subjects in the intervention group who achieved cephalic version in the first week of treatment filled in only the first of the 2 record forms used for the weekly AFM counts. The mean value for fetal movements recorded during a 1-hour observation period for 7 days was 48.45 for the subjects in the intervention group and 35.35 for the subjects in the control group (difference, 13.08; 95% CI, 10.56-15.60; t test, 10.215; $P < .001$).

Effects of 1 or 2 Moxibustion Sessions per Day

In the intervention group, the first 87 subjects received 1 stimulation per day, lasting 30 minutes, for 7 or 14 days (QD [*quaque die*] group). The last 47 subjects received 2 30-minute stimulations per day for 7 or 14 days (BID [*bis in die*] group). The 2 subgroups showed no significant

Table 2.—Main Results of the Trial

	No. (%)		P	RR (95% CI)*
	Intervention Group	Control Group		
Cephalic presentation at 35 wk	98/130 (75.4)	62/130 (47.7)	<.001	1.58 (1.29-1.94)
Cephalic presentation at birth	98/130 (75.4)	81/130 (62.3)	.02	1.21 (1.02-1.43)
Cephalic presentation at birth†	98/129 (76.0)	62/106 (58.5)	.004	1.30 (1.08-1.57)

*RR indicates relative risk; CI, confidence interval.

†Data exclude subjects treated with external cephalic version.

differences in amount of amniotic fluid during the 33rd week, frequency of straight or bent leg position during the 33rd week, placental localization, neonatal sex, treatment compliance, or adverse effects attributable to the treatment.

At the end of the first week of treatment in the BID group, 34 (79.1%) of 43 cephalic versions were obtained compared with 48 (55.2%) of 87 in the QD group ($P = .007$; RR, 1.43; 95% CI, 1.12-1.83).

During the second week of treatment, 15 additional cephalic versions were obtained in the QD group and only 1 additional version in the BID group. Thus, the following cephalic presentation results were observed on ultrasound examination at the end of the second week of treatment: 63 (72.4%) of 87 in the QD group and 35 (81.4%) of 43 in the BID group (nonsignificant difference). The same percentages were maintained to term.

Cesarean and Vaginal Deliveries

No statistically significant differences were found in the number of cesarean deliveries performed. In the intervention group, 46 cesarean deliveries (35.4% of births) were performed, 20 of which were with cephalic presentations and 26 of which were with breech presentations. The 20 cesarean deliveries in the cephalic presentations were performed for fetopelvic disproportion (14 cases), postterm pregnancy (3 cases), or fetal distress (3 cases). The 26 cesarean deliveries in the breech presentations were performed for PROM after week 37 (10 cases), large fetus (2 cases), fetal distress (1 case), oligohydramnios (2 cases), and unspecified causes (11 cases).

In the control group, 47 cesarean deliveries (36.2%) were performed, 21 of which were with cephalic presentations and 26 of which were with breech presentations. Indications for cesarean delivery in the subjects with cephalic fetuses included fetopelvic disproportion (11 cases, 1 of which was with oligohydramnios), fetal distress (4 cases, 1 of which was in a subject with toxemia of pregnancy), sacral rotation of the occiput (2 cases), placental insufficiency (1 case), toxemia of pregnancy (1 case), PROM (1 case), and deep transverse arrest (1 case). Cesarean deliveries in the breech presentations were performed

for PROM after 37 weeks (8 cases, 1 of which was with prolapse of the cord), oligohydramnios (3 cases), fetal distress (2 cases), large fetus (1 case), and unspecified causes (12 cases).

In both the intervention and control groups, cesarean delivery revealed 1 case of previously undiagnosed bicornuate uterus. In both cases, the presentation at birth was breech. Because they had been randomized, both cases were included in the statistical analysis of the data despite uterine malformations being exclusion criterion.

In regard to vaginal deliveries, the only significant difference between the 2 groups relates to the use of oxytocin, given to 7 (8.6%) of 81 subjects in the intervention group vs 25 (31.3%) of 80 in the control group (RR, 1.33 [95% CI, 1.13-1.56]; $P < .001$) before or during labor. In the intervention group, 2 vacuum-extractor and 1 forceps deliveries were performed and in the control group, 2 vacuum-extractor and 3 forceps deliveries were performed.

Apgar Scores

No neonates in the intervention group, but 7 in the control group, had Apgar scores of less than 7 at 5 minutes (Fisher exact test, $P = .006$). On grouping Apgar scores in the traditional manner, in the intervention group no neonates had Apgar scores less than 4 and 4 had scores 4 to 7; in the control group, 2 neonates had Apgar scores less than 4 and 12 had scores 4 to 7.

COMMENT

Moxibustion is a popular and much appreciated therapy for breech presentation in the People's Republic of China; thus, it would have been impossible to propose a "sham moxibustion" as a placebo for the control group.

Furthermore, moxibustion is a typical cheap, self-administered home therapy. This made blinding practically impossible. It was very difficult for investigators to persuade subjects to accept randomization and the consequent risk of having to do without the therapy. Consent was often obtained because of the availability of ECV later in pregnancy, but this is a much less popular and somewhat feared therapy; thus, only a few subjects, mostly belonging to the control group, opted for this solution.

Because the main results of the trial are of a qualitative type and were measured objectively (ultrasound), we believe that the lack of blinding and a placebo does not undermine the validity of the results. This is not entirely the case when considering fetal movement count, which was subjectively assessed.

The choice of sample (primigravidas at the 33rd week of gestation) appears to have been appropriate because the presentation did not change after the 35th week in any of the subjects (except for those undergoing ECV). This confirms the rarity of spontaneous fetal version (to either breech or cephalic presentation) among primigravidas after the 35th week.¹⁶

Two half-hour stimulations per day proved more effective in producing cephalic version than a single stimulation. On prolonging the therapy by 1 week in those cases in which cephalic version was not achieved, this difference in efficacy was partly, although not entirely, annulled. Of the 2 dosages, then, twice-daily stimulation is recommended because it did not reduce treatment compliance and had no adverse effects. Compliance with the treatment was by and large good.

In 2 cases, disorders serious enough to prompt discontinuation were observed during treatment. It was not clear whether these were adverse effects of the treatment.

No severe adverse events attributable to the treatment were observed and, in particular, there were no cases of intrauterine death or placental detachment. No cases of severe fetal anemia attributable to fetomaternal transfusion²⁰ were reported. The number of

PROMs was similar in both groups and the number of premature births was lower in the intervention group.

Moxibustion treatment did not reduce the rate of cesarean deliveries in a population in which elective cesarean delivery is not envisaged for breech presentations. On the other hand, it is possible that the significantly higher number of breech presentations at birth in the control group may have been a factor in bringing about worse Apgar scores.

The mechanism of action of moxibustion appears to be through increased AFMs, which proved significantly stronger in the treated subjects. Although a number of studies in China^{11,12,21} have investigated the neurologic path of stimulation by moxibustion and have shown evidence of its effect on maternal plasma cortisol and prostaglandins, we think that the mechanism of action of moxibustion is not entirely clear and warrants further research.

Further studies²² are needed to establish the efficacy and safety of moxibustion at more advanced gestational ages than those considered in this trial, as well as in second pregnancies or multigravidas and populations other than Chinese. Moreover, it is not clear whether moxibustion is more or less efficacious than ECV at term for obtaining cephalic presentation given the small number of subjects (nearly all belonging to the control group) who underwent ECV. Furthermore, since moxibustion and ECV must be performed at different gestational ages, we may regard them as complementary therapies to be used in succession. As we see it, if the results of this

trial are confirmed, moxibustion should be extensively used on account of its minimally invasive nature, low cost, and ease of execution. In fact, it is easy to train expectant mothers (either alone or with their partners) to administer the therapy at home. Further studies are also necessary to establish whether moxibustion treatment can reduce the rate of cesarean deliveries where these are used electively for breech presentation at birth.

Additional results regarding the effects of family history, fetal sex, cranial circumference, and leg position on the likelihood of cephalic version will be presented in a subsequent article.

On the basis of the results of the trial, moxibustion, when performed in primigravidas for 1 or 2 weeks starting in the 33rd week of pregnancy, has proved to be an effective therapy for inducing a significant increase in cephalic versions within 2 weeks of the start of therapy and in cephalic presentations at birth.

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Treatment of Irritable Bowel Syndrome With Chinese Herbal Medicine

A Randomized Controlled Trial

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Context.—Irritable bowel syndrome (IBS) is a common functional bowel disorder for which there is no reliable medical treatment.

Objective.—To determine whether Chinese herbal medicine (CHM) is of any benefit in the treatment of IBS.

Design.—Randomized, double-blind, placebo-controlled trial conducted during 1996 through 1997.

Setting.—Patients were recruited through 2 teaching hospitals and 5 private practices of gastroenterologists, and received CHM in 3 Chinese herbal clinics.

Patients.—A total of 116 patients who fulfilled the Rome criteria, an established standard for diagnosis of IBS.

Intervention.—Patients were randomly allocated to 1 of 3 treatment groups: individualized Chinese herbal formulations ($n = 38$), a standard Chinese herbal formulation ($n = 43$), or placebo ($n = 35$). Patients received 5 capsules 3 times daily for 16 weeks and were evaluated regularly by a traditional Chinese herbalist and by a gastroenterologist. Patients, gastroenterologists, and herbalists were all blinded to treatment group.

Main Outcome Measures.—Change in total bowel symptom scale scores and global improvement assessed by patients and gastroenterologists and change in the degree of interference in life caused by IBS symptoms assessed by patients.

Results.—Compared with patients in the placebo group, patients in the active treatment groups (standard and individualized CHM) had significant improvement in bowel symptom scores as rated by patients ($P = .03$) and by gastroenterologists ($P = .001$), and significant global improvement as rated by patients ($P = .007$) and by gastroenterologists ($P = .002$). Patients reported that treatment significantly reduced the degree of interference with life caused by IBS symptoms ($P = .03$). Chinese herbal formulations individually tailored to the patient proved no more effective than standard CHM treatment. On follow-up 14 weeks after completion of treatment, only the individualized CHM treatment group maintained improvement.

Conclusion.—Chinese herbal formulations appear to offer improvement in symptoms for some patients with IBS.

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IRRITABLE BOWEL syndrome (IBS) is a common functional bowel disorder that accounts for a significant proportion of patients seen in gastroenterology offices¹ and is characterized by chronic or recurrent abdominal pain and disturbed defecation. Studies in the United States

and Australia suggest that between 10% and 20% of the population have this disorder.²⁻⁵ No single available treatment is reliably effective for this condition,^{6,7} and patients use a variety of approaches for symptom management, including drugs, dietary modifications, and counseling.

To date, no strong scientific evidence available supports the use of Chinese herbal agents in IBS.⁸ However, CHM has been used for centuries in the treatment of functional bowel disorders and is routinely used for this purpose in China. Several Chinese studies have suggested the potential effectiveness of CHM for treatment of IBS, although these have all lacked rigor in clinical trial protocol⁹⁻¹³ and have had poor randomization techniques and lack of blinding.⁸

According to the fundamental principles of traditional Chinese medicine, treatment should be tailored to the individual clinical presentation of patients, even though they all may have the same medical diagnosis.^{8,14,15} Furthermore, treatment needs to be modified at different stages of the patient's illness or recovery. In this study, we evaluated the effectiveness of CHM in the treatment of IBS. We compared individualized therapy against a standard Chinese herbal formulation for IBS and a placebo using a randomized, double-blind, placebo-controlled study design.

METHODS

Setting and Patients

Patients were recruited from gastroenterology units in 2 teaching hospitals in Sydney, Australia, and through 5 private practices of gastroenterologists. After patient screening and subsequent review in these centers, patients' conditions were further diagnosed (according to Chinese medicine principles) and treated in 3 Chinese herbal clinics by 3 Chinese medicine practitioners.

A clinical trial notification was filed with the Therapeutic Goods Administration, Commonwealth Department of Health, Housing, Local Government and Community Services, Canberra, Australia. All herbal substances used in this trial were listed with the Australian Therapeutic Goods Administration, have been acknowledged as suitable for human consumption, and were administered within standard dosage levels. All herbs used in this trial are available over-the-counter throughout Australia. No product used in this trial was a controlled substance, animal product, or endangered species. The trial protocol was approved by the ethics committee of the University of Western Sydney Macarthur and the ethics committees of the 2 participating hospitals.

Patients between the ages of 18 and 75 years (inclusive) were screened by a gastroenterologist. Screening involved a routine clinical workup for IBS with diagnostic tests as determined appropriate by the specialist. Patients were assessed according to the Rome criteria, an estab-

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Table 1.—Inclusion and Exclusion Criteria

Inclusion Criteria	
Age, 18-75 y inclusive	
Colonic evaluation (colonoscopy or barium enema) within the previous 5 years (for 18-60 y) or within the previous 3 y (for 61-75 y)	
Irritable bowel syndrome by Rome Criteria	
At least 3 mo of continuous or recurrent symptoms of:	
Abdominal pain or discomfort with at least some discomfort present within the last 2 wk; and ≥ 2 of the following on at least a quarter of occasions or days	
Abdominal distention that is visible or felt by tight clothing	
Pain relief with bowel action	
More frequent stools with onset of pain	
Looser stools with onset of pain	
Mucous in stools	
Feeling of incomplete evacuation	
At least 1 marking on the visual analog scales for IBS symptoms to be at least 20 mm from the "not present" end of the scale	
Normal liver function test and full blood cell count and urea and creatinine levels (within the last 2 wk)	
Exclusion Criteria	
Pregnancy or breast-feeding	
Liver disease	
Medications: anticholinergics, lactulose, smooth muscle relaxants, motility stimulants, and/or antidepressants. Use of these is accepted provided patient is still symptomatic for IBS, medications have been used for 3 mo, and effects of medications are stable	
Current alcoholism or drug abuse	
Current psychiatric illness or dementia	
Allergies to food additives	
Lactose intolerance—no obvious clinical indications	
Inflammatory bowel disease (ulcerative colitis, Crohn disease)	
Gastric and duodenal ulcers	
Cancers of the gastrointestinal tract	
Celiac disease	
Diabetes mellitus	

lished standard for diagnosis of IBS.^{16,17} If diarrhea was a prominent symptom, lactose intolerance was excluded by hydrogen breath testing or during a 2-week lactose exclusion period. The inclusion and exclusion criteria are shown in Table 1. Written informed consent was obtained from all patients before entering the trial. Patients were free to withdraw from the study at any time.

Treatment Schedule

After initial gastroenterological screening (week 0), all patients entered a 2-week run-in period. A Bowel Symptom Scale (BSS) was completed at the beginning and end of the 2-week period to assess measurement reliability and to account for any degree of improvement based simply on admission to the trial. Patients were seen on specified days by 1 of 3 herbalists during the trial period and were not permitted to change herbalist during the course of the treatment. The first consultation with the Chinese herbalist occurred at week 2, at which time the patient was randomized (by an assistant) to placebo, standard CHM, or individualized CHM treatment. The patient was re-evaluated by the Chinese herbalist at 2-week intervals for 2 occasions and then at

Table 2.—Standard Formula (Capsule Ingredients)*

Chinese Name	Pharmaceutical Name	Powdered %
Dang Shen	<i>Codonopsis pilosulae, radix</i>	7
Huo Xiang	<i>Agastaches seu pogostami, herba</i>	4.5
Fang Feng	<i>Ledebouriales aesioidis, radix</i>	3
Yi Yi Ren	<i>Cocis lachryma-jobi, semen</i>	7
Chai Hu	<i>Bupleurum chinense</i>	4.5
Yin Chen	<i>Artemisiae capillaris, herba</i>	13
Bai Zhu	<i>Atractylodis macrocephalae, rhizoma</i>	9
Hou Po	<i>Magnoliae officinalis, cortex</i>	4.5
Chen Pi	<i>Citri reticulatae, pericarpium</i>	3
Pao Jiang	<i>Zingiberis officinalis, rhizoma</i>	4.5
Qin Pi	<i>Fraxini, cortex</i>	4.5
Fu Ling	<i>Poriae cocos, sclerotium (Hoelen)</i>	4.5
Bai Zhi	<i>Angelicae dahuricae, radix</i>	2
Che Qian Zi	<i>Plantaginis, semen</i>	4.5
Huang Bai	<i>Phellodendri, cortex</i>	4.5
Zhi Gan Cao	<i>Glycyrrhizae uralensis, radix</i>	4.5
Bai Shao	<i>Paeoniae lactiflorae, radix</i>	3
Mu Xiang	<i>Saussureae seu vladimirae, radix</i>	3
Huang Lian	<i>Coptidis, rhizoma</i>	3
Wu Wei Zi	<i>Schisandrae, fructus</i>	7

*Pharmaceutical terminology from Hsu.¹⁸

monthly intervals for 2 further occasions. Continuous treatment was administered for 16 weeks. No special instructions were given to patients regarding diet, other than to continue consumption of foods they felt comfortable with and to avoid foods known to cause them gastrointestinal tract irritation. All patients were evaluated by their gastroenterologist after 8 weeks of treatment and again at the end of the 16-week treatment period. Patients were closely monitored for any adverse effects or worsening of symptoms. Liver function tests were performed after 8 weeks of treatment. Follow-up questionnaires were sent to all patients 14 weeks after completion of the treatment period. Treatment codes were broken and revealed to patients only after completion of the follow-up questionnaires.

Randomization

Randomization was done by selection of a sealed envelope from a closed bag. Seventy sealed envelopes were prepared for each of the standard and individualized groups, and 60 envelopes were prepared for the placebo group. Patients were aware that there was a greater chance of receiving active treatment. Success in blinding was evaluated using a treatment credibility scale administered during the trial.

Herbal Preparation and Dispensing

All herbs were administered in the dried powdered form and encapsulated. A period of preparation was required before commencement of the trial to develop a suitable dispensary of 81 individual dried powdered Chinese herbs for dispensing to patients in the individualized treatment group. The standard

herbal formulation was designed by Chinese herbalists and prepared by the principal supplier, Mei Yu Imports, Sydney, Australia (Table 2).¹⁸ The placebo preparation was prepared and encapsulated by a pharmaceutical contractor and was designed to taste, smell, and look similar to a Chinese herb formula. After testing on 5 independent volunteers, the placebo was deemed indistinguishable from raw powdered Chinese herbs. All herbs and the placebo formulation were supplied in the same opaque capsules. Patients in all 3 groups were required to take 5 capsules 3 times daily.

After consulting with the Chinese herbalist, all patients were required to complete a series of questionnaires and wait 30 minutes for the preparation of their capsules. The wait time was used to avoid patients identifying whether they were receiving prepared capsules (standard or placebo) or individualized formulations that were made at the treatment center. All medication preparation occurred in a closed room by assistants who were restricted from contact with the patients. Treatment codes were held by these assistants and by the chief investigator (A.B.). A blinded primary research assistant managed all the questionnaires and was responsible for giving the capsules to the patients. All patients were treated in an equivalent fashion. Compliance was assessed by an item included in the BSS and by pill count.

Measurement Instruments

The BSS was used to assess change in IBS symptoms during the course of the treatment. The BSS consists of 100-mm visual analog scales related to a symptom of IBS (pain/discomfort, bloat-

ing, constipation, and diarrhea) and an overall severity scale. Patients and gastroenterologists completed this scale independently at the beginning and end of the treatment period. Patients also were monitored during the course of the trial using this scale. The BSS also included items for assessing rate of stool passage, rating the degree to which IBS symptoms interfered with life activities, and recording changes in medications usage and fiber consumption. To assess the success of patient blinding, a brief questionnaire was administered to patients after 2, 4, 10, and 16 weeks of treatment. This 4-item scale has been used to test credibility of different forms of psychological treatment¹⁹ but also has been successfully used in acupuncture trials and shown to have good internal consistency and test-retest reliability.^{20,21}

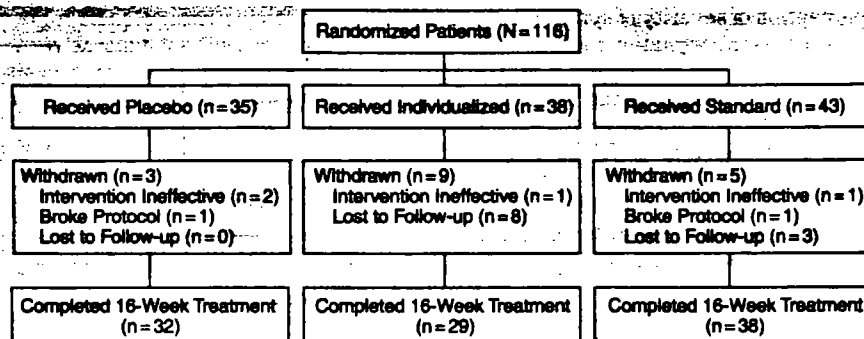
Statistical Analysis

Pearson product moment correlation was used in the analysis of reliability and validity data, and factor analysis was used to determine construct validity of the credibility scale. Outcome measures with categorical responses were analyzed using χ^2 and Fisher exact tests. For the BSS, analysis of variance was used to determine the differences among groups at baseline, end of treatment, and follow-up. All *P* values were 2-tailed, unless otherwise indicated, and the α level of significance was set at .05. Missing scale and item scores were not replaced. Data are presented according to an intention-to-treat protocol, in which patients who withdrew from the trial were recorded as having worsened (if appropriate) for categorical items only. Data for all other outcome measures are presented as per protocol analysis.

There were no reliable data that could be used to accurately predict the anticipated effect size between placebo, standard, and individualized treatment groups. We estimated that for adequate power (80%) to detect a 20% difference on the BSS scores at the $\alpha = .05$ level (1-tailed test), 35 patients were needed in each group.

RESULTS

A total of 116 subjects were recruited during an 18-month period: 35 were randomized into the placebo group, 43 into the standard group, and 38 into the individualized treatment group (Figure). Fifteen patients withdrew during the 4-month course of the trial, and 2 patients were withdrawn from the trial for commencing a variety of relevant medications during the treatment period. Patient data on study entry are shown in Table 3. Patient groups were similar in terms of age, weight, and sex distributions. There were



Patient progress through stages of the trial.

Table 3.—Patient Population Characteristics Before Treatment and Mean Total Bowel Symptom Scores*

Variables	Group, No. (SD)			<i>P</i> Values
	Placebo (n = 35)	Standard (n = 43)	Individualized (n = 38)	
Characteristic				
Weight, kg	72.1 (12.8)	68.7 (16.8)	69.1 (14.4)	.29
Age, y	45.0 (13.9)	47.6 (15.1)	47.4 (13.4)	.68
Sex ratio (male:female)	0.46	0.65	0.52	.75
Baseline data				
Gastroenterologist total BSS score	182.7 (65.4)	172.2 (72.6)	166.6 (63.6)	.59
Patient total BSS score	191.2 (69.4)	189.7 (64.8)	178.5 (69.8)	.67
End of treatment				
Gastroenterologist total BSS score	147.2 (86.6) (n = 30)	70.9 (63.2) (n = 35)	100.4 (83.6) (n = 25)	.001
Patient total BSS score	150.0 (81.6) (n = 32)	106.1 (73.7) (n = 38)	103.0 (74.7) (n = 29)	.03
At follow-up 14 weeks after study completion				
Patient total BSS score	155.7 (84.2) (n = 18)	132.6 (90.2) (n = 35)	99.4 (74.8) (n = 24)	.10

*Data are reported by patients and gastroenterologists at start and end of treatment period and at follow-up. BSS indicates Bowel Symptom Scale.

no significant differences among patients in the 3 groups in terms of total severity of symptoms as judged independently by both the patient and gastroenterologist, or in duration of the disease as reported by patients. Patients allocated to the placebo group had a higher mean score for constipation, while patients allocated to the standard treatment had a higher mean score for diarrhea. Compliance with study medication was high as measured by a questionnaire item and by random pill counts and did not differ between groups (95% for standard CHM, 94% for individualized CHM, and 95% for placebo). Fiber and nonstudy medication consumption did not change significantly for any group during the treatment period.

Reliability and Validity Testing

The reliability of the BSS (ie, consistency of the measure) was determined by a test-retest assessment during the run-in period prior to treatment commencing (week 0-2). Correlation between the BSS completed during the initial interview with the gastroenterologist and then 2 weeks later at the

clinical treatment centers was high for total score ($r = 0.7$; $P < .01$, 2-tailed) and for each individual symptom (bloating [$r = 0.8$], pain [$r = 0.6$], diarrhea [$r = 0.8$], and constipation [$r = 0.7$]).

The credibility scale also was examined for test-retest reliability. Correlation between the first and second administration of this scale was significant ($r = 0.6$; $P < .01$, 2-tailed). The correlation coefficients for each of the 4 scale items were in the range of 0.47 to 0.65. The internal consistency of the credibility scale based on interitem correlations on both occasions were uniformly high and Cronbach coefficient α (representing average interitem correlations) was .87 and .86 for the first and second occasions, respectively.

The visual analog scales within the BSS had high face validity (100-mm lines with severity marked at the extreme right and absence of symptom marked at the extreme left) and have high content validity (ie, they incorporate the key domains of interest—pain and discomfort, bloating, constipation, and diarrhea). Testing items in the scale for concurrent validity at the commencement and end of treatment showed that the gastroenterologist's assessment of the patient

correlated highly with the patient's own perception of severity of symptoms. For both, Pearson correlation coefficient was in the range of $r = -0.63$ to 0.84 for any 1 item (symptom) or for the total symptom score ($P < .01$ on all occasions).

Assessment of the credibility scale for construct validity through a principal components factor analysis based on the first administration revealed only 1 factor with an eigenvalue greater than 1 (2.89). This factor accounted for 72.2% of variance in this data set. All items had a high correlation with this first factor, suggesting satisfactory construct validity.

Main Outcome Measures

For all 5 main outcome measures—total mean BSS scores and global improvement as assessed by patients and gastroenterologists, and interference with life as assessed by patients—patients receiving the standard CHM formulation responded significantly better than patients in receiving placebo. Patients receiving individualized CHM treatment also responded significantly better on 4 of 5 scores than patients receiving placebo. Overall, patients receiving individualized CHM fared slightly worse than those receiving standard CHM treatment.

At the end of treatment, there was a significant difference between the mean total BSS scores as assessed by patients, with patients in the standard CHM group and those in the individualized CHM group responding significantly better compared with placebo (Table 3). No significant differences were noted between standard and individualized CHM treatment groups.

The BSS scores completed by the gastroenterologist at the end of treatment showed a significant difference between the mean total BSS scores for patients in each group, with patients receiving standard and individualized CHM responding significantly better compared with those taking placebo ($P = .001$). A post hoc Bonferroni test demonstrated that this difference was significant for patients in the standard group ($P = .001$) but not for those in the individualized group ($P = .08$).

Patients receiving standard herbal formulations improved by 44% (according to patients) and 59% (according to gastroenterologists), in contrast to patients in the placebo group who improved 22% (according to patients) and 19% (according to gastroenterologists). Patients receiving individualized CHM improved by 42% (according to patients) and 40% (according to gastroenterologists).

There was a significant association between the treatment groups and the change in the degree to which IBS symp-

Table 4.—Perception of Improvement by Treatment Group*

Compared With Before Trial	Group, No. (%)			P Value
	Placebo	Standard	Individualized	
Patient rating of response				
Improved	11 (33)	29 (76)	18 (64)	.007
Stayed the same	19 (57)	13 (21)	8 (29)	
Worsened	8 (9)	1 (3)	2 (7)	
Gastroenterologist rating of response				
Improved	19 (30)	29 (78)	15 (50)	.002
Stayed the same	19 (63)	7 (19)	12 (40)	
Worsened	2 (7)	1 (3)	3 (10)	

*Group differences calculated by using χ^2 .

toms caused interference with life and activities by the end of treatment ($P = .03$). Of patients receiving the standard formulation and of those receiving individual formulations, 63% and 54%, respectively, stated that treatment resulted in IBS causing less interference in their lives and activities, compared with 37% of patients in the placebo group.

At the end of the trial, the ratings of both gastroenterologists and patients who believed that the IBS symptoms had improved, stayed the same, or worsened (Table 4) showed a significant association by treatment group ($P = .007$). Of patients receiving standard CHM and of those receiving individual CHM, 76% and 64%, respectively, stated they had improved during treatment. In contrast, only 33% of patients receiving placebo stated they had improved during treatment.

The gastroenterologists' responses also demonstrated a significant association between the treatment group and how patients felt at the end of treatment ($\chi^2 = 17.1$; $P = .002$). Seventy-eight percent of patients receiving the standard CHM formulation, 50% of those receiving individual CHM, and 30% of those receiving placebo were judged by the gastroenterologist as having improved during treatment. There was significant correlation between patients' and gastroenterologists' assessment of global improvement and of total BSS scores at the beginning and end of the trial (all $r > 0.5$, all significant to $P \leq .01$ level, 2-tailed).

Adverse Effects

Two patients withdrew from the trial because of discomfort associated with the treatment. One patient developed upper gastrointestinal discomfort while taking the standard CHM formulation. A second patient developed headaches (although a history of headaches existed), which gradually subsided on discontinuation of therapy. Recommencement of treatment caused gastrointestinal discomfort, and the patient was subsequently withdrawn from the study. No other major adverse effects were noted. Liver function tests ob-

tained after 8 weeks of treatment showed no abnormal values.

Follow-up Assessment

Results of the BSS administered to patients 14 weeks after completion of the course of treatment (but before treatment codes were revealed) demonstrated that the treatment effect weakened, with only the individualized CHM group maintaining improvement ($P < .10$) (Table 3). However, there was significant association between the treatment group and how patients felt at the 14-week follow-up ($P = .02$). Of patients who had received the standard CHM formulation and of those who had received individual CHM formulations, 63% and 75%, respectively, stated that they still felt an improvement compared with 32% of patients who received placebo.

Blinding

The success of blinding patients to treatment was tested at the beginning, end, and on 2 other occasions during the course of treatment. At 2 weeks into treatment, the overall mean on this 6-point scale was 4, indicating that patients on average viewed CHM as only moderately credible and were not a self-selected group with a bias in favor of complementary medicine. No significant difference was noted between groups at outset and at end of treatment. However, the mean credibility score decreased slightly with time for the placebo group and remained strong within the standard CHM group. Since the standard CHM treatment proved the most effective, the increased difference in credibility toward the end of the treatment may be a reflection that this group of patients was receiving the most benefit. There was a significant negative correlation between the final credibility score and the final patient-rated BSS score ($r = -0.43$; $P < .01$) and the final gastroenterologist-rated BSS score ($r = -0.58$; $P < .01$).

COMMENT

To our knowledge, this is the first clinical trial in CHM that fully adheres to the

traditional Chinese diagnostic treatment processes while using a strict and accepted methodological protocol. Our study demonstrated that CHM is effective in the management of symptoms related to IBS with, in some cases, effects lasting up to 14 weeks after completion of treatment. Patients receiving standard or individualized CHM treatment demonstrated significantly better outcomes (both clinically and statistically) than patients receiving the placebo on all 5 key outcome measures. However, patients receiving individualized CHM formulations had less improvement during treatment than patients receiving the standard formula, although this difference was not statistically significant.

The first null hypothesis that CHM treatment of IBS with a standard herbal formula is of no value is rejected. The second null hypothesis that individualized treatment of IBS according to the principles of traditional CHM is of no added value to treatment with a standard formula is partially accepted. While there were no significant differences between patients receiving standard or individualized treatment at the end of the treatment period, on follow-up, patients in the individualized treatment group had maintained more substantial improvement.

Three Chinese herbalists with contrasting Chinese medicine education backgrounds participated in this trial. In theory, their degree of education in Chinese herbalism should affect their ability to successfully tailor treatment for patients. While outcome differences between practitioners were observable for this cohort of patients, sample sizes were too small to make reliable conclusions. Furthermore, the overall differences between standard and individualized CHM may be relatively small (as both

are active treatments) and may require larger sample sizes. This does not, however, account for the notable improvement that was maintained in the individualized CHM group after cessation of treatment.

One plausible explanation may be that the standard CHM formulation was suitably designed to treat the complex presentations of IBS but was incapable of successfully dealing with underlying causes for most patients as viewed by Chinese medicine. The tailored formulations may have permitted the herbalists to individually address these underlying causes and deficiencies. Moreover, there may be active ingredients in the CHM formulation with properties similar to antispasmodic or anxiolytic drugs. Chinese herbal formulas are complex and viewed as a number of active ingredients working together, rather than 1 specific active substance. The standard formulation used in this study is not a sedative or anxiolytic preparation in traditional CHM terms but is a formulation considered to regulate and strengthen bowel function.

In our study, all efforts were made for the approach in the 3 treatment groups to be indistinguishable. The credibility scale was demonstrated to be a reliable and valid instrument and presents strong evidence that blinding was maintained throughout the trial. The slight decrease in credibility score seen in the placebo group toward the end of the trial was accounted for by its significant correlation with the actual treatment outcome. The authors are convinced that patients, herbalists, and gastroenterologists were all successfully blinded.

There were minimal adverse effects reported during the study. Liver function screening was included as a precaution because liver dysfunction associated

with the use of Chinese herbs has been noted in other studies.²² Liver dysfunction was not expected with the type and form of herbs used in this study. In our study, liver function was reassessed after 8 weeks of treatment. We have no data on liver function after that time, and therefore cannot comment on longer-term safety of these CHM products. Raw herbs used as starting products are partly regulated in Australia.

We conclude that Chinese herbal formulations may offer symptom improvement to some patients with IBS. In this randomized, double-blinded, placebo-controlled trial CHM was shown to be effective in the management of IBS. Patients receiving the standard CHM formulation fared best during the course of treatment, while patients receiving the individualized treatments found that the benefit gained lasted beyond the treatment period. Although not all patients responded to this therapy, our findings support the consideration of further investigation of Chinese herbal medicine as a treatment option for IBS.

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Acupuncture and Amitriptyline for Pain Due to HIV-Related Peripheral Neuropathy

A Randomized Controlled Trial

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Context.—Peripheral neuropathy is common in persons infected with the human immunodeficiency virus (HIV) but few data on symptomatic treatment are available.

Objective.—To evaluate the efficacy of a standardized acupuncture regimen (SAR) and amitriptyline hydrochloride for the relief of pain due to HIV-related peripheral neuropathy in HIV-infected patients.

Design.—Randomized, placebo-controlled, multicenter clinical trial. Each site enrolled patients into 1 of the following 3 options: (1) a modified double-blind 2 × 2 factorial design of SAR, amitriptyline, or the combination compared with placebo, (2) a modified double-blind design of an SAR vs control points, or (3) a double-blind design of amitriptyline vs placebo.

Setting.—Terry Bein Community Programs for Clinical Research on AIDS (HIV primary care providers) in 10 US cities.

Patients.—Patients with HIV-associated, symptomatic, lower-extremity peripheral neuropathy. Of 250 patients enrolled, 239 were in the acupuncture comparison (125 in the factorial option and 114 in the SAR option vs control points option), and 136 patients were in the amitriptyline comparison (125 in the factorial option and 11 in amitriptyline option vs placebo option).

Interventions.—Standardized acupuncture regimen vs control points, amitriptyline (75 mg/d) vs placebo, or both for 14 weeks.

Main Outcome Measure.—Changes in mean pain scores at 6 and 14 weeks, using a pain scale ranging from 0.0 (no pain) to 1.75 (extremely intense), recorded daily.

Results.—Patients in all 4 groups showed reduction in mean pain scores at 6 and 14 weeks compared with baseline values. For both the acupuncture and amitriptyline comparisons, changes in pain score were not significantly different between the 2 groups. At 6 weeks, the estimated difference in pain reduction for patients in the SAR group compared with those in the control points group (a negative value indicates a greater reduction for the "active" treatment) was 0.01 (95% confidence interval [CI], -0.11 to 0.12; $P = .88$) and for patients in the amitriptyline group vs those in the placebo group was -0.07 (95% CI, -0.22 to 0.08; $P = .38$). At 14 weeks, the difference for those in the SAR group compared with those in the control points group was -0.08 (95% CI, -0.21 to 0.06; $P = .26$) and for amitriptyline compared with placebo was 0.00 (95% CI, -0.18 to 0.19; $P = .99$).

Conclusions.—In this study, neither acupuncture nor amitriptyline was more effective than placebo in relieving pain caused by HIV-related peripheral neuropathy.

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PERIPHERAL NEUROPATHIES are diagnosed in 30% to 35% of patients with human immunodeficiency virus (HIV) and cause pain and dysesthesias.^{1,2} Symptomatic treatment includes antidepressants, nonnarcotic and narcotic analgesics, anticonvulsants, and acupuncture.^{2,3} The use of these treatments is based on anecdotal information and trials in other disease conditions.⁵

We chose to examine the efficacy of 2 commonly used treatments, amitriptyline hydrochloride and acupuncture, for HIV-related peripheral neuropathy. Amitriptyline is frequently prescribed for neuropathic pain and has been shown to be an effective treatment for diabetic, hereditary, toxic, and idiopathic neuropathies.^{6,7}

Although several trials that reported examining acupuncture for chronic painful conditions claim efficacy,^{8,9} these studies have methodological limitations, including small sample sizes and inadequate controls for the nonspecific effects of acupuncture.⁹⁻¹¹ Meta-analyses of studies of acupuncture for chronic pain show a response rate of approximately 70% for acupuncture, 50% for "sham" acupuncture (needling points not considered effective), and 30% for control treatments, such as sham transcutaneous electrical nerve stimulation.^{9,10,12,13}

To evaluate the effect of both a non-standard and standard medical therapy for peripheral neuropathy, we performed a multicenter, modified double-blind, randomized, placebo-controlled study of the separate and combined efficacy of a standardized acupuncture regimen (SAR) and amitriptyline for the relief of pain caused by HIV-related peripheral neuropathy.

METHODS

Study Design

We used a 2 × 2 factorial design to determine whether SAR, amitriptyline, or the combination was more effective than placebo. The SAR consisted of acupuncture points chosen by the study acupuncturists and several consultants to be effective for peripheral neuropathic pain. This regimen was compared with control points that were not "true" points defined by any standard acupuncture text¹⁴ (Figure 1). We compared the efficacy of amitriptyline with placebo capsules of identical appearance. Enrollment in the factorial design began in May 1993, but patients at some sites were re-

- * Standardized Acupuncture Regimen
- † Supplemental Acupuncture Points
- ‡ Control Points

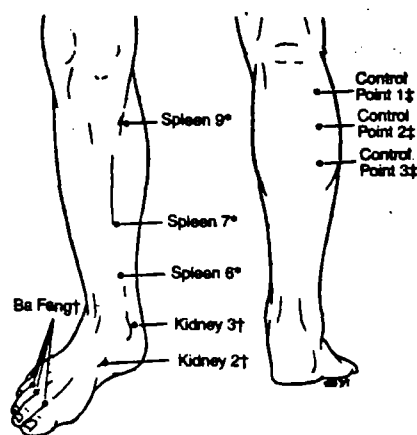


Figure 1.—Standardized acupuncture regimen and control points.

luctant to be randomized to receive amitriptyline and some clinicians were unwilling to provide amitriptyline to their patients because it was a commonly abused drug in their communities. The study design was modified in March 1995 so that sites could choose only 1 of 3 options. Each site could (1) continue to enroll into the factorial design (factorial option), (2) enroll into a single-factor design of SAR vs control points (acupuncture option), or (3) enroll into a single-factor design of amitriptyline vs placebo (amitriptyline option) (Figure 2).

Randomization schedules were prepared using random blocks stratified by unit. Patients were randomized to treatment by the study units by telephoning the Statistical Center at the University of Minnesota, Minneapolis. The unit pharmacists were the only people unblinded to the placebo vs amitriptyline assignment, and the acupuncturists were the only people unblinded to the SAR vs control points assignments. The pain diaries and the assessments of pain relief were collected by study staff who were blinded to the treatment assignments.

Study Population

Patients were recruited from 11 units of the Terry Bein Community Programs for Clinical Research on AIDS, an organization sponsored by the National Institutes of Health, which conducts clinical trials in primary care settings. The study was approved by each institutional review board. All participants gave written informed consent. To be eligible, participants had to be aged 13 years or older; have documented HIV infection; have symptoms of HIV-related lower extremity peripheral neuropathy, diagnosed by

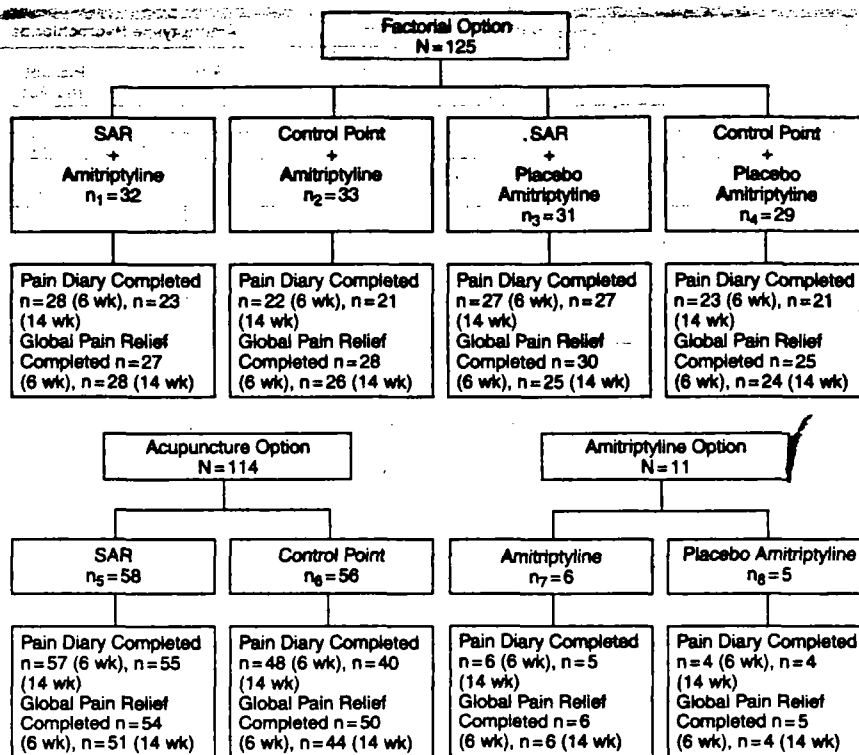


Figure 2.—The standardized acupuncture regimen (SAR) vs control points (CPs) compares n₁ + n₃ + n₅ with n₂ + n₄ + n₆. The amitriptyline vs placebo compares n₁ + n₂ + n₇ with n₃ + n₄ + n₈.

a physician based on history and clinical examination; and have completed a baseline pain diary prior to randomization. Antiretroviral therapy was allowed and dosages of analgesic medication or herbal therapies used at randomization were maintained or reduced. The initiation of new treatments during the study was discouraged but allowed when necessary. Patients were excluded if they were being treated for an acute opportunistic infection or malignancy except nonsystemic Kaposi sarcoma, were pregnant, or had taken a tricyclic antidepressant or monoamine oxidase inhibitor 2 weeks before randomization.

Treatment Regimens

For the acupuncture comparison, patients were randomly assigned to receive SAR or control points twice weekly during a 6-week induction phase, followed by weekly treatment during an 8-week maintenance phase. This SAR was based on a Chinese theory that peripheral neuropathy caused by diabetes and HIV-related peripheral neuropathy have similar mechanisms. The SAR included spleen points 9, 7, and 6, with the additional supplemental points of Ba Feng (M-LE-8) for complaints of pain or numbness in the toes, Ran Gu (kidney 2) for complaints of pain or numbness in the soles, and Tai Ki (kidney 3) for complaints of pain or numbness in the heel (Figure 1).¹⁴ The

control points were located on the back of the leg (Figure 1). For the SAR and control points, acupuncture needles were inserted to a specified depth. Each location was manipulated both superiorly and inferiorly. Then the needles were reinserted into the specified point. After 10 to 15 minutes, the needles were remanipulated and replaced into the original location for another 5 to 10 minutes. The depth of insertion was between 1.28 to 2.54 cm (0.5 to 1.0 in) for spleen point 9, 2.54 to 3.81 cm (1.0 to 1.5 in) for spleen point 7, and 1.5 to 3.05 cm (0.6 to 1.2 in) for spleen point 6. For the control points, insertion was less than 1.28 cm (0.5 in). Study acupuncturists received standardized training in the technique. In addition, a videotape of the acupuncture and the control treatment was provided to each of the acupuncturists in the study. To maintain blinding and to determine the need for supplemental points, the acupuncturists asked all patients a series of standard questions, irrespective of treatment arm. For those in the SAR group, spleen points 9, 7, and 6 were always used. Supplemental acupuncture points were used only if the patient answered "yes" to the corresponding question. The control points consisted of only 3 specified points.

For the amitriptyline comparison, the patients were randomized to receive a 14-week course of either amitriptyline or placebo capsules by mouth once a day.

Table 1.— Characteristics of Study Participants*

Characteristics	Acupuncture		Amitriptyline Hydrochloride	
	SAR (n = 121)	Control Points (n = 118)	Active (n = 71)	Placebo (n = 65)
Age, mean (SD), y	40.9 (6.6)	41.7 (8.3)	40.1 (7.1)	39.9 (5.9)
Sex, % male	88	82	84	88
Race, %				
Latino/Hispanic	52	46	11	42
Black	30	39	28	22
White	55	61	58	63
Other	3	4	3	3
Baseline pain score, mean (SD)	1.11 (0.3)	1.06 (0.4)	1.10 (0.3)	1.13 (0.3)
Karnofsky score, mean (SD)	84.5 (11.7)	84.7 (11.0)	83.7 (11.5)	83.1 (10.2)
<80, %	21	19	24	15
Disease progression history, %†	53	47	62	48
Current use of antiretrovirals, %	61	65	58	57
Current use of pain medications, %	48	46	47	54
Type of pain, %‡				
Aching/cramping	41	45	51	40
Burning/heat	35	30	28	35
Throbbing	23	22	27	12
Stabbing/sharp	36	36	35	39
Numbness/tingling	68	87	69	66
Other	24	22	30	22

*SAR indicates standardized acupuncture regimen. Values are mean percentage unless otherwise indicated.

†Defined as history of an opportunistic infection or malignancy.

‡These categories are not mutually exclusive.

They were instructed to take them between 1 to 2 hours before bedtime. An initial daily dose of 25 mg of amitriptyline hydrochloride was increased every 2 to 3 days until a maximum dosage of 75 mg/d was reached.^{15,16} The placebo capsules were identical in appearance and taste to the active capsules. Patients were followed up for the 14-week study period and for adverse event monitoring for an additional 8 weeks after the study treatment had discontinued.

Results were monitored by the HIV Therapeutic Trials Data Safety and Monitoring Board of the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. Data monitoring used the Lan-De Mets method¹⁷ as a guideline for early stopping to account for increased type I error probability by examining the data before the designed study end.

Evaluation

Patients rated their pain in a diary once daily, choosing from the Gracely scale of 13 words that describe the intensity.¹⁸ The scale ranges from no pain (0.0), weak (0.45), mild (0.74), moderate (1.09), strong (1.36), to extremely intense (1.75). The words had been assigned magnitudes on the basis of ratio-scaling procedures that demonstrated internal consistency, reliability, and objectivity.¹⁸ The scale has distinguished active from control interventions in experimental and clinical pain studies.^{6,18,19} At the end of both the induction and maintenance phases, patients reported their global pain relief (complete, a lot, moderate, slight, none, or worse)

after they were asked the following question: "Since the beginning of the study, how would you rate the relief of pain and/or discomfort in your legs and feet?" A study physician, trained in neurologic examination, tested the patient at randomization and at 14 weeks. A neurologic summary score was computed as an average of 3 separate scores for muscle strength, sensory ability, and reflex. Each physician who performed the neurologic assessment reviewed a videotape that detailed how the examination was to be completed. The patients also completed a self-administered, 39-item, quality-of-life assessment tool.²⁰ The complete tool, consisting of 11 different dimensions, was administered at baseline and 14 weeks, and the dimension corresponding to physical functioning was also administered at 6 weeks. To assess the effectiveness of the blinding, all patients were asked to guess their treatment assignments at 14 weeks. Patients were monitored for grade 4 adverse events and death. Adverse experiences occurring within 8 weeks of study treatment were graded on a 5-point severity scale (grade 5 corresponding to death) according to a standardized toxicity scale. Any grade 4 or 5 event was reportable irrespective of presumed relationship to study treatment.

Statistical Analysis

Comparison of treatment groups for the primary end point of change in pain, as measured by the pain diary, used a linear model with baseline characteristics, clinical unit, and option (factorial or single

factor) as covariates. If the average weekly pain score for the sixth week of treatment was present, it was used. If it was missing, the closest weekly average within the 6-week visit window of 4 to 10 weeks was used. Similarly, this was done for the 14-week end point and the visit window of 11 to 16 weeks. A linear repeated measures analysis of the pain averages was also performed, with the same explanatory variables.²¹ Estimates of the difference between SAR and control points were calculated for each of the 14 weeks. The global pain relief rating was analyzed using a log-linear model, with likelihood ratio tests for difference among treatment groups, which were adjusted for option.²²

We verified that results from the 3 treatments could be pooled by checking that the interaction term between acupuncture and amitriptyline in the factorial option and the option by treatment interaction were nonsignificant.

Secondary outcomes were the permanent discontinuation of study treatments, changes in quality of life, and changes in neurologic summary scores, which were analyzed similarly to the primary end point. All analyses were on an intent-to-treat basis. The evaluation of the blinding compared the patients' guesses of the therapy received with the treatment group. Using a log-linear model, we adjusted for option and for whether the patient reported moderate or more pain relief with the 14-week global pain relief rating.

For the original 2 × 2 factorial, n, a sample size of 260 patients was calculated to provide a 90% power of detecting a mean difference between treatments of 0.20 (half the difference between "moderate" and "mild" pain) on the Gracely pain intensity scale using a type I error of .05 (2-sided). After the study design was modified, sample size requirements were estimated at 260 per group. In February 1997, the monitoring board recommended closing the study because it concluded that the results were definitive for both acupuncture and amitriptyline comparisons.

RESULTS

Study Population

From May 1993 to February 1997, 250 patients were enrolled. Of those, 239 were in the acupuncture comparison (125 in the factorial option and 114 randomized to SAR or control points), and 136 were in the amitriptyline comparison (125 from the factorial option and 11 randomized to either active or placebo amitriptyline) (Figure 2). Baseline characteristics (Table 1) were similar in the active and control groups for both comparisons.

Table 2.—Mean Changes in Weekly Pain Diary Scores, Neurologic Score, and Quality of Life at 6 and 14 Weeks*

	Acupuncture						Amitriptyline Hydrochloride					
	SAR			Control Points			Active			Placebo		
	No.	Mean Change	No.	Mean Change	Difference (95% CI)†	P Value‡	No.	Mean Change	No.	Mean Change	Difference (95% CI)‡	P Value‡
Primary Outcomes												
Pain diary, 6 wk	112	-0.21	93	-0.20	0.01 (-0.11 to 0.12)	.88	56	-0.23	54	-0.18	-0.07 (-0.22 to 0.08)	.38
Pain diary, 14 wk	105	-0.29	82	-0.19	-0.08 (-0.21 to 0.06)	.26	49	-0.26	52	-0.30	0.00 (-0.18 to 0.19)	.99
Secondary Outcomes												
Neurologic score, 14 wk	94	2.1	80	-1.4	2.2 (-1.9 to 6.3)	.30	49	0.8	49	-0.4	0.6 (-4.3 to 5.4)	.62
Quality of life												
Physical functioning, 6 wk	110	6.0	102	5.6	0.4 (-5.4 to 6.1)	.90	61	5.9	60	5.1	0.3 (-8.3 to 8.9)	.94
Physical functioning, 14 wk	97	3.4	90	1.3	3.4 (-3.3 to 10.0)	.32	52	7.1	51	0.6	6.4 (-2.7 to 15.5)	.17
Overall P value, 14 wk§						.64						.60

*SAR indicates standardized acupuncture regimen; CI, confidence interval.

†SAR minus control points, adjusted for unit, baseline score, and amitriptyline assignment (active, placebo, or none).

‡Active minus placebo, adjusted for unit, baseline score, and acupuncture assignment (SAR or not SAR).

§P value from combining 11 dimensions using method of O'Brien.²²

Effects of Treatment

SAR vs Control Points.—The change in pain was not significantly different between the 2 groups at either 6 or 14 weeks (Table 2). Both groups showed improvement in pain from an average intensity of "moderate" to "mild" (Figure 3). The estimated difference of the SAR group compared with the control points group was 0.01 at 6 weeks (95% confidence interval [CI], -0.11 to 0.12; $P = .88$) and -0.08 at 14 weeks (95% CI, -0.21 to 0.06; $P = .26$). At 6 weeks, the SAR group had less pain relief than patients in the control points group by 0.01 U and at 14 weeks, the SAR group had 0.08 U more relief than patients in the control points group. Repeated measures analyses of weekly pain averages during the entire 14-week period gave weekly effects, which were small and nonsignificant (P values ranging from .10 to .94).

There were no significant differences in the quality of life, neurologic summary score (Table 2), number of grade 4 adverse events, deaths, or discontinuations. By 14 weeks, 20% of patients randomized to the SAR group and 25% of those randomized to control points group had discontinued treatment. Three patients assigned to the SAR option and 10 assigned to the control points experienced a grade 4 adverse event ($P = .06$).

The difference in the global pain relief rating between the 2 groups was not significant at 6 weeks ($P = .65$). However, at 14 weeks, there was a nominally significant difference ($P = .03$) with a slightly higher proportion of patients in the SAR group reporting moderate or more pain relief than those in the control points group (Table 3). However, after adjustment for multiple comparisons, the result is not significant.

Amitriptyline vs Placebo.—The change in pain score at 6 and 14 weeks was not significantly different between the active and placebo groups (Table 2). As with the SAR

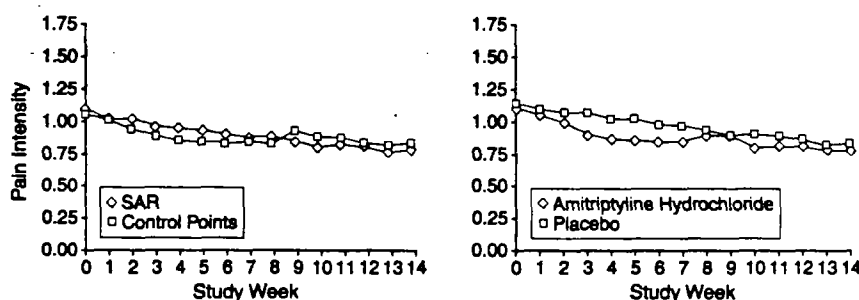


Figure 3.—Average pain intensity scores for single factor options by study week. The mean weekly values of the descriptors of pain intensity are plotted. There was no statistically significant difference between the effects of the standardized acupuncture regimen (SAR) vs control points or between amitriptyline vs placebo. Pain intensity is described and rated as no pain (0.0), faint (0.04), very weak (0.36), weak (0.45), very mild (0.59), mild (0.74), moderate (1.09), barely strong (1.10), slightly intense (1.35), strong (1.36), intense (1.59), very intense (1.64), and extremely intense (1.75).¹⁸

vs control points comparison, both groups showed improvement over time (Figure 3). The estimated difference of amitriptyline compared with placebo was -0.07 at 6 weeks (95% CI, -0.22 to 0.08; $P = .38$) and 0.00 at 14 weeks (95% CI, -0.18 to 0.19; $P = .99$). That is, at 6 weeks, patients taking amitriptyline had more pain relief by 0.07 U than those taking placebo and there was no difference at 14 weeks. Repeated measures analyses of weekly pain averages indicated that the largest beneficial effect was at week 3 ($P = .05$), but after adjusting for multiple comparisons, the result was not statistically significant.

There were no statistically significant differences in quality of life, neurologic summary scores (Table 2), number of grade 4 adverse events, or deaths. Six patients assigned to the amitriptyline and 2 assigned to placebo options experienced grade 4 adverse events ($P = .20$). By 14 weeks, 35% of patients randomized to either the amitriptyline or placebo groups had discontinued drug treatment. The difference in the global pain relief rating between the 2 groups was not significant at 6 weeks ($P = .68$) or 14 weeks ($P = .81$) (Table 3).

Factorial Option.—The test for interaction in change of pain between the 2 factors was not significant at either 6 or 14 weeks ($P = .17$ and $P = .31$, respectively). There was no significant difference in the change in pain among the 4 groups at either 6 or 14 weeks ($P = .37$ and $P = .64$, respectively). All study groups in the factorial option showed improvement in pain.

Completeness of Data

Figure 2 shows the number of patients providing pain diary data and global pain relief ratings at 6 and 14 weeks. To examine the sensitivity of the conclusions to missing data, the analyses were repeated using 2 common methods to impute missing data. The first assumes that the patients' missing data indicated no change in their pain from baseline; the second uses the last value of the weekly pain reported to calculate the end point. Under both methods to impute the missing pain diary data, the results of the study did not reach statistical significance for either comparison at either 6 or 14 weeks.

Table 3.—Global Pain Relief Rating at 6 and 14 Weeks*

Global Pain Relief	Acupuncture				Amitriptyline Hydrochloride			
	SAR		Control Points		Active		Placebo	
	No.	Cumulative %	No.	Cumulative %	No.	Cumulative %	No.	Cumulative %
6 weeks								
Complete	3	2.7	2	1.9	3	4.3	8	5.0
A lot	17	18.0	14	15.5	6	14.8	10	21.7
Moderate	37	51.4	36	50.5	22	50.8	16	46.7
Slight	29	77.5	19	68.9	14	73.8	13	68.3
None	16	91.9	22	80.3	11	81.8	11	86.7
Pain worse	9	100.0	10	100.0	5	100.0	8	100.0
No. of patients with rating	111		103		61		80	
P value†				.65				.88
14 weeks								
Complete	8	7.8	2	2.1	1	1.7	0	0.0
A lot	19	26.5	27	30.9	12	22.4	12	22.6
Moderate	31	56.9	16	47.9	14	46.4	15	50.9
Slight	23	79.4	18	67.0	13	69.0	13	75.5
None	19	98.0	26	94.7	16	96.6	11	96.2
Pain worse	2	100.0	5	100.0	2	100.0	2	100.0
No. of patients with rating	102		94		58		53	
P value†				.03				.81

*SAR indicates standardized acupuncture regimen.

†Likelihood ratio test for the conditional independence of relief and treatment arm; SAR vs control points comparison is adjusted for the level of the other factor (active amitriptyline, placebo amitriptyline, and no amitriptyline). Amitriptyline vs placebo comparison is adjusted for the level of the other factor (SAR, control points, or no acupuncture).

Table 4.—Effectiveness of Participants' Blinding to Treatment Assignment*

Patient Guess	Acupuncture, No. (%)		Patient Guess	Amitriptyline Hydrochloride, No. (%)	
	SAR	Control		Active	Placebo
Moderate or more relief†					
SAR	47 (81.0)	28 (62.2)	Active	20 (74.1)	9 (33.3)
Control points	2 (3.4)	6 (13.3)	Placebo	4 (14.8)	16 (59.3)
Cannot guess	9 (15.5)	11 (24.4)	Cannot guess	3 (11.1)	2 (7.4)
Less than moderate relief†					
SAR	14 (31.8)	10 (20.4)	Active	19 (61.3)	8 (30.8)
Control points	12 (27.3)	22 (44.9)	Placebo	6 (19.4)	15 (57.7)
Cannot guess	18 (40.9)	17 (34.7)	Cannot guess	6 (19.4)	3 (11.5)
P value‡		.02			<.001

*SAR indicates standardized acupuncture regimen.

†Global pain relief rating at 14 weeks.

‡Likelihood ratio test for independence of guess and treatment adjusted for global pain relief rating at 14 weeks (moderate or more vs less than moderate).

Assessment of Treatment Blinding

For the acupuncture comparison, although the patients' guesses and the treatment assignments were not independent ($P = .007$, data not shown), there was a strong association between the guess and the global pain relief rating. Those reporting moderate or more relief at 14 weeks tended to guess that they received the SAR. After adjusting for option and the reported relief being moderate or more, the patients' guesses and the treatment assignments were not independent ($P = .02$), but the association was small. This differed in the amitriptyline comparison, in which a large proportion of patients correctly guessed the study treatment, irrespective of their level of pain relief ($P < .001$) (Table 4).

COMMENT

The main findings of this study show that treatment with this SAR had little or no effect on HIV-related peripheral neuropathy compared with the control points. Similarly, amitriptyline, as commonly used, was not significantly more effective than placebo (Table 2 and Figure 3). All treatment groups improved during the study period by the amount hypothesized in the design, suggesting that the modest decline in pain scores in all groups was either attributable to a placebo effect or patients entered the study at times of symptomatic flares and improved spontaneously thereafter.

For the acupuncture comparison, the results were strengthened by 2 methodological features of the trial. First, the sample size of approximately 120 patients

per treatment group is many times larger than those in previously published trials of acupuncture,⁹ and the CIs were narrow, making it unlikely that a large positive treatment effect was missed by chance. Second, the control points appeared reasonably effective in preserving the blinding (Table 4). Many of the study participants and, presumably, the study participants were favorably disposed toward acupuncture. If patients were able to guess their treatment better than randomly, the resulting placebo effects would be expected to bias the result in favor of this SAR,^{10,12,24} thus making our finding of a similar effect even more convincing.

We cannot completely rule out the possibility that the SAR had a modest and delayed analgesic effect, in view of the nominally significant result of SAR compared with control points on the global pain relief rating at 14 weeks, although this was not seen at 6 weeks. This is unlikely, however, in view of the finding of no significant difference in the pain diary scores. Our study was designed with a sample size that provided sufficient power to detect even a small difference between the SAR and control points. The CIs at both 6 and 14 weeks rule out any clinically meaningful beneficial effects of SAR based on the primary end point of the pain diary scores.

One possible explanation for the lack of efficacy of the SAR is that we chose the wrong "active points." Consensus on the SAR was reached by 8 acupuncturists before protocol implementation. Another explanation is that the use of nonclassical points as a control provided a real effect and was not an inert control. There is evidence from animal and human studies that acupuncture at either classical or nonclassical locations may have analgesic effects^{9,25,26} by mechanisms such as the release of endogenous opioids²⁷ or activation of other brain and spinal cord pathways that reduce pain.²⁸

There is controversy over what constitutes an acceptable control group for acupuncture studies.^{6,29} It is possible that the novelty of an experience like acupuncture may generate a placebo effect quite apart from specific effects produced by needling specific points.³⁰ Unless the study includes a "sham" acupuncture group as a control, such nonspecific effects may bias toward a result in favor of the active intervention.

The SAR chosen for this study differed from the practice of most acupuncturists who treat patients with individualized regimens.³¹ We chose to study standardized points to test the hypothesis that these specific points promote analgesia for chronic foot and leg pain¹² and because such a study is easier to blind and replicate. If the acupuncturists had individualized

visualized treatment, the results would not be generalizable to other acupuncturists, and the treatment, if efficacious, could not be used by other practitioners. Our approach enabled us to derive a conclusion about these acupuncture points but not about individualized treatments.

Amitriptyline is used in the treatment of HIV-related peripheral neuropathy³² but was not effective in this study. The lack of efficacy at 14 weeks was confirmed by the analysis of the secondary end points. Although the 6-week CI did not completely rule out the beneficial effect of 0.20 that the study was designed to detect, there was no supporting evidence of beneficial effect from any of the secondary end points. In addition, another study in HIV-related peripheral neuropathy agrees with our findings.³³ The indication that the blinding was not maintained also confirms the lack of efficacy because unblinding tends to bias toward a hypothesized active intervention.^{24,34}

It is possible that a higher dose of amitriptyline would have resulted in a larger treatment effect. We chose this dose based on common clinical practice and on the only 2 published prospective randomized dose-response studies of tricyclic antidepressants used for chronic pain.^{15,16}

No previously controlled trials of amitriptyline in neuropathic pain have followed up patients for longer than 8 weeks.^{33,36} Clinical trials of amitriptyline for neuropathies of diabetic and nondiabetic etiologies have shown larger, short-term, clinically meaningful effects.^{6,7,19} Mechanisms for this include facilitation of the analgesic action of norepinephrine and serotonin released by endogenous analgesic systems^{16,19} and the blockade of sodium channels in peripheral sprouts from damaged nerves.³⁶ Presumably, the neuropathological features of the HIV-associated distal axonal neuropathy generate painful discharges resistant to the analgesic actions of tricyclic antidepressants.^{37,38}

In conclusion, this is the largest reported randomized, placebo-controlled, clinical trial of symptomatic treatment for HIV-related peripheral neuropathy. Overall, our results indicate that neither this SAR given over 14 weeks nor amitriptyline hydrochloride, 75 mg/d, was effective in relieving pain and neither therapy can be recommended for the treatment of HIV-related peripheral neuropathy. Additional clinical trials are needed because there are no effective treatments for this chronic debilitating condition.³⁹

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Garcinia cambogia (Hydroxycitric Acid) as a Potential Antiobesity Agent

A Randomized Controlled Trial

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Context.—Hydroxycitric acid, the active ingredient in the herbal compound *Garcinia cambogia*, competitively inhibits the extramitochondrial enzyme adenosine triphosphate-citrate (pro-3S)-lyase. As a citrate cleavage enzyme that may play an essential role in de novo lipogenesis inhibition, *G cambogia* is claimed to lower body weight and reduce fat mass in humans.

Objective.—To evaluate the efficacy of *G cambogia* for body weight and fat mass loss in overweight human subjects.

Design.—Twelve-week randomized, double-blind, placebo-controlled trial.

Setting.—Outpatient weight control research unit.

Participants.—Overweight men and women subjects (mean body mass index [weight in kilograms divided by the square of height in meters], approximately 32 kg/m²).

Intervention.—Subjects were randomized to receive either active herbal compound (1500 mg of hydroxycitric acid per day) or placebo, and both groups were prescribed a high-fiber, low-energy diet. The treatment period was 12 weeks. Body weight was evaluated every other week and fat mass was measured at weeks 0 and 12.

Main Outcome Measures.—Body weight change and fat mass change.

Results.—A total of 135 subjects were randomized to either active hydroxycitric acid (n = 66) or placebo (n = 69); 42 (64%) in the active hydroxycitric acid group and 42 (61%) in the placebo group completed 12 weeks of treatment (P = .74). Patients in both groups lost a significant amount of weight during the 12-week treatment period (P < .001); however, between-group weight loss differences were not statistically significant (mean [SD], 3.2 [3.3] kg vs 4.1 [3.9] kg; P = .14). There were no significant differences in estimated percentage of body fat mass loss between treatment groups, and the fraction of subject weight loss as fat was not influenced by treatment group.

Conclusions.—*Garcinia cambogia* failed to produce significant weight loss and fat mass loss beyond that observed with placebo.

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EXCESSIVE ADIPOSITY and its concomitant health risks are among the most common conditions managed by health care practitioners. The limited long-term effectiveness of conventional weight management, including behavioral therapy,¹ is the impetus of major

efforts aimed at developing alternative pharmacologic² and surgical weight reduction treatment strategies.³ A rapidly growing therapeutic area, and one widely embraced by the general public, is the use of herbal weight loss products.

An herb-derived compound, hydroxycitric acid, is now incorporated into many commercial weight loss products. Obtained from extracts of related plants native to India, mainly *Garcinia cambogia* and *Garcinia indica*, hydroxycitric acid was first identified by Watson and Lowenstein^{4,5} in the late 1960s as a po-

tent competitive inhibitor of the extramitochondrial enzyme adenosine triphosphate-citrate (pro-3S)-lyase. These investigators and others subsequently demonstrated both in vitro and in vivo that hydroxycitric acid in animals not only inhibited the actions of citrate cleavage enzyme and suppressed de novo fatty acid synthesis,⁶ but also increased rates of hepatic glycogen synthesis,⁷ suppressed food intake,⁸ and decreased body weight gain.⁹

Although hydroxycitric acid appears to be a promising experimental weight control agent, studies in humans are limited and results have been contradictory¹⁰⁻¹⁴ (also R. Ramos, J. Flores Saenz, F. Alarcon, unpublished data, 1996, and G. Kaats, D. Pullin, L. Parker, S. Keith, unpublished data, 1996). Supporting evidence of human hydroxycitric acid efficacy for weight control is based largely on studies with small sample sizes,^{11,12} studies that failed to include a placebo-treated group,¹⁰ and use of inaccurate measures of body lipid change.¹² Although hydroxycitric acid effectiveness remains unclear, at least 14 separate hydroxycitric acid-containing products are presently sold over-the-counter to consumers.¹⁵ This investigation was designed to overcome limitations of earlier studies and examine the effectiveness of hydroxycitric acid for weight loss and fat mass reduction in a rigorous controlled trial.

METHODS

Protocol

We tested 2 primary hypotheses in a randomized, double-blind, placebo-controlled trial: (1) *G cambogia* produces a greater reduction in body weight than placebo, and (2) *G cambogia* produces a greater reduction in total body fat mass than placebo. Advertisements were placed in local newspapers, and over-

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weight subjects who responded and met entry criteria during a telephone screening interview were scheduled for a baseline visit. The evaluation included a physical examination, electrocardiogram, and screening blood studies. Subjects meeting entry criteria were seen within 2 weeks for randomization at treatment week 0. Subjects were assigned to placebo or active compound with equal probability through a random number generator.

The protocol with active herbal compound included *G cambogia* extract (50% hydroxycitric acid by chemical analysis), taken 3 times daily as two 500-mg caplets 30 minutes before meal ingestion. Total daily dose was *G cambogia* extract, 3000 mg, and hydroxycitric acid, 1500 mg. Placebo-treated subjects followed an identical protocol in which active compound was replaced with inert ingredients. Subjects taking active compound or placebo were provided a high-fiber, 5040-kJ/d diet plan, with 20%, 50%, and 30% of energy as fat, carbohydrate, and protein, respectively. The recommended daily food provision was divided into 3 meals with an evening snack. Subjects were asked to maintain a stable physical activity level and return for evaluation every 2 weeks for a total treatment interval of 12 weeks. Body weight was measured at each visit, and clinical information, including potential herb or weight loss adverse effects, was obtained. Bi-weekly pill counts and diaries were used to check patient medication compliance. Diet compliance was not quantitatively monitored during the study.

The study was approved by the institutional review board of St Luke's-Roosevelt Hospital Center, New York, NY, and all subjects gave written consent prior to participation.

Subjects

Subjects were overweight but otherwise healthy adults aged 18 to 65 years who had a body mass index (BMI, defined as weight in kilograms divided by the square of height in meters) of more than 27 kg/m² and at most 38 kg/m². Subjects were excluded if they were pregnant, had any clinically significant medical condition, were taking prescription medications or appetite suppressants on a regular basis, had a history of alcohol or other drug abuse, were allergic to any of the study products, or had dieted with weight loss in the past 6 months.

Body Composition

Body weight and height were measured to the nearest 0.1 kg and 0.5 cm using a digital scale (Weight Tronix, New York, NY) and stadiometer (Holtain, Crosswell, Wales), respectively.

Table 1. Baseline Subject Characteristics

Group	No. of Patients	Age, y	Weight, kg	BMI, kg/m ²	Total Body Fat Mass, %
Treatment					
Men	5	43.1 (2.8)	100.8 (11.0)	33.0 (3.7)	28.4 (2.6)
Women	61	38.2 (7.8)	82.9 (8.8)	31.1 (2.7)	41.9 (7.3)
Total	66	38.8 (7.7)	83.8 (10.1)	31.2 (2.6)	41.1 (7.8)
Placebo					
Men	14	40.5 (5.5)	101.7 (11.8)	32.3 (2.5)	36.8 (5.9)
Women	55	39.6 (7.6)	84.8 (10.9)	31.4 (3.2)	43.8 (4.2)
Total	69	39.4 (7.2)	88.2 (13.0)	31.9 (3.1)	42.0 (5.6)

*Data (except number of patients) are presented as group mean (SD).

†BMI indicates body mass index, defined as weight in kilograms divided by the square of height in meters.

Total body fat mass was measured at baseline and at the 12-week visit using several different procedures.

A pencil-beam dual-energy x-ray absorptiometry (DXA) scanner (Lunar DPX, Madison, Wis) was used to estimate total body fat mass. Subjects completed the slow-mode whole body scan and fat mass estimates were provided by Lunar, Version 3.6g, software.¹⁶ The technical error of DXA percentage fat mass estimates in our laboratory is 3.1%.¹⁷ The remaining body fat mass measurement methods used in our laboratory for this study included underwater weighing,¹⁸ skinfold thicknesses,¹⁹ and bioimpedance analysis.²⁰

Statistical Analysis

Based on previous research,¹ we estimated that a study that included at least 30 completed subjects in each of 2 groups would have more than 80% power at the 2-tailed α level of .05 to detect any significant differences in body weight.

The 2 study hypotheses were tested in separate sets of statistical analyses. Statistical models were used in which the outcome variable, either loss of body weight or percentage of fat mass, was set as dependent variable and assigned treatment and other covariates were set as independent variables in an intent-to-treat analysis.²¹ Within the intent-to-treat analysis, missing data due to measurement failure or subject dropout were imputed by carrying the last observation forward (LOCF).²² The baseline value of the dependent variable (ie, initial body weight or percentage of fat mass) served as a potential independent variable in each analysis. Patient age and sex also served as additional independent variables. All analyses were conducted at the 2-tailed α level of .05.

For each of the 2 dependent variables, a set of secondary analyses were conducted, including (1) evaluation of completers only; (2) imputation of all missing data with a regression procedure rather than the LOCF; (3) imputation of missing data using the EM²³ algorithm rather than the LOCF; (4) use of weight loss slopes as outcomes²⁴ rather than the

simple baseline to final measurement change when more than 2 time points for weight were available; (5) performance of a full repeated-measures analysis of variance using all time points; and (6) performance of a multivariate analysis of covariance using all time points simultaneously in the statistical model. In no case did any of these secondary sensitivity analyses lead to different conclusions than the primary LOCF intent-to-treat analysis. We therefore report only the results of the primary intent-to-treat analysis.

At baseline, DXA readings were unavailable for several subjects who had technically poor scans or who were evaluated during a brief period in which the DXA system was undergoing repair. However, each of these subjects had 1 or more measurements of fat mass taken with the other techniques mentioned herein and summarized in earlier articles.¹⁶⁻²⁰ Estimates of total body fat mass for these subjects by DXA were inferred using single imputation plus random error models based on multiple regression analysis of all other available measurements of fat mass for that subject, as described by Graham et al.²⁵ Similarly, several subjects completed the entire course of treatment and received some measurement of body fat mass after treatment but not by DXA. For these subjects, estimates of total body fat mass by DXA also were imputed using the same statistical methods and the other available measurements of body fat mass.

The purported fat-mobilizing properties of hydroxycitric acid were evaluated by computing the slope of change in fat mass vs change in body weight for the 2 treatment groups. Assuming approximately a zero intercept for this relation, the anticipated regression line slopes should approach 0.7 to 0.8, the generally acknowledged fraction of weight loss as fat mass in obesity trials.²⁶ Promotion of fat mass loss by active hydroxycitric acid would be associated with an increased fraction of weight loss as fat mass.

Group results are expressed as mean (SD) in text and tables. Data were analyzed using the statistical programs

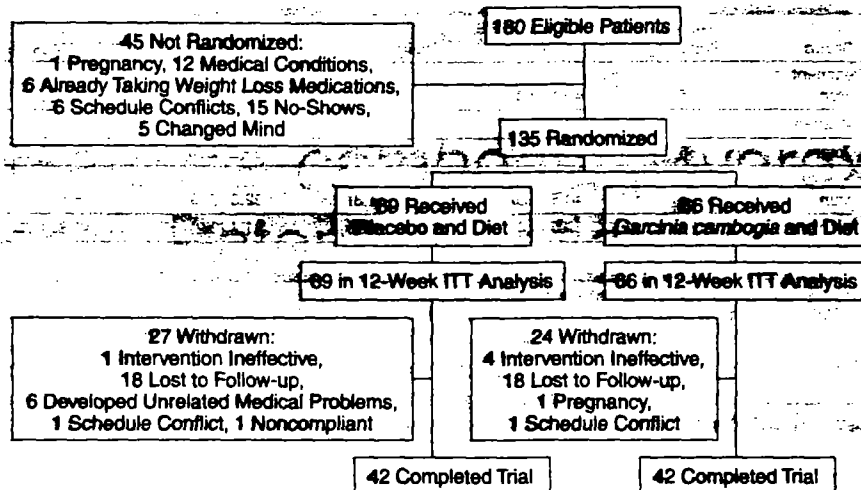


Figure 1.—Study CONSORT flow diagram. ITT indicates intent-to-treat.

SPSSWIN, Version 7.5, and SPSSMVA, Version 7.5 (SPSS Inc, Chicago, Ill).

RESULTS

Baseline Characteristics

At baseline, 180 moderately overweight subjects were screened and, of those, 135 were randomized to placebo and active compound (Table 1 and Figure 1). There were 69 subjects (BMI, 31.9 [3.1] kg/m²) in the placebo-treated group (14 men and 55 women) and 66 subjects (BMI, 31.3 [2.8] kg/m²) in the *G. cambogia*-treated group (5 men and 61 women).

Of the 69 placebo-treated subjects, 42 (61%) completed the 12-week protocol. The reasons for subject withdrawal (27 cases) are summarized in Figure 1. Of the 66 subjects randomized to active compound, 42 (64%) completed the 12 weeks of treatment. The reasons for subject withdrawal from this group (24 cases) are also summarized in Figure 1. There were no significant differences in age, body weight, or BMI between subjects who withdrew from the study and those who completed the 12-week protocol. There was also no significant difference between the 2 groups in the proportion of subjects who completed the entire course of treatment ($\chi^2 = 0.11$, $P = .74$). Among subjects completing the 12 weeks of treatment, medication compliance was 88.6% (10.9%) and 92.1% (10.0%) in the treatment and placebo groups, respectively ($P = .30$).

Weight Loss

Primary Analysis.—The weight loss curves for placebo and treatment groups are shown in Figure 2 for subjects in the intent-to-treat analysis with LOCF. The estimated mean (SD) [median (interquartile range)] weight loss for the placebo group was 4.1 (3.9) [3.9 (4.7)] kg and

for the treatment group was 3.2 (3.3) [2.6 (4.1)] kg. The weight loss within each group was significantly different from baseline ($t_{134} = 11.795$, $P < .001$), although between-group weight loss differences were not statistically significant ($t_{133} = 1.474$, $P = .14$). Body weight change differences remained nonsignificant after controlling for patient starting weight, sex, and age. Assumptions of the applied parametric statistical analysis such as homogeneity of variance and normality of residuals were tested and no meaningful violations were detected. Given the lack of significant findings, questions of statistical power are important. Therefore, using the observed distributions of weight change and the within-group SD thereof, we estimated that the power of the current study to detect differences between the treatment and placebo groups in terms of weight change was 89% to detect a between-group difference in weight loss as small as 2 kg at the 2-tailed α level of .05.

Secondary Analyses.—In no case did any secondary analysis indicate any statistically significant effect for the active compound to produce more weight loss than placebo.

Fat Mass Loss

Primary Analysis.—Results for body fat mass analysis were imputed for 9 baseline and 4 post-weight loss subjects. With the LOCF intent-to-treat analysis, the estimated mean (SD) [median (interquartile range)] percentage of body fat mass loss for the placebo group was 2.16% (2.06%) [2.20% (2.7%)] and the estimated percentage of fat mass loss for the treatment group was 1.44% (2.15%) [1.60% (1.9%)]. This difference was tested using the Welch test because the variances were significantly hetero-

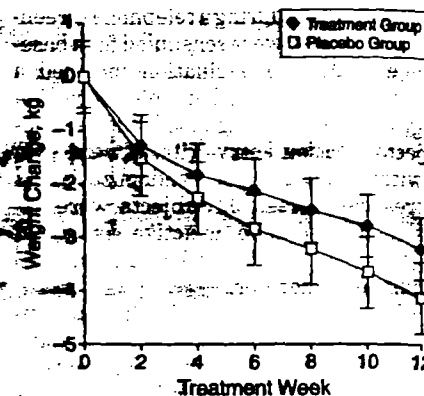


Figure 2.—Weight-change curves for 2 study groups. Results are plotted for group means ($\pm 95\%$ confidence limits) for 69 subjects in the placebo group and 66 subjects in the treatment group. Data are from last-observation-carried-forward intent-to-treat analysis.

geneous by the Levene test (P for variance heterogeneity = .03). Using the Welch test, the placebo and treatment group mean differences were not statistically significant ($t_{129} = 1.7$, $P = .08$). This finding was consistent with that of the ordinary t test ($t_{132} = 1.78$, $P = .08$). Using analysis of covariance with age, sex, and pretest percentage of fat mass as covariates, the percentage of fat mass differences also was nonsignificant ($F_{1,129} = 1.57$, $P = .21$).

Secondary Analyses.—As for weight loss, all of the secondary analyses were consistent with the primary analysis. That is, in no case did analysis indicate any statistically significant effect for the active compound to produce a different percentage of body fat mass loss than the placebo.

Examination of the change in fat mass relative to change in body weight derived using least squares regression analysis for all subjects combined resulted in the relation, $\Delta \text{fat mass (kg)} = 0.77 \times \Delta \text{body weight (kg)} - 0.44$, with $r = 0.89$ and $P < .001$. The association was not changed significantly ($P > .91$) by adding treatment group as a second independent variable, even after adjusting for 3 additional potential covariates: initial body weight, sex, and age.

Adverse Events

No patient was removed from the study protocol for a treatment-related adverse event, and the number of reported adverse events was not significantly different between the placebo and treatment groups (eg, headache, 12 vs 9, respectively; upper respiratory tract symptoms, 13 vs 16, respectively; and gastrointestinal tract symptoms, 6 vs 13, respectively).

Table 2.—Summary of Previous *Garcinia cambogia* Studies*

Author(s)	Publication Type	Study Design	Study Agent(s)	Sample	Duration, wk	Major Observations
Badmaev and Majed ¹⁰	Industrial	Single arm, open label	GCE, 500 mg, chromium picolinate, 100 µg, 3 times per day and healthy eating/exercise	77 obese adults, with 55 completing trial	8	5.5% weight loss in women, 4.9% in men; combined, $P<.001$ vs baseline
Conte ¹¹	Peer-reviewed	Randomized, double-blind, placebo controlled	<i>Garcinia indica</i> extract 500 mg, nickel chromium, 100 µg, 3 times per day and low-fat substitution diet	54 obese subjects randomized, with 39 completing trial	8	Active, 11.14 lb, vs placebo, 4.2 lb†‡
Ramos et al (unpublished data)	Abstract	Randomized, double-blind, placebo controlled	GCE, 500 mg, 3 times per day, and low-fat 4200-6300 kJ/d diet	40 obese subjects randomized, with 35 completing trial	8	Active, 4.1 (1.8) kg, vs placebo, 1.3 (0.9) kg ($P<.05$)§
Kaals et al (unpublished)	Abstract	Randomized, double-blind, placebo controlled	GCE, 1500 mg/d, chromium picolinate, 600 µg/d, L-carnitine, 1200 mg/d, and low-fat, high-fiber diet	200 subjects randomized, with 186 completing trial	4	Active, -2.84 lb, vs placebo, -1.4 lb fat mass loss ($P<.01$)†
Thorn ¹²	Abstract	Randomized, double-blind, placebo controlled	Hydroxycitric acid, 1320 mg/d, in 3 divided doses, and 5040-kJ/d low-fat diet	60 subjects randomized; number completing trial not reported	8	Active, 6.4 kg, vs placebo, 3.8 kg weight loss ($P<.001$); weight loss as fat, 87% in active vs 80% in placebo group†‡
Rothacker and Waitman ¹³	Abstract	Randomized, double-blind, placebo controlled	GCE, 800 mg, natural caffeine, 50 mg, and chromium polynicotinate, 40 µg, 3 times per day, and 5040-kJ/d diet	50 obese subjects randomized, with 48 completing trial	6	Active, -4.0% (3.5%) vs placebo, -3.0% (3.1%) body fat mass ($P=.30$)
Girola et al ¹⁴	Peer-reviewed	Randomized, double-blind, placebo controlled	GCE, 55 mg, chrome, 19 mg, and chitosan, 240 mg; randomized to 1 of 3 groups, active medication twice per day, placebo twice per day, or 1 placebo and 1 active medication per day; all groups treated with hypocaloric diet	150 obese subjects; number completing trial not reported	4	Active, twice per day, -12.5% (1.2%); active, once per day, -7.9% (0.9%); twice per day placebo, -4.3% (1.0%); "overweight reduction" ($P<.01$ for all 3 vs baseline)§

*GCE indicates *Garcinia cambogia* extract.

†No SDs reported.

‡No statistical analysis reported

§Numbers in parentheses are SD.

COMMENT

In 1883 von Lippmann isolated hydroxycitric acid, a minor constituent of sugar beets.²⁷ More than half a century later, in 1941, Martius and Maué²⁸ discovered that the (+) isomer of a racemic hydroxycitric acid mixture is attacked by the enzyme isocitrate dehydrogenase. The (-) hydroxycitric acid isomer of hydroxycitric acid was first isolated by Lewis and Neelakantan in 1964,²⁹ and by 1969 Watson and colleagues⁵ reported the powerful inhibition by (-) hydroxycitric acid of citrate cleavage enzyme. Evidently, the additional hydroxyl group's steric position, compared with citric acid, enhances its binding affinity and competitively inhibits catalytic action by the enzyme. Citrate, entering the cytoplasm from mitochondria, cannot be cleaved to release acetyl coenzyme A, the substrate for de novo fatty acid synthesis. Despite these century-old, well-grounded observations, there has been little effort to critically test the basic assumption underlying therapeutic use of hydroxycitric acid in overweight humans: that hydroxycitric acid inhibition of lipid synthesis will significantly reduce body fat mass beyond that observed with a placebo capsule.

The present study, carried out during a 12-week evaluation period and using accepted experimental design and in

vivo analytic methods, failed to support the hypothesis that hydroxycitric acid as prescribed promotes either additional weight or fat mass loss beyond that observed with placebo. Specifically, body weight and fat mass change during the 12-week study period did not differ significantly between placebo and treatment groups. These results apply to both the primary and secondary statistical analyses. Additionally, there were no observed selective fat-mobilizing effects specifically attributable to the active agent, hydroxycitric acid.

Seven earlier *G cambogia* trials have appeared in peer-reviewed literature,^{11,14} as abstracts,^{12,13} and in industrial publications as an open-label study¹⁰ and randomized controlled trials.¹¹⁻¹⁴ We chose to collectively review these studies even though *G cambogia* typically was used in combination with other ingredients for the claimed purpose of enhancing weight loss.

Of the 7 studies reviewed, 5 reported significant ($P<.05$) effects of *G cambogia* alone or in combination with other ingredients on body weight or fat mass loss in overweight humans (Table 2). These earlier studies all have limitations when specifically considering *G cambogia* as a weight loss agent, including lack of placebo control or double-blinding in 1 study,¹⁰ coadministration of *G cambogia* in combination with other potentially ac-

tive ingredients in 5 studies,^{10,11,13,14} use of an inaccurate body composition method (near-infrared interactance)¹² in 1 study, and failure as of yet to publish study results in peer-reviewed literature in all but 2^{13,14} of the 7 studies. However, our present investigation, carried out using accepted clinical trial design procedures and applying accurate body composition methods, failed to support a specific weight loss effect of *G cambogia* administered as recommended. The present 12-week study period also exceeded in duration all previous study treatment periods, which ranged from 4 to 8 weeks.

In our present investigation we failed to detect a weight loss or fat-mobilizing effect of active herb. The question therefore arises whether there exist conditions differing from those used in the present study that might support hydroxycitric acid efficacy. The 5040-kJ/d low-fat diet recommended in our current study was intended to mimic diets commonly prescribed as a component of weight control programs. The possibility exists that the lipid synthesis-inhibiting properties of hydroxycitric acid may be more evident in subjects relapsing following a failed diet attempt, particularly if high-carbohydrate foods are ingested.³⁰

Another concern is related to the timing and dosage considerations of hy-

hydroxycitric acid. Sullivan and colleagues²¹ showed that the effects of hydroxycitric acid in animals depend on time of administration in relation to a meal, with hydroxycitric acid maximally effective when administered 30 to 60 minutes prior to feeding. The approach used in our study and the others we reviewed suggested hydroxycitric acid ingestion about 90 minutes prior to meal intake, the lower end of the maximally effective range. A related concern is that hydroxycitric acid provided in divided doses also was found to be more effective than the same amount given as a single dose.⁶ Although divided doses typically are used in weight loss protocols, human doses ranging between 750 and 1500 mg/d of hydroxycitric acid are at the extreme low end of the in vivo dose-response range established by Sullivan and colleagues.²² Thus, in light of the many requirements for its effective use, it seems unlikely that the maximal effects of hydroxycitric acid will be realized in human weight loss studies unless treatment conditions are well defined

and patient diet and medication compliance are tightly monitored.

Our study explored product safety only in the form of clinical evaluations and reported adverse events. No significant differences were observed between placebo and treatment groups in number of reported adverse events and no subjects were removed from the study for a treatment-related adverse event. Additional studies, potentially with larger subject groups, are needed to gather specific information on the long-term safety of *G cambogia*.

An important concern in all pharmacological trials, particularly those in which herbal products are evaluated, is the amount and bioavailability of the active agent. As standard procedure, we confirmed the presence and quantity of hydroxycitric acid in the supplied capsules using an independent testing laboratory. However, we did not measure hydroxycitric acid blood levels or evaluate tissue or cytosolic citrate-cleavage enzyme activity. Although the format of our experiment closely resembles cur-

rent use of *G cambogia* as a weight loss product, our conclusions should not be interpreted as a failure to support the validity of the biochemical effects of hydroxycitric acid identified by earlier investigators.

In conclusion, our study evaluated the hypothesis that the active ingredient of *G cambogia*, hydroxycitric acid, elicited weight and fat mass loss effects. Our findings, obtained in a prospective, randomized, double-blind study, failed to detect either weight loss or fat-mobilizing effects of hydroxycitric acid beyond those of placebo. These observations, the first, to our knowledge, to appear in a peer-reviewed article using currently accepted experimental and statistical methods, do not support a role as currently prescribed for the widely used herb *G cambogia* as a facilitator of weight loss.

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Preliminary Communication

Yoga-Based Intervention for Carpal Tunnel Syndrome

A Randomized Trial

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Rosemary Reshetar, EdD; H. Ralph Schumacher, Jr, MD

Context.—Carpal tunnel syndrome is a common complication of repetitive activities and causes significant morbidity.

Objective.—To determine the effectiveness of a yoga-based regimen for relieving symptoms of carpal tunnel syndrome.

Design.—Randomized, single-blind, controlled trial.

Setting.—A geriatric center and an industrial site in 1994-1995.

Patients.—Forty-two employed or retired individuals with carpal tunnel syndrome (median age, 52 years; range, 24-77 years).

Intervention.—Subjects assigned to the yoga group received a yoga-based intervention consisting of 11 yoga postures designed for strengthening, stretching, and balancing each joint in the upper body along with relaxation given twice weekly for 8 weeks. Patients in the control group were offered a wrist splint to supplement their current treatment.

Main Outcome Measures.—Changes from baseline to 8 weeks in grip strength, pain intensity, sleep disturbance, Phalen sign, and Tinel sign, and in median nerve motor and sensory conduction time.

Results.—Subjects in the yoga groups had significant improvement in grip strength (increased from 162 to 187 mm Hg; $P = .009$) and pain reduction (decreased from 5.0 to 2.9 mm; $P = .02$), but changes in grip strength and pain were not significant for control subjects. The yoga group had significantly more improvement in Phalen sign (12 improved vs 2 in control group; $P = .008$), but no significant differences were found in sleep disturbance, Tinel sign, and median nerve motor and sensory conduction time.

Conclusion.—In this preliminary study, a yoga-based regimen was more effective than wrist splinting or no treatment in relieving some symptoms and signs of carpal tunnel syndrome.

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CARPAL TUNNEL syndrome (CTS) is a common problem in the workplace and causes significant morbidity. In addition to its potentially debilitating physical aspects, CTS has a negative financial impact resulting from lost time from work and increasing medical ex-

penses.¹ Traditionally, CTS has been treated with wrist splints, anti-inflammatory agents, avoidance of occupational duties, career changes, injection therapy, and surgery. However, many of these options have provided less than satisfactory symptom relief.¹

Yoga and relaxation techniques have been used to help alleviate musculoskeletal symptoms.² However, except for a previous study on osteoarthritis of the hand,³ to our knowledge, these methods have not been studied in a prospective controlled trial. Our previous investigation showed significant improvement in range of motion, decreased tenderness, and decreased hand pain during activity in patients with osteoarthritis who followed a supervised program of yoga and relaxation.

The purpose of this study was to evaluate whether a program of yoga and relaxation techniques might offer an effective treatment alternative for patients with CTS. Yoga was proposed to be helpful because stretching may relieve compression in the carpal tunnel, better joint posture may decrease intermittent compression, and blood flow may be improved to decrease ischemic effects on the median nerve. In this article, we report the results of a randomized controlled trial examining the effects of an intervention using supervised yoga and relaxation techniques specifically designed for patients with CTS.

METHODS

Subject Selection

Approximately 400 potential subjects were recruited through advertisements in the city newspaper and notices posted at study sites. After initial screening by telephone, 72 interested, available, and suitable patients with characteristic symptoms of CTS were interviewed in person and examined; 51 subjects met the criteria for inclusion in the study.

Entry criteria included the presence of at least 2 of 5 of the following clinical findings: positive results on Tinel sign, positive results on Phalen sign, pain in the median nerve distribution, sleep disturbances resulting from hand symptoms, and numbness or paresthesias in the median nerve distribution. All potential subjects were required to have abnormal median nerve conduction latencies on neuroelectrical testing.⁴ All subjects were required to agree not to change medications, receive other new treatments, or change work duties during the study. Exclusion criteria were previous surgery for CTS, rheumatoid arthritis or other recognized inflammatory arthritis, CTS related to systemic disease (such as hypothyroidism), and pregnancy.

The study took place at Ralston House, the Geriatric Center of the University of Pennsylvania in Philadelphia, and at QVC

From the Department of Medicine, Division of Rheumatology, University of Pennsylvania School of Medicine (Drs Garfinkel, Singhal, Katz, and Schumacher), the Arthritis-Immunology Center, Veterans Affairs Medical Center (Dr Schumacher), University of Pennsylvania Health System/Presbyterian Medical Center (Drs Katz and Allan), and the American Board of Internal Medicine (Dr Reshetar), Philadelphia, Pa. Dr Garfinkel is now with Cooper Health System and Center for Health and Wellness, Cherry Hill, N.J. Dr Singhal is now in private practice in Mesquite, Tex. Dr Reshetar is now with the Educational Testing Service, Princeton, N.J.

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Table 1.—Yoga Postures Used for Carpal Tunnel Syndrome*

1. Sitting with extension of the trunk (dandasana).—Sit on a chair with the trunk upright. Press hands into the seat. Press shoulder blades into the back. Move shoulders back and down.
2. Hands in prayer position (namaste).—Press palms and fingers of each hand together, with fingers away from their position of ulnar deviation. Release and repeat, pressing palms together with fingers spread as widely as possible. Repeat by pressing metacarpals of each finger. Pull fingers back into hyperextension, increasing distance between fingers of each hand.
3. Arms extended overhead (urdhva hastasana).—Stretch arms and fingers forward and up, with hands facing vertically. Open palms, keep fingers together and lock the elbows. Lift sides of the body. Keep arms straight.
4. Arms extended overhead with fingers interlocked (parvatasana).—Interlock fingers with the right thumb base over the left, with the base of the fingers in contact. Turn palms out and stretch arms forward and up. Lock elbows and keep arms straight. Raise trunk by lifting the arms and pull arms further back. Lower arms. Repeat with left thumb over the right.
5. Arms interlocked in front of the body (garudasana).—Bend elbows, crossing arms in front of the chest with the forearms stretching up and thumbs facing the head. Cross left elbow over the right. Move right hand toward the head and the left hand away; cross hands and place fingers of the right hand on left palm. Stand and raise elbows to shoulder level and bend them. Stretch hands and fingers. Release arms and stand straight.
6. Chair twists (bharadvajasana).—Sit sideways on a chair, with right hip and thigh against the back of chair. Stretch the trunk up and pull shoulders back. Keep knees and feet together, turn toward the back of chair. Place hands on back of chair. Pull left hand to bring left side toward back of chair and push with right hand to turn right side away. Turn body then the head to look over right shoulder.
7. Standing, mountain pose (tadasana).—Stand straight in bare feet, facing forward, feet together, toes and heels in line, with big toes and centers of the inner ankles touching. Balance weight evenly on inner and outer edges of both feet and heels and soles. Lift knee caps into the joints. Raise upper chest and collarbones.
8. 90-Degree forward bend to wall (half uttanasana).—Stand with feet 1 foot apart. Stretch the arms over head. Bend from the hips, extending entire body toward the wall, hands touching the wall. Stretch forward.
9. Arms extended overhead with palms together in prayer position (virabhadrasana 1, arms only).—Stand in tadasana. Stretch arms to sides at shoulder level keeping fingers together. Turn arms circularly in their sockets, palms facing the ceiling. Keeping arms straight, extend them over the head until they are parallel. While moving arms upward, stretch the sides of chest and armpits. Take arms back, and bring them closer together; join palms, with the fingers stretching upward. Lock elbows.
10. Dog pose with chair, with special emphasis on hand placement (urdhva mukha svanasana).—Stand, feet hip width apart, facing the seat of a chair. Bend, placing palms on the seat, shoulder width apart. Straighten arms and lift waist, hips, and knees a few inches above chair. Turn arms out and curve trunk back between them. Bring coccyx, sacrum, and lumbar spine forward, keeping buttocks tight. Stretch front of the body from the pubis. Raise sternum and ribs. Hold shoulders back. Press shoulder blades and dorsal spine in.
11. Hands joined in prayer position behind the back (namaste).—Stand in tadasana. Join palms behind the back, fingers pointing down and in line. Turn hands toward the trunk and then up. Raise them as high as possible between the shoulder blades. Join heels of the hands and press little fingers into the dorsal spine. Stretch fingers up. Turn upper arms outward and press shoulders back and down.
12. Relaxation.—Lie flat on the back. Keep arms slightly away from thighs, palms up, heels together, and toes apart. Close eyes. Breathe deeply. Concentrate on soft, slow exhalation. Relax lower jaw, tongue, and pupils of the eyes. Relax completely and exhale slowly. Remain in pose for 10 to 15 minutes.

*Hold positions 1 through 11 for 30 seconds and breathe through the nose. Do not tense the throat and keep the shoulders away from the ears. Repeat each position. The Iyengar system of hatha yoga emphasizes structural alignment. These postures are described in abbreviated form. A detailed description of the yoga intervention is available on request from the author.

Corporation, an industrial site in West Chester, Pa. Participants from QVC were actively employed and were compensated to arrive 1 hour before their shift began. Ralston House participants included employed and retired subjects. The study was approved by the institutional review boards of Presbyterian Medical Center, Philadelphia, Pa, and the University of Pennsylvania Medical Center. Written informed consent was obtained from study subjects.

Interventions

Subjects were randomized into 2 groups by having them select sealed envelopes containing a group assignment. Subjects in the control group were offered a standard wrist splint with a metal insert (if not already in use) to supplement their current treatment. Subjects in the yoga-based intervention group received a program focused on upper body postures: improving flexibility; correcting alignment of hands, wrists, arms, and shoulders; stretching; and increasing awareness of optimal joint position during use. We used the Iyengar approach to hatha yoga, which emphasizes proper structural alignment of the body and is based on the

teachings of yoga master B. K. S. Iyengar.^{5,6} The method of study is orderly and progressive, and postures are adjusted to meet the physical conditions of the subjects. With education in the postures (asanas), habitual poor posture can improve. As musculoskeletal alignment improves, the ability to perform the asanas also should improve. Potential benefits of this method include improvements in strength, coordination, and flexibility and an increased sense of well-being.

The sequence of postures used in this study was designed to focus on the upper body for subjects with CTS. The exercises were performed while the subject was sitting and standing and were designed to take each joint in the upper body through its full range of motion with strengthening, stretching, and balancing each part.⁵ Instructions for the 11 asanas used and the relaxation technique are shown in Table 1.

Every session ended with relaxation using the relaxation response of savasana (corpse pose), which is proposed to help counteract the energy-draining effects of prolonged stress and chronic pain.⁵ During relaxation, the body remains still and movement is not possible.

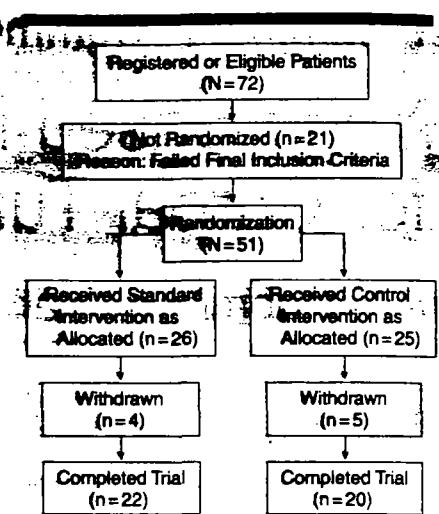


Figure.—Progress through the various stages of a randomized controlled trial, including flow of participants, withdrawals, and timing of primary and secondary outcome measures.

The yoga program was given for 1 to 1½ hours twice weekly by 1 instructor (M.S.G.) for 8 weeks.

Measurements

Subjects reported the approximate number of hours of disturbed sleep per night during the previous week. Subjects indicated the intensity of pain for the previous week on a visual analog scale of 0 to 10, with 10 indicating the greatest level of pain.⁶ Phalen⁷ sign (90 seconds) and Tinel sign⁸ were assessed, with results recorded as positive or negative for each involved wrist. Patterns of paresthesia and numbness were recorded on hand diagrams. Grip strength was measured with a sphygmomanometer cuff that was rolled, taped, and inflated to 20 mm Hg. The subject was encouraged to squeeze with maximum strength and the best of 3 efforts was recorded for each hand.

An electroneurometer⁴ (NERVE-PACE, NeuMed [Neurotron Medical], Lawrenceville, NJ) was used to measure the distal latency of the median nerve across the wrist. This electroneurometer has been validated to show comparable specificity to standard nerve conduction studies.⁹ All tests were assessed at baseline and were repeated at the end of 8 weeks. The assessments all were conducted by 1 physician (A.S.) who was blinded to the patient's group assignment and the intervention.

Statistical Analysis

Differences between the pretest and posttest changes were examined using repeated-measures analysis of variance for within-group differences in improvement for continuous measures of grip strength and nerve conduction times (sensory and motor) for each involved

Table 2.—Characteristics of Study Subjects by Group

Characteristic	Yoga Group* (n = 22)	Control Group (n = 20)
Age, mean (median) [range], y	48.9 (45) [17-68]	48.7 (42) [18-70]
Sex		
Women	18	12
Men	5	8
Race		
Black	3	3
White	18	17
Smokers	2	5

*Demographic data missing for 1 subject. Data are presented as number of subjects unless otherwise indicated.

Table 4.—Improvement in Phalen Sign, Tinel Sign, and Sleep Disturbance*

Variable	Yoga Group	Control Group	χ^2	P Value
Phalen sign				
Improved	12	2	9.72	.008
Same	18	19		
Worsened	2	7		
Tinel sign				
Improved	7	3	1.88	.39
Same	22	21		
Worsened	4	6		
Sleep disturbance				
Improved	4	2	2.68	.26
Same	13	14		
Worsened	0	2		

*Data are presented as number of involved wrists for Phalen sign and Tinel sign, and as number of subjects for sleep disturbance.

Table 3.—Comparison Between Grip Strength, Pain, and Sensory and Motor Nerve Conduction Times*

Variable	n†	Mean (SD)			P Value‡
		Pretest	Posttest	Improvement	
Grip strength, mm Hg					
Yoga	33	161.6 (70.4)	187.4 (68.8)	25.8 (41.4)	.009
Controls	29	183.9 (69.5)	190.5 (68.2)	6.6 (41.1)	.37
Pain, visual analog scale (1-10)					
Yoga	22	5.0 (2.8)	2.9 (2.2)	2.1 (3.1)	.02
Controls	20	5.2 (2.1)	4.3 (2.2)	0.9 (2.8)	.16
Median nerve sensory conduction, ms					
Yoga	35	4.40 (1.5)	3.97 (1.5)	.42 (1.8)	.18
Controls	32	4.66 (1.4)	4.36 (1.6)	.29 (1.5)	.28
Median nerve motor conduction, ms					
Yoga	33	4.79 (1.3)	4.27 (1.4)	.52 (1.7)	.08
Controls	29	4.78 (1.1)	4.52 (1.1)	.26 (0.8)	.09

*Repeated measures analysis for each of the variables (grip strength, pain, and sensory and motor conduction time) showed none of the test results was significant at the .05 level for between-group differences.

†Data are presented as number of involved wrists for grip strength and median nerve conduction times, and as number of subjects for pain.

‡P values are 2-tailed and reflect paired differences within groups.

wrist, and for pain intensity for each subject. Paired difference *t* tests were conducted to examine pretest vs posttest differences on continuous variables within each group. χ^2 Tests were used to examine the relationship between group membership and categorically coded variables of improvement on Phalen sign, Tinel sign, and sleep disturbance. The *P* < .05 level of significance was used. Post hoc analysis was carried out to calculate the appropriate sample size to detect clinically meaningful differences in each of the proposed tests. For variables measured on a continuous scale this sample size would yield a power of 80%, and for variables measured on a categorical scale power would be 64%.

RESULTS

Of the 51 subjects who met inclusion criteria and were randomized, 9 dropped out or were excluded (Figure 1). Final data were analyzed for 42 subjects (67 unique wrists with CTS), 22 (35 wrists) in the yoga group and 20 subjects (32 wrists) in the control group (Table 2).

Table 3 shows a comparison between pretest and posttest results for pain, grip strength, and nerve conduction time (sensory and motor) in the yoga-treated

and control groups. Patients in the yoga-treated group had statistically significant improvements for grip strength and pain reduction. Trends toward improvement also were observed within the yoga-treated group in pretest to posttest measures of motor nerve conduction time, Phalen sign, Tinel sign, and sleep disturbance, although these trends were not statistically significant. Both groups also showed trends toward improvement in sensory and motor nerve conduction times, but no significant differences between pretest and posttest values were found. Results of repeated-measures analyses for between-group differences were not statistically significant for any of the variables. Improvement on Tinel sign, Phalen sign, and reported sleep disturbance were more common in the yoga-treated group, but were statistically significant only for improvement in Phalen sign (Table 4).

COMMENT

Occupationally related health problems such as CTS are the leading cause of lost earnings in the workplace.¹⁰ As a result of cumulative trauma disorders, businesses sustain substantial losses annually due to medical expenses and lost

productivity. In this study, a program of yoga-based simple stretching and postural alignment, which does not require drugs, expensive equipment, or surgery, reduced pain and improved grip strength for patients with CTS.

Yoga classes such as the one used in this study can improve awareness of proper postures and use of the upper extremities. Although not studied here, we propose that a properly supervised program may be helpful not only to treat symptoms, but also to prevent recurrences or the onset of symptoms.

Our study was designed as a preliminary study and as such has several limitations including small sample size, lack of generalizability, and the use of a simple wrist splint as a control. We did not obtain data on medication use, time lost from work, or patient compliance with wrist splint use or other therapies.

Although not systematically studied, many subjects in the yoga group reported that they maintained improvement in their CTS symptoms 4 weeks after conclusion of the program. Further studies are needed to ascertain whether a single course of yoga intervention with occasional reinforcement can be effective for long-term relief. Programs could be initiated at workplaces with a high incidence of CTS, perhaps with 2 classes per week for 8 to 10 weeks, with monthly follow-up sessions to monitor home practice. Continued evaluations of outcomes are needed to evaluate long-term effects of yoga on CTS symptoms, lost time from work, and patient satisfaction.

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Saw Palmetto Extracts for Treatment of Benign Prostatic Hyperplasia

A Systematic Review

Timothy J. Wilt, MD, MPH; Areef Ishani, MD; Gerold Stark, MD; Roderick MacDonald, MS; Joseph Lau, MD; Cynthia Mulrow, MD, MS

Objective.—To conduct a systematic review and, where possible, quantitative meta-analysis of the existing evidence regarding the therapeutic efficacy and safety of the saw palmetto plant extract, *Serenoa repens*, in men with symptomatic benign prostatic hyperplasia (BPH).

Data Sources.—Studies were identified through the search of MEDLINE (1966-1997), EMBASE, Phytodok, the Cochrane Library, bibliographies of identified trials and review articles, and contact with relevant authors and drug companies.

Study Selection.—Randomized trials were included if participants had symptomatic BPH, the intervention was a preparation of *S repens* alone or in combination with other phytotherapeutic agents, a control group received placebo or other pharmacological therapies for BPH, and the treatment duration was at least 30 days.

Data Extraction.—Two investigators for each article (T.J.W., A.I., G.S., and R.M.) independently extracted key data on design features, subject characteristics, therapy allocation, and outcomes of the studies.

Data Synthesis.—A total of 18 randomized controlled trials involving 2939 men met inclusion criteria and were analyzed. Many studies did not report results in a method that permitted meta-analysis. Treatment allocation concealment was adequate in 9 studies; 16 were double-blinded. The mean study duration was 9 weeks (range, 4-48 weeks). As compared with men receiving placebo, men treated with *S repens* had decreased urinary tract symptom scores (weighted mean difference [WMD], -1.41 points [scale range, 0-19] [95% confidence interval (CI), -2.52 to -0.30] [n = 1 study]), nocturia (WMD, -0.76 times per evening [95% CI, -1.22 to -0.32] [n = 10 studies]), and improvement in self-rating of urinary tract symptoms; risk ratio for improvement (1.72 [95% CI, 1.21-2.44] [n = 6 studies]), and peak urine flow (WMD, 1.93 mL/s [95% CI, 0.72-3.14] [n = 8 studies]). Compared with men receiving finasteride, men treated with *S repens* had similar improvements in urinary tract symptom scores (WMD, 0.37 International Prostate Symptom Score points [scale range, 0-35] [95% CI, -0.45 to 1.19] [n = 2 studies]) and peak urine flow (WMD, -0.74 mL/s [95% CI, -1.66 to 0.18] [n = 2 studies]). Adverse effects due to *S repens* were mild and infrequent; erectile dysfunction was more frequent with finasteride (4.9%) than with *S repens* (1.1%; $P < .001$). Withdrawal rates in men assigned to placebo, *S repens*, or finasteride were 7%, 9%, and 11%, respectively.

Conclusions.—The existing literature on *S repens* for treatment of BPH is limited in terms of the short duration of studies and variability in study design, use of phytotherapeutic preparations, and reports of outcomes. However, the evidence suggests that *S repens* improves urologic symptoms and flow measures. Compared with finasteride, *S repens* produces similar improvement in urinary tract symptoms and urinary flow and was associated with fewer adverse treatment events. Further research is needed using standardized preparations of *S repens* to determine its long-term effectiveness and ability to prevent BPH complications.

SYMPTOMATIC BENIGN prostatic hyperplasia (BPH) is one of the most common medical conditions in older men. As many as 40% of men aged 70 years or older have lower urinary tract symptoms consistent with BPH.¹ Treatment goals in the vast majority of men are to relieve irritative (urgency, frequency, and nocturia) and obstructive (weak stream, hesitancy, intermittency, and incomplete emptying) symptoms. In the United States, treatment of BPH exceeds \$2 billion in costs, accounts for 1.7 million physician office visits,² and results in more than 300 000 prostatectomies annually.³ Treatment options include lifestyle modification, device and surgical therapies, and pharmaceutical and phytotherapeutic preparations.^{4,5}

Phytotherapy or the use of plant extracts for treating BPH symptoms was first described in Egypt in the 15th century BC. Currently, phytotherapy is common in Europe and is increasing in the western hemisphere. The sale of all botanical medications in the United States is \$1.5 billion per year and the use of phytotherapies increased nearly 70% among US adults in the past year.^{6,7} Phytotherapeutic agents represent nearly half the medications dispensed for treatment of BPH in Italy, compared with 5% for α -

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blockers and 5% for 5 α -reductase inhibitors.⁸ In Germany and Austria, phytotherapy is the first-line treatment for mild-to-moderate lower urinary tract symptoms and represents more than 90% of all drugs prescribed for the treatment of BPH.⁹ In the United States, phytotherapies for BPH are readily available as nonprescription dietary supplements. Most of these compounds are unlicensed and often promoted to "maintain a healthy prostate" and as a natural and harmless treatment of BPH symptoms.

There are about 30 phytotherapeutic compounds used for the treatment of BPH.¹⁰ The most widely used is the extract of the dried ripe fruit from the American dwarf saw palmetto plant *Serenoa repens* (also known by its botanical name *Sabal serrulata*). Berries from saw palmetto were first used by the American Indians in Florida in the early 1700s to treat testicular atrophy, erectile dysfunction, and prostate gland swelling or inflammation.¹⁰ The medicinal value of *S repens* for relief of prostate gland swelling has been reported in medical literature since the 1800s. The mechanism of action of *S repens* is not known but may include alteration of cholesterol metabolism,¹¹ antiestrogenic, antiandrogenic, and anti-inflammatory effects,¹²⁻¹⁴ and a decrease in available sex hormone-binding globulin.¹⁵ Although *S repens* has been evaluated in several randomized trials its clinical efficacy has not been clearly demonstrated.

Our goal was to systematically review the existing evidence regarding the therapeutic efficacy and safety of the saw palmetto plant extract *S repens*. We specifically assessed whether *S repens* is more effective than placebo and as effective as other pharmacological therapies in improving symptoms and/or urodynamic measurements in men with BPH.

METHODS

Inclusion Criteria

Randomized controlled trials were included if participants had symptomatic BPH; the treatment intervention was a preparation of *S repens* (*S serrulata*, *Sabal serrulata*, *Serenoa serrulata*, Permixon, PA109, Serendax, Talso, Curbicin, Prostagutt, Prostaselect, Prostagalen, Prostavigol, Strogen forte, and SPRO 160/120) alone or in combination with other phytotherapeutic agents; a control group received either placebo or other pharmacological therapies for BPH; and the treatment duration was at least 30 days.

Identification of Relevant Trials

We searched MEDLINE for studies from 1966 to 1997 by crossing an opti-

mally sensitive search strategy for trials from the Cochrane Collaboration with the medical subject headings *prostatic hyperplasia*, *phytosterols*, *plant extracts*, *sitosterols*, *Serenoa repens*, or *Sabal serrulata*, including all subheadings.¹⁶ EMBASE, (1974-July 1997), Phytodok (Munich, Germany), and the Cochrane Library, including the database of the Cochrane Prostatic Diseases and Urologic Malignancies Group and the Cochrane Field for Complementary Medicine, were searched in a similar fashion. Reference lists of all identified trials and previous reviews were searched for additional trials. Expert relevant trialists and pharmaceutical companies were asked to identify additional published or unpublished trials. There were no language restrictions.

Data Extraction and Study Appraisal

Study characteristics, demographic information, enrollment criteria, therapy allocation, adverse effects, outcomes and numbers, and reasons for dropouts were extracted independently by 2 reviewers. Missing information was sought from authors and/or sponsors. Extracted data were reviewed by the principal reviewer and discrepancies resolved by discussion.

The main outcome was the efficacy of *S repens* vs placebo or active control in improving urologic symptom scale scores or global report of urinary tract symptoms (improved vs stable or worsened). Secondary outcomes included peak and mean urine flow, residual urine volume, prostate size, and nocturia.

As a measure of overall methodological study quality, we assessed the quality of concealment of treatment allocation according to a scale developed by Schulz et al,¹⁷ assigning 1 as poorest quality and 3 as best quality. The treatment allocation included (1) trials in which concealment was inadequate (eg, such as alternation or reference to case record numbers or to dates of birth); (2) trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories; and (3) trials deemed to have taken adequate measures to conceal allocation (eg, central randomization; numbered or coded bottles or containers; drugs prepared by the pharmacy; serially numbered, opaque, sealed envelopes, etc, that contained elements convincing of concealment). Additionally, we assessed whether study participants and investigators were blinded to the treatment provided.

Statistical Methods

A random-effects model was used to combine data for all outcomes. For continuous variables weighted mean differ-

ences and their 95% confidence intervals (CIs) were calculated using RevMan 3.0 software.¹⁸ For categorical variables weighted risk ratios (RRs) and 95% CIs were calculated.¹⁹ For continuous measurements, a difference between treatment means and its correlated SE of the difference were calculated using the methods of Lau¹⁹ and Laird and Mosteller.²⁰ Because studies did not report the SE of the difference between the means (*S repens* and control), analyses were carried out for 3 different assumed values of correlation (0.25, 0.50, 0.75). This approach was taken to test the sensitivity of the results to this unknown parameter. Because there were no statistically significant differences in the outcomes, according to the different correlation coefficients, we used SEMs calculated with a correlation coefficient of 0.50. χ^2 Tests were used for analysis of bivariate comparisons. To assess the percentage of patients having improvement in urologic symptoms, a modified intention-to-treat analysis was performed (ie, men who dropped out or were lost to follow-up were considered to have had worsening symptoms).²¹ The denominator for the modified intention-to-treat analysis included the number randomized to treatment at baseline, and the numerator included the number completing the trial and showing improvement.

RESULTS

The combined search strategies identified 24 reports of trials; 18 met inclusion criteria.²²⁻³⁹ Reasons for exclusion included duration unknown or less than 30 days ($n = 2$ trials)^{40,41}; no clinical outcomes (examining enzyme or tissue effects ($n = 3$))^{15,42,43}; and no indication of randomization ($n = 1$).⁴⁴ Main comparisons in the remaining studies were *S repens* alone vs placebo ($n = 10$); *S repens* in combination with other phytotherapeutic agents vs placebo ($n = 3$); *S repens* alone vs active control ($n = 2$); *S repens* vs another phytotherapeutic agent and vs placebo ($n = 1$); *S repens* in combination with other phytotherapeutic agents vs active control ($n = 1$); and *S repens* orally vs a rectal suppository form of *S repens*, a therapeutic bioequivalence study ($n = 1$). A total of 2939 participants were randomized in the 18 trials (1118 in trials of *S repens* alone or in combination vs placebo and 1821 in trials of *S repens* alone or in combination vs active control).

A description of the individual studies is available from the authors on request. The mean age of enrollees was 65 years (range, 40-88 years). The mean study duration was 9 weeks (range, 4-48 weeks). The percentage of men who dropped out

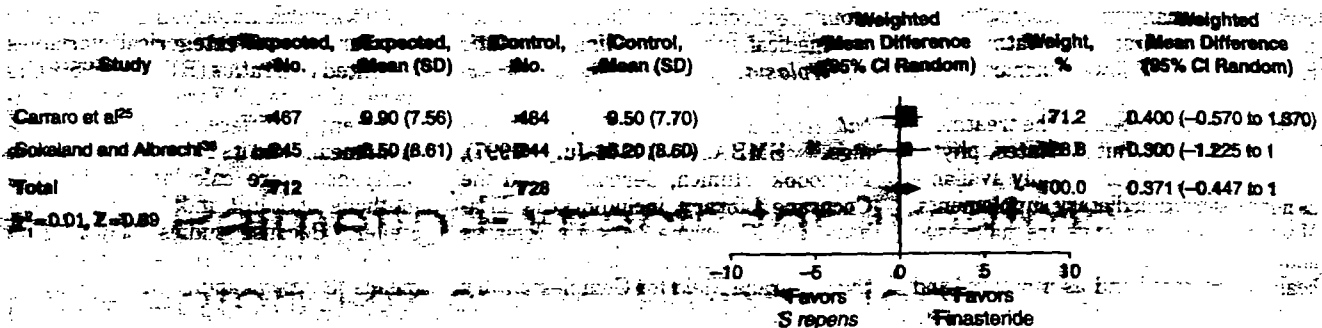


Figure 1.—Weighted mean differences in International Prostate Symptom Scale scores for men treated with *Serenoa repens* vs finasteride. CI indicates confidence interval.

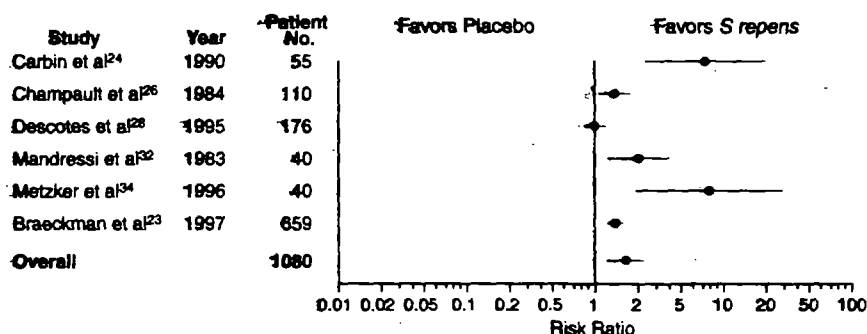


Figure 2.—Weighted risk ratios for self-rating of improvement in urinary tract symptoms for men treated with *Serenoa repens* vs placebo.

or were lost to follow-up was 9.6% (n = 283) and ranged from 4% to 15%. Treatment allocation concealment was adequate in 9 studies (50%) and 16 studies (89%) were double-blinded.

Baseline and outcome data from individual studies for urologic symptoms, nocturia, peak urine flow, and residual urine volume are available from the authors on request. These results indicate that on average, participating men had urinary tract symptoms and urinary flow measures consistent with moderate BPH. The mean (SD) baseline values for these variables did not differ by treatment group and included urologic symptom scale score (International Prostate Symptom Scale [IPSS]) in 2 studies with active control (14.4 [5.9] points; scale range, 0-35; moderate BPH symptoms, 8-19); urologic symptom scale score in 1 study with placebo (7.0 [2.8] points; scale range, 0-19, based on an addition of subscores for 6 variables: pollakiuria, nocturia, dysuria, hesitancy, urgency, and perineal heaviness); nocturia (2.5 [1.47] times per night; peak urine flow, 11.2 [3.9] mL/s; and residual urine volume, 55.8 [41.5] mL). Baseline values (SD) for mean urine flow (5.7 [2.1] mL/s) and prostate volume (43.9 [21.6] cc) also did not differ by treatment group. Symptom score results were reported in 10 stud-

ies, nocturia results in 12 studies, peak urine flow in 13 studies, and residual volume in 12 studies. Many studies did not report results in a method that permitted data to be combined in a meta-analysis.

Weighted Summary Differences in Outcomes

Urinary Tract Symptoms.—Summary treatment effect sizes were determined for *S repens* alone or in combination vs placebo and vs active controls. Results from participant and physician assessment indicated that *S repens* was superior to placebo and comparable with finasteride in improving urologic symptoms. The weighted mean difference for urinary symptom scale scores for *S repens* vs placebo was -1.41 points (scale range, 0-19) (28% absolute improvement vs placebo) (95% CI, -2.52 to -0.30) (n = 1 study) and vs finasteride was 0.37 IPSS points (scale range, 0-35) (37% absolute improvement from baseline for *S repens* vs 40% absolute improvement from baseline for finasteride) (95% CI, -0.45 to 1.19) (n = 2 studies) (Figure 1). The weighted mean difference for the combination preparation *Sabal-Urtica* vs placebo was -3.50 IPSS points (scale range, 0-35) (17% absolute improvement vs placebo) (95% CI, -6.75 to -0.25) (n = 1 study).

Participants and their physicians were both more likely to report improvement in symptoms in men treated with *S repens* than with placebo. The weighted RR for participant self-rating of improvement in urinary tract symptoms for *S repens* vs placebo was 1.72 (95% CI, 1.21-2.44) (n = 6 studies) (Figure 2). The weighted RR for physician rating of improved urologic symptoms for *S repens* vs placebo was 1.72 (95% CI, 1.11-2.65) (n = 3 studies). Overall, 242 (74%) of 329 men (6 studies) taking *S repens* reported an improvement of urologic symptoms compared with 168 (51%) of 330 men taking placebo (P < .001). Physician-assessed improvement of symptoms was reported in 165 (63%) of 262 men taking *S repens* and 101 (38%) of 262 men taking placebo (P < .001) (3 studies).

Serenoa repens reduced nocturia 25% (absolute difference) compared with placebo. The weighted mean difference was -0.76 times per evening vs placebo (95% CI, -1.21 to -0.32) (n = 10 studies) (Figure 3). *Serenoa repens* was comparable with active controls regarding nocturia. The weighted mean difference was -0.05 (95% CI, -0.49 to 0.39) (n = 1 study) vs finasteride and -0.20 (95% CI, -1.69 to 1.29) (n = 1 study) vs *Pygeum africanum*.

Urinary Flow Measures and Prostate Size.—*Serenoa repens* was superior to placebo and comparable with finasteride in improving peak and mean urine flow rates and residual urine volume. The weighted mean differences for peak urine flow were 1.93 mL/s vs placebo (24% absolute improvement vs placebo) (95% CI, 0.72-3.14) (n = 8 studies) (Figure 4), -0.74 mL/s vs finasteride (95% CI, -1.66 to 0.18) (n = 2 studies), 2.0 mL/s vs gestonorone caproate (95% CI, 1.36-2.64) (n = 1 study), and 1.6 mL/s for *Sabal-Urtica* vs placebo (95% CI, -0.67 to 3.87) (n = 1 study). The weighted mean differences for mean urine flow were 2.22 mL/s vs placebo (28% absolute improvement vs placebo) (95% CI, 1.17-3.27) (n = 4 studies) and -0.40 mL/s vs finasteride (95% CI, -0.15-0.95) (n = 1 study).

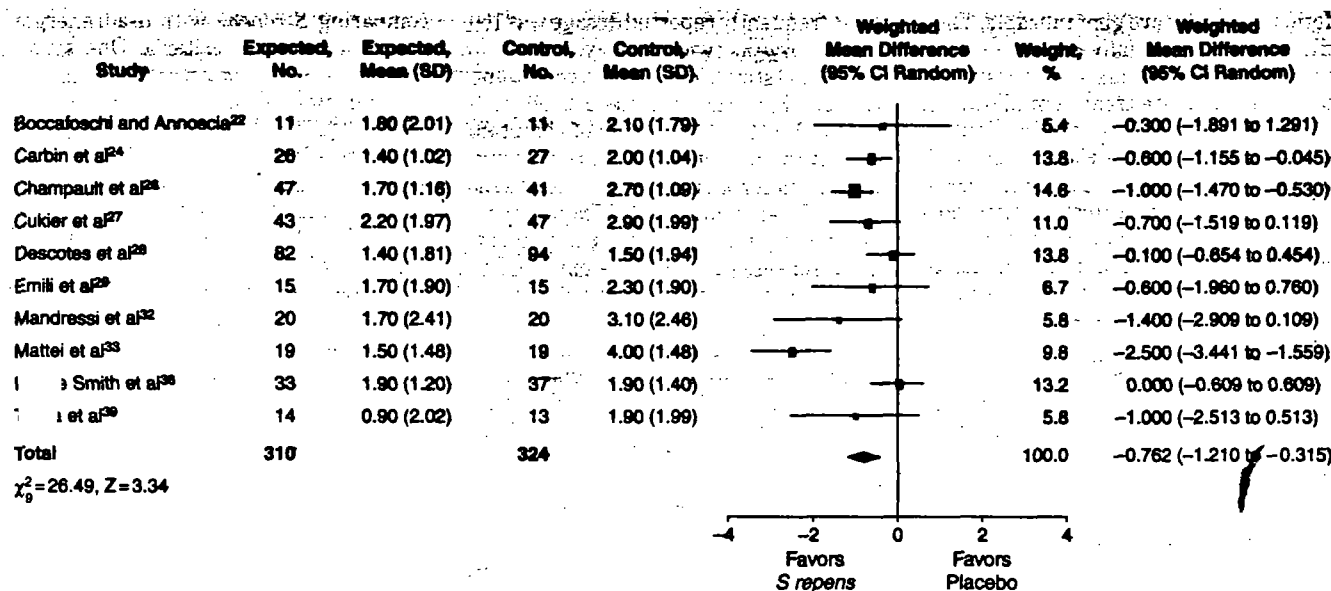


Figure 3.—Weighted means differences in nocturia for men treated with *Serenoa repens* vs placebo. CI indicates confidence interval.

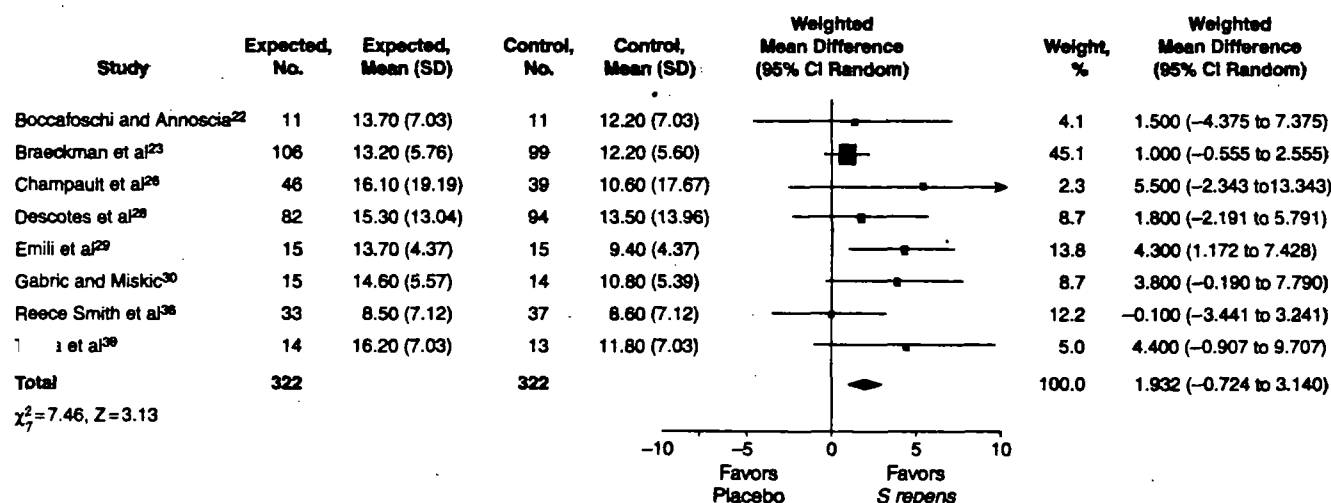


Figure 4.—Weighted mean differences in peak urinary flow rates for men treated with *Serenoa repens* vs placebo. CI indicates confidence interval.

For residual volume the weighted mean difference was -22.05 mL vs placebo (43% absolute decrease vs placebo) (95% CI, -40.78 to -3.32) ($n = 6$ studies) and 5.70 mL vs finasteride (95% CI, -5.42 to 16.82) ($n = 1$ study). *Serenoa repens* did not reduce prostate size; the weighted mean differences for prostate size were -2.14 cc (95% CI, -10.92 to 6.65) ($n = 2$ studies) vs placebo, and 4.08 cc (95% CI, 1.42-8.18) ($n = 1$ study) vs finasteride.

Adverse Effects

Adverse effects due to *S repens* were generally mild and comparable with placebo. Withdrawal rates were *S repens*, 9.1%; placebo, 7.0%; and finasteride, 11.2% ($P = .02$ for *S repens* vs placebo and $P = .87$ vs finasteride). Erectile dysfunction

was reported in 1.1% of men taking *S repens*; placebo, 0.7%; and finasteride, 4.9% ($P = .58$ for *S repens* vs placebo and $P < .001$ vs finasteride). Gastrointestinal adverse effects were reported in 1.3% of men taking *S repens*, placebo, 0.9%; and finasteride, 1.5% ($P > .50$ vs placebo and finasteride).

COMMENT

This systematic review summarizes the evidence from randomized controlled trials regarding the efficacy and safety of extracts from the saw palmetto berry *S repens* in men with lower urinary tract symptoms attributable to BPH. The available data indicate that *S repens* (alone or in combination with other phytotherapeutic agents) im-

proves urinary tract symptoms and urinary tract flow measures. Compared with placebo, *S repens* improved urinary tract symptoms by 28%, nocturia by 25%, peak urine flow by 24%, mean urine flow by 28%, and residual urine volume by 43%. Men taking *S repens* were nearly twice as likely to report improvement in symptoms than men taking placebo. When compared with finasteride, *S repens* provided similar responses in urologic symptoms and flow measures and was associated with a lower rate of erectile dysfunction.

Participant baseline characteristics regarding age, prostate volume, peak urine flow, and symptom scale scores were comparable with previous trials and meta-analyses involving pharmaco-

logical manager of BPH.⁴⁴⁻⁴⁶ Therefore, our results are generalizable. They did not substantially change when we restricted our analysis to studies that had adequate treatment allocation concealment (level 3) or were double-blinded. Furthermore, the treatment effect sizes with regard to symptom scale scores, peak and mean urinary flow, nocturia, and residual volume are considered clinically important and similar to effects reported with other pharmacological agents.⁴⁵⁻⁴⁸

METHODOLOGICAL ISSUES

Previous reviews of phytotherapy in the treatment of BPH were not structured systematic reviews or quantitative meta-analyses.^{9,10} They included information from nonrandomized or uncontrolled studies and, therefore, may have overestimated treatment effectiveness. The number of randomized trials included in these previous studies was less than we identified. The inclusion of an EMBASE and Phytodok search identified 5 studies not listed in MEDLINE. If our search had been restricted to English-language journals, we would have missed 12 trials (67%).

Our results should be viewed with caution. Despite abstracting and analyzing 18 randomized trials that included nearly 3000 participants, many studies did not report outcomes data in a consistent fashion. Several did not report means and SDs making completion of a quantitative systematic review difficult. Funnel plot analysis for urinary tract symptoms comparing study weight with weighted mean difference revealed no publication bias.⁴⁹ Multiple attempts to contact the trialists enabled us to obtain information from additional studies.⁵⁰

Only 3 studies reported results from standardized and validated urologic symptom scales.^{25,24,38} One trial reported results from a scale that had not been standardized or validated.²⁸ All these studies were rated as having adequate treatment allocation concealment. Most studies were conducted prior to the development of validated urologic symptom scale scores. Results from these scales have been demonstrated to be the most valid and clinically relevant end points for assessing treatment effectiveness in men with mild to moderate symptoms of BPH.³ Secondary outcomes were combined in only a minority of trials: mean urine flow (5 trials), peak urine flow (12 trials), residual volume (6 trials), nocturia (11 trials), and prostate size (3 trials). The treatment duration was short with only 2 studies having follow-up of at least 6 months' duration. Studies used different doses and preparations of *S repens* or were performed in combination with

other phytotherapeutic compounds. The most frequently reported dosage was 160 mg of *S repens* twice per day.

Several statistical issues in combining the data in our analysis need to be mentioned. For the "self-rating of symptom improvement" outcome, there was significant heterogeneity in the treatment effects. Ideally, when significant heterogeneity of treatment effect is present, meta-regression should be explored to understand reasons for the differences. However, this was not possible here because of an insufficient number of studies and lack of standardized reporting of meaningful clinical covariates. Nonetheless, if an overall quantitative estimate is deemed to be useful, then a random-effects model that incorporates between-studies heterogeneity would be more appropriate as we have done. The random-effects model typically produces wider CIs compared with the fixed-effects model. Five of 6 studies^{23,24,26,32,34} had significant treatment effects and the second largest study also had trends in the same direction, thus reducing the likelihood that the pooling produced a false-positive result.

Because of the high baseline response rate in the control groups and the wide range of the baseline rates of several studies, the choice of treatment effect metric used to combine outcomes may also affect the results. Compared with the pooled random-effects RR (RR, 1.71; 95% CI, 1.22-2.39), the pooled odds ratio (OR) is much higher (OR, 5.74; 95% CI, 2.14-15.35). The OR is frequently used to approximate the RR in the clinical trial setting. In this case, the high pooled OR creates a false impression that *S repens* is far more efficacious. We chose the more conservative metric provided by the RR in our analysis.

We were not able to determine if *S repens* prevented long-term complications of BPH, such as acute urinary retention or the need for surgical interventions. Previous studies have demonstrated that, in men with large prostates (ie, >40 cc) producing moderate to severe symptoms, finasteride is effective in relieving BPH symptoms and reducing the development of acute urinary retention and the need for surgical intervention.^{45,46} However, fewer than one third of men with BPH have prostate glands more than 40 cc in size.⁶¹ In men with "large prostates," the absolute rate of acute urinary retention or symptomatic progression requiring surgical intervention is less than 3% per year. In our review, the mean prostate volume in studies reporting prostate size was 44 cc. The available data did not allow us to determine if prostate volume was an important predictor of outcomes. Addi-

tionally, there were no reported studies comparing *S repens* with α -adrenergic blockers that met criteria. One study compared *S repens* with alfuzosin, but the duration of follow-up was only 3 weeks.⁴¹

The medication charges of *S repens* are less than other pharmacological therapies. A 90-day supply of saw palmetto berry (320 mg/d of *S repens*) is between \$10 and \$50. However, available dosages and preparations frequently vary from those used in the published trials. The pharmacy charges for a 90-day supply of finasteride or terazosin (5 mg/d) are approximately \$200 and \$120, respectively.⁴

Additional placebo-controlled trials are needed as well as studies that compare *S repens* with α -antagonists.^{47,48} Future trials should be of sufficient size and duration to detect important differences in clinically relevant end points. At a minimum, these studies should assess and report the means and SDs at baseline and conclusion for the following variables: age, number enrolled and completing the study, standardized urologic symptom scale scores, mean and peak urine flow, voided volume, prostate size, residual urine volume, complications from BPH, need for subsequent therapy, and long-term adverse effects of *S repens*. Until then, this systematic review provides the most complete assessment regarding the efficacy and safety of *S repens* for treatment of symptomatic BPH.

In conclusion, the available evidence suggests that extracts from the saw palmetto plant, *S repens*, improve urinary tract symptoms and flow measures in men with BPH. Compared with finasteride, *S repens* produces similar improvements in urinary tract symptoms and flow measures, has fewer adverse treatment effects, and costs less. The long-term effectiveness and safety of *S repens* and its ability to prevent complications from BPH are not known.

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Medical Malpractice Implications of Alternative Medicine

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Although use of alternative therapies in the United States is widespread and growing, little is known about the malpractice experience of practitioners who deliver these therapies or about the legal principles that govern the relationship between conventional and alternative medicine. Using data from malpractice insurers, we analyzed the claims experience of chiropractors, massage therapists, and acupuncturists for 1990 through 1996. We found that claims against these practitioners occurred less frequently and typically involved injury that was less severe than claims against physicians during the same period. Physicians who may be concerned about their own exposure to liability for referral of patients for alternative treatments can draw some comfort from these findings. However, liability for referral is possible in certain situations and should be taken seriously. Therefore, we review relevant legal principles and case law to understand how malpractice law is likely to develop in this area. We conclude by suggesting some questions for physicians to ask themselves before referring their patients to alternative medicine practitioners.

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MANY AMERICANS seek medical care from practitioners of alternative medicine. (We define *alternative medicine* as medical interventions not taught widely at US medical schools or generally available at US hospitals.) In 1990, chiropractors, acupuncturists, massage therapists, naturopaths, and a variety of other practitioners of alternative medicine received 425 million visits, for which patients paid \$10.3 billion in out-of-pocket expenses.¹ Financial analysts have suggested that consumer spending on alternative medicine may have surged 69% since 1989,² and the market may be growing as fast as 30% annually.³ Employers and insurers, including several major managed care organizations such as Oxford Health Plans and Health Net, have recently begun to respond to this demand by adding alternative therapies to their insurance products.⁴⁻⁶ As well, state legislatures have enacted laws that require health

insurers to include alternative treatments in the benefits they cover.⁹

Despite this activity, coordination between alternative and conventional medical care remains poor. An estimated 90% of patients using alternative medical care are not referred by their physicians (MDs or DOs) but are, instead, self-referred.¹ This lack of communication and the absence of proactive referral for alternative treatment or, when appropriate, professional advice to avoid alternative care are unfortunate from a quality perspective. Various measures to improve the coordination between physicians and alternative medicine practitioners have been proposed.¹⁰

Improved quality of care in this area is frustrated by a longstanding professional rivalry between organized medicine and unorthodox health care practitioners.^{11,12} However, a more fundamental obstacle is physicians' lack of knowledge about the appropriateness and efficacy of alternative medicine. While anecdotal evidence abounds, only a few well-designed clinical studies have examined the efficacy of alternative medicine therapies.¹³⁻¹⁹ Additional outcomes studies and randomized trials are only now being launched.²⁰

A subset of these general doubts and concerns about alternative medicine relates to medical malpractice.²¹⁻²⁶ We believe physicians worry that they will be sued if a patient they refer to an alternative medicine practitioner suffers a poor outcome. Even when patients have independently chosen to submit to alternative treatment, physicians may be reluctant to discover or discuss this care with them for fear that, if they know about it, they will be deemed to endorse it.

To address these issues, we have examined available data on rates of claims against chiropractors, acupuncturists, and massage therapists. Next, we explore the kinds of situations in which physicians may be exposed to liability for the referrals they make. Finally, we note the approach courts have adopted in assessing the malpractice liability of alternative medicine practitioners. We conclude that malpractice concerns alone should not inhibit physicians from referring patients to alternative medicine practitioners, particularly where those practitioners are licensed and accredited. A caveat to our conclusions is that legal principles in this area are not well devel-

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Table 1.—Selected Claims Information for Massage Therapy, Chiropractic, and Medicine, 1990-1996

	Claims per 100 Policy Holders			Average Indemnity Payment per Paid Claim, \$			Claims Paid, %		
	Massage Therapy*	Chiropractic†	Medicine (Primary Care)‡	Massage Therapy	Chiropractic	Medicine (Primary Care)§	Massage Therapy	Chiropractic	Medicine (Primary Care)
1990	...	2.7	7.7 (5.9)	...	33 625	137 900 (129 213)	...	49.1	31.9 (32.5)
1991	...	2.7	8.2 (5.7)	...	43 670	159 788 (148 533)	...	49.0	33.1 (32.0)
1992	...	2.8	9.1 (6.9)	...	40 621	183 541 (143 730)	...	47.5	33.2 (33.9)
1993	0.2	3.0	9.8 (7.1)	12 011	52 231	185 243 (147 084)	38.5	56.9	30.3 (30.7)
1994	0.2	2.7	9.5 (6.7)	4251	65 597	182 003 (151 001)	44.8	46.0	31.7 (30.2)
1995	0.2	2.6	9.0 (6.2)	4864	52 385	179 732 (149 028)	63.0	49.5	30.2 (30.3)
1996	0.1	2.2	...	4253	60 985	202 772 (166 379)	23.8	46.0	28.6 (29.9)

*Data from Albert H. Wohlers & Co, Park Ridge, Ill. Ellipses indicate data were not available prior to 1993.

†Data from the NCMIC Insurance Company, Des Moines, Iowa.

‡Data from Gonzales.²⁹

§Data from PIAA Data Sharing System, Rockville, Md.

oped—a situation that is poised to change as conventional and unconventional medicine become increasingly integrated in health care delivery systems.⁸

CLAIMS EXPERIENCE

Alternative medicine accounts for approximately 5% of the total medical malpractice insurance market, and coverage is provided by fewer than 50 insurers.²⁶ We collected claims information from the leading indemnity insurers in the country serving chiropractors, massage therapists, and acupuncturists. Together these 3 groups of practitioners account for approximately two thirds of the estimated 425 million visits made annually to offices of alternative medicine practitioners.¹

Chiropractic data were obtained from NCMIC Insurance Company (NCMIC) of Des Moines, Iowa. NCMIC insured 25 103 chiropractors in 1996, nearly half of all licensed chiropractors practicing in the United States.²⁷ We obtained data on claims against massage therapists from Albert H. Wohlers and Co of Park Ridge, Ill. Wohlers has provided professional indemnity insurance services to members of the American Massage Therapy Association (AMTA) since 1993 and currently insures approximately 27 000 massage therapists throughout the country—again, almost half of all licensed practitioners in this area. Acupuncture Insurance Services of Elmhurst, Ill, provided information on acupuncture claims. With approximately 1500 policyholders in 1996, it is the largest carrier of insurance for acupuncturists in the United States.

The data used to describe the claims experience of physicians are drawn from 2 sources. Information on claims paid against physicians comes from the Physician Insurers Association of America's (PIAA's) Data Sharing Project.²⁸ Information on claims frequency comes from the American Medical Association's annual core survey of a national sample of physicians. In contrast to our other claims data, the survey data reflect the experience of a general physician population (excluding federally employed physicians) rather than a discrete population defined by a specific insurer.²⁹

To maximize comparability of the data, we specified a number of parameters: (1) a claim was defined as a formal demand for compensation arising from health care (ie, incident reports were excluded); (2) multiple claims against a single insured

that related to the same incident were counted as a single claim; (3) claims against multiple practitioners relating to the same incident were counted separately; (4) all claims for which a nonzero indemnity payment was made to the plaintiff were counted as paid claims; and (5) claims were assigned to years according to file date, and payment figures were assigned to years according to closure date.

Table 1 compares the claims rates, average amount on paid claims, and percentage of claims among massage therapists, chiropractors, and primary care physicians for 1990 through 1996. Claims rates against chiropractors insuring through NCMIC have remained steady at 2 to 3 claims per 100 policyholders per year through the 1990s. The average severity of claims against chiropractors, as measured by average indemnity amounts on paid claims, increased by 81%. Conventional medicine experienced this same trend with a 47% increase. NCMIC resolved approximately half of its claims with payment, 18% more on average than did PIAA insurers. Table 2 shows the percentage of claims received by NCMIC in various injury categories during 1992 through 1996.

Table 1 also shows that rates of claims against massage therapists are less than one tenth of those against physicians and decreased in 1996. Table 3 shows the percentage of claims against AMTA members received by Wohlers in various injury categories during 1993 through 1996. Most claims (61%) relate to minor injuries, although a significant proportion (14%) relate to sexual misconduct.

Less information is available on rates of claims against other practitioners of alternative medicine. We were unable to obtain comprehensive data on claims against acupuncturists; however, some information on claims history was obtained from Acupuncture Insurance Services. Although this company insures one sixth of the 8900 licensed acupuncturists in the country,³⁰ it has had ongoing difficulties underwriting its policies because of its relatively small insurance pool.

After working through several offshore underwriters during the 1980s, a relatively stable relationship with a domestic underwriter was disrupted when a single acupuncturist apparently infected 35 people with hepatitis B,³¹ 21 of whom filed claims (Martin Shaw, president, Acupuncture Insurance Services, oral communication, March 1997). The other major

Table 2.—Categories of Claims Against Chiropractors, 1992-1

Type of Injury	Total Claims, %	Paid Claims, %
Disk	27.1	27.6
Failure to diagnose	12.2	11.3
Fracture	13.5	10.3
Aggravation of existing condition	7.6	9.9
Cerebral vascular	6.4	2.9
Vicarious liability	3.5	4.5
Other	30.7	23.5

*Data obtained from the NCMIC Insurance Company, Des Moines, Iowa.

claims experienced by Lincoln in its 15 years of operation include a case of irreversible nerve damage, several burns, and 2 cases involving pneumothorax.

The best explanation for the relative infrequency and lower severity of claims against alternative medicine practitioners concerns the nature of alternative therapies. Since rates of medical injury increase with invasiveness of therapy,³² fewer bases for suit are likely to present in the largely noninvasive alternative medicine setting. Moreover, injuries that do occur may not be as severe.

Another explanation may be the immature state of medical malpractice law and claims consciousness outside conventional clinical medicine—a phenomenon that may change as use and awareness of alternative therapies grow and as these therapies are progressively integrated into health care delivery systems. A third explanation may be that personal characteristics of alternative medicine practitioners and their patients or the dynamics of that patient-practitioner relationship are associated with a reduced propensity to sue, whether or not negligence occurred.

From the perspective of a physician who is concerned about the malpractice implications of referring to alternative medicine practitioners or comanaging patients with them, these findings should offer a degree of reassurance: they diminish the practical importance of situations in which practitioners might be exposed to liability for mere referral. Nonetheless, such situations can arise and should be taken seriously, particularly in light of uncertainty about how courts will decide medical malpractice cases.

LIABILITY FOR REFERRAL TO ALTERNATIVE MEDICINE PRACTITIONERS

As a general rule, a physician's mere referral of a patient to another physician, without more, does not expose the referring physician to liability.³³⁻³⁶ This rule has been applied by courts throughout the country in cases involving referral among physicians. Yet in certain circumstances—alluded to in the qualification, "without more"—the rule does not hold. These exceptional situations in the context of alternative medicine can be divided into 2 categories: (1) situations in which a decision to refer the patient for alternative medical treatment is negligent and (2) situations in which the referring physician is held liable for the treating practitioner's negligence because the physician supervised the care, jointly treated the patient, or knew the practitioner to whom the physician referred the patient was incompetent.

In the first category, the referral itself falls short of the reasonable practice standard and is sufficient to form the basis of a malpractice lawsuit, regardless of the quality of care delivered by the practitioner to whom the referral is made. The law still requires that the patient suffer injury causally related

Table 3.—Categories of Claims Against Therapists, 1992-1

Type of Injury	Claims, %
Minor	61
Major	5
Graves	1
Nonphysical	15
Sexual misconduct	14
Other	4

*Data obtained from Albert H. Wohlers & Co, Park Ridge, Ill.

†Includes soft tissue injuries, minor fractures, and minor scarring with no residuals.

‡Includes fractures, serious internal injuries, serious back injuries (ie, fusions, ruptured disks, laminectomies), loss of vision in 1 eye, and serious scarring.

§Includes brain damage, quadriplegia, severe burns, fatalities, dismemberment of 1 or more major limbs, and extremely serious multiple fracture cases.

to the substandard referral. But if, for example, a physician refers a patient to an alternative medicine practitioner instead of to some other, more appropriate practitioner and the referral delays, decreases, or eliminates the opportunity for the patient to receive important care, the referring physician could be held liable.³⁶

Available empirical evidence on alternative medicine use suggests that this type of referral liability may be a theoretical concern more than a practical one: the most commonly used alternative therapies treat minor ailments or serious conditions for which conventional medicine can offer little in the way of therapeutic benefit.¹ Nonetheless, it does highlight an important reason why physicians who refer to alternative medicine practitioners should be familiar with the efficacy of various alternative therapies. As knowledge about the appropriateness of alternative therapies expands, courts may determine that physicians act negligently when they refer patients for particular therapies that they know or should know offer no practical benefit to the patient.³⁷

Another complicating issue with regard to the choice of referral is the increasingly complex set of influences brought to bear on physician decision making. Guidelines, incentives, and restrictions aimed at influencing physicians' referral decisions are hallmarks of the managed care environment.^{38,39} Managed care organizations typically seek to minimize the use of specialist care and limit expensive tests that offer little or no marginal benefit.^{40,41} Analogously, a plan that covers alternative medicine services may, for example, determine that its enrollees should be referred to chiropractors rather than to orthopedic surgeons, given certain clinical indications. Were liability for this type of referral to be considered by the court, the plan's guidelines or incentives could potentially mitigate the referring physician's exposure to liability, although such "reallocation" of liability has been slow to develop because of a range of barriers to holding managed care organizations liable for malpractice.⁴² Yet another complication is the increasingly common practice of using alternative medical care as an adjunct to allopathic care.

The second category of exceptions to the general rule of nonliability for referral arises when the practitioner to whom a patient is referred renders negligent care that injures the patient and for which the referring physician is then considered partially or wholly responsible. There are several situations in which courts may impute liability in this way, all of which involve *vicarious liability*, defined as liability of a person or organization for the negligence of an employed individual. (Vicarious liability includes liability of supervisors [*respondeat superior*] and apparent authority, that is, when an individual apparently represents an organization.)

First, when physician A refers a patient to physician B then exerts authority over the way physician B treats that patient, physician A may be held liable for physician B's negligent acts. In finding vicarious liability, the law considers that physician B merely acts as physician A's agent. The question of whether an agency relationship exists and hence whether vicarious liability may be appropriate for that reason depends on the level of actual (or apparent) control maintained by the referring physician.

Courts have generally been reluctant to find that one physician controls another, setting a fairly high threshold for plaintiffs who attempt to establish liability on this basis.^{35,43-45} However, referral to an allied health professional—for example, a nurse practitioner or physician assistant—presents a slightly different situation. A physician may be held liable for the negligent acts of allied health professionals, such as nurses, when the physician takes charge or supervises the care provided.^{46,47} The same is true if a health care organization supervises the allied health professional. Moreover, by requiring the adoption of written protocols for collaboration, professional regulation in many states explicitly commits physicians to a supervisory role over allied health professionals such as nurse practitioners, physical therapists, and physician assistants, particularly in the area of drug prescription.^{48,49}

Leading cases addressing this type of vicarious liability have considered care delivered in the operating room setting, rather than referrals^{46,47,50}; they have also involved practitioners using the same approach to healing (ie, conventional medicine). Nonetheless, the manner in which alternative medicine services are integrated with conventional medical services will be important in determining whether referral involves the requisite level of actual or apparent control that courts have demanded to establish the agency relationship and so constitute an exception to the general rule of nonliability for referral.

Physicians who maintain a supervisory role over the patient's care or who refer in circumstances where the patient might reasonably expect that care will be supervised could be held to account for the negligent acts of the treating practitioner. From the perspective of physicians and health plans, the agency exception to the general rule of nonliability for referral would suggest good reasons for allowing alternative medicine practitioners to practice their craft freely once referral is made and also for ensuring that patients understand that referral initiates a new and separate patient-practitioner relationship. These recommendations would, however, be qualified if the alternative medicine practitioner is not licensed or is in an organization subordinate to the referring physician.

Second, liability may be extended to the referring physician in situations when the care given exhibits characteristics of a joint undertaking. Cases that have bound defendants together in this manner have looked for a fairly high degree of unity in the practitioners' approach to treatment.^{51,52} In fact, joint undertakings typically involve practitioners who act in concert, simultaneously administering treatment to a patient, rather than being separated by the referral process.

Under current health care arrangements, it seems unlikely that this kind of situation will arise between physicians and alternative medicine practitioners. However, it could emerge as a possibility if the practitioners are employed by the same hospital or health plan and collaborate closely in providing patient care. This level of collaboration could also exist in situations where physicians and alternative medicine practitioners

render care in a jointly owned or operated clinic. Similarly, as alternative medicine practitioners begin to deliver care alongside physicians in "integrated" units within a hospital or clinic, the possibility of a joint-undertaking situation does arise.

Third, the general rule of nonliability for referral may not apply when the referring physician knows that the practitioner to whom she or he refers the patient is incompetent.^{54,55,58} For example, if a physician is aware that a particular acupuncturist uses unsterilized needles or that the acupuncturist has recently been the subject of serious disciplinary action by a professional board, then the physician may be considered negligent if a patient referred to that acupuncturist suffers iatrogenic injury.

While the physician's own liability is certainly a consideration in the above scenario, the courts have been far more active in holding institutions accountable in this area. Hospitals⁵⁴ and managed care organizations^{55,56} have a legal obligation to be diligent in selecting, retaining, and evaluating health care professionals; this same obligation will extend to their relationship with alternative medicine practitioners. Therefore, the plan that credentials an incompetent acupuncturist may face liability as a corporation when a physician refers a patient to this practitioner for treatment, especially when it has established incentives or guidelines to facilitate this referral.

All of the above recommendations are contingent on the assumption that courts are not prepared to make presumptive judgments about the incompetence of alternative medicine practitioners, based solely on their idiosyncratic approaches to health care. If the courts were so prepared, this possibility has serious legal ramifications because it would allow liability of the referring physician to be inferred in a much wider range of cases—not merely those in which there is knowledge about a particular practitioner's incompetence. Once again, the courts do not yet appear to have considered this issue directly. However, we can find important clues about how they might deal with the situation by returning to litigation against alternative medicine practitioners and examining more closely how these cases have been decided.

REGULATION AND LIABILITY OF ALTERNATIVE MEDICINE PRACTITIONERS

A widely accepted rule of medical malpractice states that "a physician is entitled to have his treatment of his patient tested by the rules and principles of the school of medicine to which he belongs, and not by those of some other school."⁵⁷⁻⁶⁰ Although this rule is most often used as a basis for delineating different standards of care among conventional medical specialties, it has also been used to set standards for practitioners of alternative medicine in schools ranging from chiropractic to homeopathy, naturopathy (the resurgent remnants of the "drugless practitioners" of an earlier era⁶¹), and even Christian Science healing.^{62,63} An important rationale underlying school-specific standards is that, when a patient elects or gives informed consent to receive care from a particular practitioner, the patient is presumed to have also elected to be treated with an ordinary level of skill and care common to that practitioner's field of practice.⁶⁴

But courts have not applied a school-specific standard of care in situations where they do not recognize the school to which a defendant claims membership. How do judges make this decision? Licensure has thus far been the decisive piece of evidence in determining whether an identifiable school of

Table 4.—Statutory Licensure of Alternative Medicine Practitioners

Chiropractic			
Licensed in 50 states and District of Columbia*			
Massage Therapy			
AL	\$34-43-2	NM	61-12C-1
AK	\$17-86-102	NY	\$7802
CT	\$20-206	ND	43-25-01
DE	24 Del C 5306	OH	\$503.42
DC	\$2-3305	OR	\$687.011
FL	\$480.033	RI	\$23-20.8-1
HI	\$452.3	SC	\$40-30-110
IA	\$152C	TN	\$63.18-201
LA	37-3556	TX	4512K
ME	32 MRS 14306	UT	58-47b-304
MD	HOcc 3-5A-04	VT	26 VSA 3405
MA	c140 §51	VA	\$54.1-3029
NE	\$71-1278	WA	18.108.005
NH	328-B.4		
Acupuncture			
AK	\$08.06.030	NH	328-E:12
AZ	\$32-2901	NJ	45-9B-8
AR	\$17-102-101	NM	61-14A-4†
CA	BPC §4925†	NY	\$8214
CO	\$12-29.5	NC	\$90-455
CT	\$20-206bb	OR	\$677.759†
DC	\$2-3302.3	PA	63 PS §1803
FL	\$457.105†	RI	\$5-37.2-12
HI	\$436E-3	SC	\$40-47-40
IL	225 ILCS 2/15	TN	\$63-1-102
IA	\$148E.3	TX	4495b
LA	37-1357	UT	58-72-101
ME	32 MRS 12511	VT	26 VSA 3401
MD	HOcc 1A-201	VA	\$54.1-2900
MA	c112 §152	WA	18.06.050†
MN	\$147B.02	WV	\$30-36-1
MT	37-13-301†	WI	451.04
NV	\$634A.120†		
Naturopathy			
AK	\$08.45.020	ME	32 MRS 12521
AZ	\$32-1555	MT	37-26-401
CT	\$20-34	NH	328-E:14
DC	\$2-3309.1	OR	\$685.02
FL	\$462.18	UT	58-71-102
HI	\$455-3	VT	26 VSA 3401
KS	\$65-2872a	WA	18.36A.030
Homeopathy			
AZ	\$32-2915	NE	\$630A.230
CT	\$20-10	WA	18.36A.030

*Mandates for coverage of chiropractic services are in force in all but 8 states (CO, HI, ID, NH, OR, SD, VT, WY) and the District of Columbia.

†Coverage of acupuncture services in health insurance products is mandated by state law.

medicine exists⁶⁶⁻⁶⁷; the regulatory apparatus that accompanies licensure defines its scope. As one court stated: "Through the enactment of this legislation, the legislature has recognized the practice . . . as a separate and distinct health care discipline."⁶⁶ Another piece of evidence likely to be important in signaling a school's identity and validity is state legislative mandates that compel insurance companies to cover certain alternative medicine treatments in all policies sold.

The chiropractic profession is the best example of an easily recognizable school of alternative medicine. Chiropractors are licensed in all 50 states and the District of Columbia (Table 4).⁶⁸ Forty-two states mandate coverage of chiropractic services in health insurance policies (Susan S. Laudicina, director of state services research, BlueCross BlueShield Association, oral communication, March 1998). Courts apply a standard of care in malpractice actions against chiropractors enunciated by experts in the chiropractic profession itself. They will rarely hear the testimony of a physician for purposes of establishing the appropriate chiropractic standard of care.^{69,70,71}

Other schools of alternative medicine besides chiropractic have established systems of licensure and regulation (Table 4). Thirty-five states license acupuncturists (with 7 states mandating insurance coverage of acupuncture services), 27 states license massage therapists, 14 states license naturopaths, and 4 states license homeopaths. Few reported cases in the modern era have considered the liability of licensed practitioners of alternative medicine practicing in these areas. Nonetheless, it is entirely consistent with prevailing legal principles to expect that their conduct will be judged in the same way as chiropractic medicine.

In contrast, where practitioners of alternative medicine are unlicensed, courts tend not to recognize them as belonging to an identifiable school of medicine and hence do not apply a school-specific standard of care. Instead, the allegation of negligence will be judged according to conventional medical⁷⁰ or lay^{66,67} standards of care. A court's decision to adopt either of these alternate standards, rather than standards set by the defendant practitioner's own school, has a significant bearing on case outcome: it becomes more likely that the conduct under scrutiny will be judged negligent.

CONCLUSION

Opening a professional dialogue between physicians and practitioners of alternative medicine is crucial to better health care for those patients who choose alternative therapies. This need can be expected to grow with use of alternative therapies, particularly as health insurance plans include such therapies in the benefits they offer. The larger solution lies with better education for physicians about alternative medicine and further outcome studies and randomized trials that comprehensively assess the efficacy and relative safety of alternative therapies. Some of this work has begun, spurred by such developments as the Office of Alternative Medicine at the National Institutes of Health.⁷¹ However, clarification of the medical liability issues involved should remove a significant obstacle to integration and continuity of patient care.

Physicians who currently refer patients to practitioners of alternative medicine or who are contemplating doing so should not be overly concerned about the malpractice liability implications of their conduct. The same commonsense considerations applicable to other referrals will be a reasonably reliable guide regarding acceptable practice. However, it may be useful to ask the following questions. First, is there evidence from the medical literature to suggest that the therapies a patient will receive as a result of the referral will offer no benefit or will subject the patient to unreasonable risks? Second, is the practitioner licensed in my state? (Some added comfort can be derived from knowing that the practitioner carries malpractice insurance.) Third, do I have any special knowledge or experience to make me think that this particular practitioner is incompetent? And fourth, will this be the usual kind of referral (ie, basically at arm's length, without ongoing and intrusive supervision of the patient's management)?

If the answers to the first and third of these questions are no and the answers to the second and fourth questions are yes, then this should remove many of the concerns a physician has that the referral decision itself will be construed as negligent. This conclusion holds even if the patient suffers an injury caused by the alternative medicine practitioner's negligence. That practitioner should be held accountable for his or her autonomous actions and should be judged according to standards set by fellow practitioners.

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- 42 USC §225g.

Alternative Medicine—Learning From the Past, Examining the Present, Advancing to the Future

Medical practices outside the mainstream of "official" medicine have always been an important part of the public's health care. Healers and herbalists, bonesetters and barbers, shamans and spiritualists have offered the public a multiplicity of ways to address the confusion and suffering that accompany disease. A century ago in the United States there was a period of "enchantment" with unorthodox medicine. Homeopaths, herbalists, psychic and magnetic healers, and "eclectics" proliferated—most with little to no training, regulation of practice, or standards for quality of care. The prominence and configuration of these "irregulars," as they were called, has waxed and waned, depending on the perceived value of orthodox medicine, the needs of the public, and the changing values of society. The prominence of these practices subsided with the development of scientific medicine in this century and its dramatic advances in the understanding and treatment of disease.¹

Historically, orthodox medicine fights these practices vigorously by denouncing and attacking them, restricting access to them, labeling them as antiscientific and quackery, and imposing penalties for practicing them. When these therapies persist and even rise in popularity despite this, mainstream medicine then turns more friendly, examining them, identifying similarities they have with the orthodox, and incorporating or "integrating" them into the routine practice of medicine.² In the past, orthodox medicine has benefited from their selective integration by abandoning ineffective therapies such as bloodletting, adopting new drugs such as digitalis, and developing more rigorous scientific methods with which to test these practices, such as blinding and randomization.^{2,3}

The increasing popularity of complementary and alternative medicine (now used by more than 40% of the public) reflects changing needs and values in modern society in general.⁴ This includes a rise in prevalence of chronic disease, an increase in public access to worldwide health information, reduced tolerance for paternalism, an increased sense of entitlement to a quality life, declining faith that scientific breakthroughs will have relevance for the personal treatment of disease, and an increased interest in spiritualism.⁵⁻⁷ In addition, concern about the adverse effects and escalating costs of conventional health care are fueling the search for alternative approaches to the prevention and management of illness.^{6,7} As the public's use of healing practices outside conventional medicine accelerates, ignorance about these practices by physicians and scientists risks broadening the communication gap between the public and the profession that serves them.^{4,8}

Today, the overwhelming effort is toward attempts at "integrating" alternative practices into the mainstream. Sixty percent of medical schools have begun to teach about alternative medicine practices,⁹ hospitals are creating complementary and integrated medicine programs, health suppliers are offering expanded benefits packages that include the services

of alternative practitioners,¹⁰ and biomedical research organizations are investing more substantial amounts toward the investigation of these practices. For example, the Office of Alternative Medicine at the National Institutes of Health has just become the National Center for Complementary and Alternative Medicine, with a budget of \$50 million. The activities of the Office of Alternative Medicine¹¹ and the publication of this issue of *JAMA* illustrate that quality scientific research can be conducted and published on alternative medicine topics. It appears that complementary and alternative medicine has again "come of age" in the United States. However, the rush to embrace a new integration of alternative and conventional medicine should be approached with great caution. Alternative medicine, like conventional medicine, has pros and cons, promotes bad ideas and good ones, and promises to hold both benefits and risks. Without critical assessment of what should be integrated and what should not, we risk developing a health care system that costs more, is less safe, and fails to address the management of chronic disease in a publicly responsible manner. The potential risks and benefits of alternative medicine must be examined carefully before heading into a new but not necessarily better health care world.

Risks of Embracing Alternative Medicine

Quality of Care.—The formal components of medical physician licensure usually are not required of alternative medicine practitioners. These include the content and length of time of training, testing and certification, a defined scope of practice, review and audit, and professional liability with regulatory protection and statutory authorization complete with codified disciplinary action.¹² All 50 states do provide licensure requirements for chiropractic practice, but only about half do so for acupuncture and massage therapy and fewer do for homeopathy and naturopathy. Many of these practitioners operate largely unmonitored.¹³

Quality of Products.—The "natural" products used by alternative medicine practitioners also are largely unmonitored and their quality is uncontrolled. These products are available on the market as dietary supplements and may be contaminated or vary tremendously in content, quality, and safety.¹⁴ Garlic, for example, claimed for many years to have cholesterol lowering effects, may not produce such effects if processed in certain ways.¹⁵ Thus, even if one product is proven safe and effective, other similar products on the market may have quite different effects that preclude consistent dosing. Fifteen million Americans are taking high-dose vitamins or herbal preparations along with prescription drugs, thereby risking adverse effects from unknown interactions.⁴

Quality of Science.—The use of science for understanding alternative medicine is frequently missing from such practices. Most alternative medicine systems have been largely unchanged for hundreds or thousands of years. Often they begin from the teachings of a charismatic leader that are not advanced with new observations, hypothesis-driven testing, innovation, and peer-review. Claiming that their practices are too "individual" or "holistic" to study scientifically, many al-

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ative cine practices hide behind anecdote, series, or "outcomes" research.¹⁶ To accept such views is to falsely label conventional medicine as nonholistic and reject the hard-fought gains made in the use of basic biological knowledge, the randomized, controlled clinical trial, and evidence-based medicine for health care decision making.¹⁷

To adopt alternative medicine without developing quality standards for its practices, products, and research is to return to a time in medicine when quackery and therapeutic confusion prevailed. Modern conventional medicine excels in the areas of quality health care and the use of science: alternative medicine must change to adopt similar standards. Conventional medicine is also the world's leader in the management of infectious, traumatic, and surgical diseases, in the study of pathology, and in biotechnology and drug development. All medical practices have the ethical obligation to retain these strengths for the benefit of patients.

Risks of Conventionalizing Alternative Medicine

Healing.—Most alternative medicine systems carefully attend to the illness and suffering that accompanies all disease. The time spent with each patient by an alternative medicine practitioner usually exceeds that spent by the average conventional physician, and patients are often more satisfied with their interactions with unorthodox than orthodox medical practitioners.¹⁸ Alternative medicine practitioners provide patients with understanding, meaning, and self-care methods for managing their condition. Empowerment, participation in the healing process, time, and personal attention are essential elements of all medicine. These elements are easily lost in the subspecialization, technology, and economics of modern medicine. Conventional medicine must develop a better language for managing illness and suffering or lose this essential message that alternative medicine provides.

Adverse Effects.—In the last century, unconventional medicine increased in popularity because of the use of severe treatments such as bloodletting, purging, and toxic metals by conventional medicine.² The popularity of alternative medicine in this century is also driven by the perception that conventional treatments are too harsh to use for chronic and non-life-threatening disease.^{6,7} Iatrogenic disease caused by conventional medicine is a major cause of death and hospitalization in the United States. While some alternative medicine practices have important toxicities, many have reduced potential for adverse effects when properly delivered.¹⁹ Conventional medicine can learn from alternative medicine how to "gentle" its approach by focusing on the patient's inherent capacity for self-healing.²⁰

Costs.—Skyrocketing costs of conventional medicine also are driving the search for alternatives. Savings from managed care now are maximized and health care costs are predicted to double in the next 10 years.²¹ If low-cost interventions such as lifestyle changes, diet, supplement therapy, and behavioral medicine can be delivered as substitutes for high-cost drugs and technological interventions, true cost reductions and the compression of morbidity might be achieved.²²

If there is a single strength of alternative medicine that risks being lost in its "integration" with conventional care, it is an emphasis on self-healing as the lead approach for both improving wellness and for the treatment of disease. All the major alternative medicine systems approach illness first by trying to support and induce the self-healing processes of the person. If recovery can occur from this, the likelihood of adverse effects and the need for high-impact, high-cost interventions is reduced.²³ It is this orientation toward self-healing and health promotion (salutogenesis rather than pathogenesis) that makes alternative medicine approaches to chronic disease especially attractive.²⁴

The Future of Alternative Medicine

The main "obstacles to discovery," writes Daniel Boorstin,²⁵ are "the illusions of knowledge." Indeed, the capacity of humans to fool themselves by making claims of truth, postulating unfounded explanations, and denying the reality of observations they cannot explain is endless. Science has emerged as one of the few truly powerful approaches for mitigating this self-delusory capacity. The clinical experimental method, in the form of the randomized, controlled trial, examines to what extent attributions and explanations of these therapies are accurate.²⁶

The goals of medicine, no matter what the label, are the same for all practices.²⁶ Is the current trend toward "integrated" medicine a deluded temptation that will turn out to be a nightmare of unscientific practices? Or will these newfound tools of scientific medicine be used to look deeper into the processes of healing for their utility in treating disease and alleviating suffering? In the last 50 years, powerful social forces have transformed medicine.⁵ If a new evidence-based "integrated" medicine does emerge, it will likely be subject to the same forces shaping the future of medicine in general. This includes the continued takeover of medicine by managed care, a more refined ability to manipulate individual susceptibilities using nanotechnology, and the ability to track quality of care and individual patient outcomes with networks of information monitoring.²⁷ Research in alternative medicine will help identify what is safe and effective and will further the understanding of biology by exploring, rather than marginalizing, unorthodox medical claims and findings.²⁸ Alternative medicine is here to stay. It is no longer an option to ignore it or treat it as something outside the normal processes of science and medicine. The challenge is to move forward carefully, using both reason and wisdom, as we attempt to separate the pearls from the mud.

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Alternative Medicine Meets Science

There is no alternative medicine. There is only scientifically proven, evidence-based medicine supported by solid data or unproven medicine, for which scientific evidence is lacking. Whether a therapeutic practice is "Eastern" or "Western," is unconventional or mainstream, or involves mind-body techniques or molecular genetics is largely irrelevant except for historical purposes and cultural interest. We recognize that there are vastly different types of practitioners and proponents of the various forms of alternative medicine and conventional medicine, and that there are vast differences in the skills, capabilities, and beliefs of individuals within them and the nature of their actual practices. Moreover, the economic and political forces in these fields are large and increasingly complex and have the capability for being highly contentious. Nonetheless, as believers in science and evidence, we must focus on fundamental issues—namely, the patient, the target disease or condition, the proposed or practiced treatment, and the need for convincing data on safety and therapeutic efficacy.

Despite the increasing use of alternative medicine (also termed *complementary, integrative, or unconventional medicine*) in the United States and throughout the world, most alternative therapies have not been evaluated using rigorously conducted scientific tests of efficacy based on accepted rules of evidence. The lack of properly designed and conducted randomized controlled trials is a major deficiency. For some published studies, serious concerns have been raised regarding methodological quality. A National Institutes of Health expert panel concluded that current evidence is inadequate for development of practice guidelines for alternative therapies, largely because of lack of relevant outcomes data from high-quality clinical trials.¹ However, some advocates of alternative medicine argue that many alternative therapies cannot be subjected to the standard scientific method and thus, instead must rely on anecdotes, beliefs, theories, testimonials, and opinions to support effectiveness and justify continued use.

Regardless of the origin or type of therapy, the theoretical underpinnings of its mechanism of action, or the practitioner who delivers it, the critical questions are the same. What is the therapy? What is the disease or condition for which it is being used? What is its purported benefit to the patient? What are the risks? How much does it cost? And, perhaps most important, does it work? For virtually all medical therapies and interventions, whether conventional or alternative, determination of effectiveness and recommendations for clinical application should be based on the strength of the scientific evidence using explicit criteria for grading the quality of evidence^{2,3} (Table) and ratings for technology assessment⁴ (ie, "established," "promising," "investigational," "doubtful," or "unacceptable.")

While acknowledging that many therapies used in conventional medical practice also have not been as rigorously evaluated as they should be, we agree that most alternative medicine has not been scientifically tested.⁵ However, for alternative medicine therapies that are used by millions of patients every

day and that generate billions of dollars in health care expenditures each year, the lack of convincing and compelling evidence on efficacy, safety, and outcomes is unacceptable and deeply troubling. We believe that physicians should become more knowledgeable about alternative medicine and increase their understanding of the possible benefits and limitations of alternative therapies. By doing so, physicians will be able to serve as more useful sources of information for their patients and advise them appropriately. As with conventional therapies, advice should be based on data and scientific information rather than anecdotal information, misperceptions, or preconceived or unfounded notions about effectiveness or lack thereof.

This theme issue of *JAMA* and the annual coordinated theme issues of the 9 American Medical Association *Archives Journals* published this month on alternative medicine represent a planned, concerted effort by the editors of these scientific journals to address some of these issues by providing physicians and other health care professionals with clinically relevant, reliable, fresh scientific information on alternative therapies. In response to our call for papers on alternative medicine,⁶ we received more than 200 manuscript submissions to *JAMA* and many more manuscripts were received by the *Archives Journals*. The result, after our usual rigorous review process, is publication of more than 80 articles and editorials on alternative medicine in our 10 scientific journals, including 18 randomized trials and systematic reviews, on more than 30 different topics, and from more than 16 different countries.

This issue of *THE JOURNAL* includes 6 randomized clinical trials that evaluate the use of 6 diverse alternative medicine therapies for treatment of common clinical conditions. The results are intriguing. Bove and Nilsson⁷ report that chiropractic spinal manipulation is not effective for episodic tension headache. Cardini and Weixin⁸ found that moxibustion (stimulation of an acupuncture point by heat generated from burning a specific herb) is helpful for correction of breech presentation in late pregnancy. Bensoussan and colleagues⁹ document that a Chinese herbal medicine formulation improves symptoms of irritable bowel syndrome. Shlay and coinvestigators¹⁰ demonstrate that acupuncture is no more effective than amitriptyline or placebo for relieving pain due to human immunodeficiency virus-related peripheral neuropathy. Heymsfield and coworkers¹¹ determined that *Garcinia cambogia*, a common component of commercial weight-loss products, lacks efficacy as an

Categories for Rating Quality of Scientific Evidence for Effectiveness of an Intervention*

Quality of Evidence	
I.	Evidence obtained from at least 1 properly randomized controlled trial
II-1.	Evidence obtained from well-designed controlled trials without randomization
II-2.	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 center or research group
II-3.	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III.	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Information is from Lawrence et al.²

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antiobesity agent. In a preliminary study, Garfinkel and co-workers¹² report that a yoga-based intervention appears to hold promise for relieving some symptoms of carpal tunnel syndrome. In addition, a systematic review by Wilt and colleagues¹³ suggests that saw palmetto extracts improve urologic symptoms in patients with benign prostatic hyperplasia.

Perhaps just as important as the results of their studies, these investigators demonstrate that alternative medicine therapies and interventions can and should be evaluated using explicit, focused research questions¹⁴ along with established and accepted rigorous research methods¹⁵ (eg, appropriate controls, effective blinding procedures, adequate power, state-of-the-art techniques for systematic reviews); incorporating measurable, objectively assessed end points (eg, blinded assessment); and reporting meaningful patient-centered outcomes.

Two other studies in this issue provide additional new information on alternative medicine. In a replication of their previous nationally representative survey,¹⁶ Eisenberg et al¹⁷ report that the prevalence of use of at least 1 of 16 specific alternative therapies during the previous 12 months has increased significantly (from 33.8% in 1990 to 42.1% in 1997), that the estimated number of visits to alternative medicine practitioners increased dramatically (from 427 million in 1990 to 629 million in 1997), and that only 38.5% of those who used alternative therapies discussed them with their physician. Total out-of-pocket expenditures associated with use of alternative medicine in 1997 were estimated at \$27 billion. In an analysis of data from malpractice insurers from 1990 through 1996, Studdert and colleagues¹⁸ found that claims against chiropractors, massage therapists, and acupuncturists generally occurred less frequently and usually involved less severe injury than claims against medical doctors. The authors also summarize the legal issues and principles for physicians to consider when advising or contemplating referral of patients to alternative medicine practitioners.

Taken together, the articles published in this issue of THE JOURNAL and in the Archives Journals' theme issues on alternative medicine add a substantial amount of new information and scientific data on alternative therapies to the peer-reviewed mainstream medical literature. However, given the burgeoning use of alternative medicine therapies, the increasing numbers of patients who consult both medical doctors and alternative medicine practitioners, and the increasing number of insurance companies and managed care organizations offering programs and benefits for alternative medicine,¹⁹ the need for additional, carefully conducted, high-quality research is essential.

Priority for research funding for alternative medicine should be given to investigations of relevant clinical problems for which well-designed studies have shown encouraging results for alternative therapies, especially for conditions that are common and those for which conventional medicine has not been effective. Attention should be given to evaluation of safety and efficacy, but also to examining the effectiveness of a treatment strategy, with consideration of community practice settings, patient expectations and compliance, and cost-effectiveness.²⁰ Collaborative research, especially among the federally funded centers for alternative medicine research in the US and with international alternative medicine research centers, may improve efficiency in answering important research questions. We encourage high-quality, rigorous research on alternative medicine and invite authors to submit their best papers for our objective evaluation and consideration for publication.

However, until solid evidence is available that demonstrates the safety, efficacy, and effectiveness of specific alternative medicine interventions, uncritical acceptance of untested and unproven alternative medicine therapies must stop. Alternative therapies that have been shown to be of no benefit (aside from possible placebo effect) or that cause harm should be abandoned immediately. Physicians, insurance plans, medical centers and hospitals, managed care organizations, and government policymakers should base decisions regarding incorporation of and payment for alternative medicine therapies on evidence-based research and objective cost-effectiveness analyses¹⁹ rather than on consumer interest, market demand or competition, well-publicized anecdotal reports, or political pressures from well-organized and influential interest groups.

Ultimately, answering fundamental questions about efficacy, safety, appropriate clinical applications, and meaningful outcomes for all medical therapies, including those considered alternative medicine, requires critical and objective assessment using accepted principles of scientific investigation and rigorous standards for evaluation of scientific evidence. For patients, for physicians and other health care professionals, and for alternative medicine practitioners—indeed, for all who share the goal of improving the health of individuals and of the public—there can be no alternative.

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Resident Forum

Resident Physicians Section

Integrating Alternative Medicine Into Practice

Residents and other physicians may wonder whether alternative medicine offers new hope to patients or if such therapies constitute quackery. The notion of alternative medicine as quackery has been reinforced by a once commonly heard definition that equates alternative with any medical treatment not taught in accredited US medical schools. That definition is no longer valid, as more medical schools have added nontraditional courses in response to growing public interest in alternative therapies.

The change in attitudes toward these therapies can be seen in the change in language used to describe them; the terms now current imply a relationship between the different approaches to medicine. The word *alternative* is often replaced by the words *complementary* and *integrative*. *Complementary* implies that these modalities are performed as adjunct to, and not simply in place of, conventional western medicine. The newest term, *integrative medicine*, implies an even closer relationship—one in which western and alternative modalities are used together. Proponents of integrative medicine are creating clinics at which a physician evaluates a patient, makes a medical diagnosis, and then recommends a combination of therapies that may include pharmaceuticals, herbs, acupuncture, or even a massage.

Use of alternative medicine among the general population has skyrocketed in the last decade. Studies show that the percentage of people in the United States using alternative therapies has risen from 34% in 1990 to 69% in 1998.^{1,2} Patients spend more out-of-pocket money on alternative medicine than on visits to their primary care physician.¹ People are using alternative medicine for several reasons: they may have grown up with it as folk medicine, they have chosen a holistic lifestyle, or they have had a negative experience with conventional western medicine.

Fortunately, people still like their physicians. The majority of alternative therapies are used as an adjunct rather than as a replacement for conventional medicine. Only 4% of Americans use alternative therapies exclusively, and only 15% think these therapies are more effective than western medicine.³

The main reason physicians distrust alternative medicine is because most of these therapies have not been studied well. Research into alternative therapies is difficult for several reasons. Dietary supplements cannot be patented, hence companies that produce herbal products have no incentive to fund expensive research studies. Some have argued that traditional research cannot take into account all of the variables that are important to alternative therapies such as a person's "energy pattern." Nonetheless, research can assess meaningful patient outcomes.

Although the research is still scant, physicians must recognize that alternative medicine is not just a fad and recognize that our patients may already be using alternative therapies. We must be willing to discuss these therapies with patients. If we dismiss a patient's interest in an alternative therapy, the patient may choose to use it without the physician's knowledge. If, instead, we discuss the efficacy of an alternative therapy in a balanced manner, we are more likely to gain the patient's trust and respect. If we lose that trust, our patients may choose to get their health care advice from sales clerks at holistic stores.

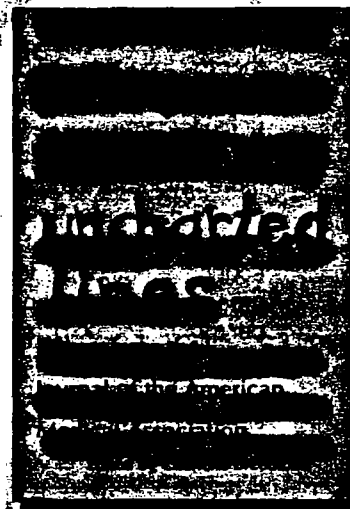
Even while keeping an open mind toward these therapies, physicians must demand that alternative therapies meet the same rigorous scientific standards as western medicine. Physicians should review the literature on alternative therapies, which is scarce but growing. The burden is truly on clinicians to explain to patients the importance of science over anecdotal evidence.

In addition to keeping an open mind, adventurous physicians might even try an alternative therapy such as acupuncture, meditation, or Tai Chi. Evaluate your experiences and the literature in a critical, unbiased fashion for the benefit of yourself and your patients.

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Poetry related to medicine has burgeoned over the past decade, becoming a recognizable genre in its own right. As health and medicine encompass ever more of our public and private concerns, the rising poetic response from those whose lives brush against illness seems a vibrant sign



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Factors That Shape Alternative Medicine

THE LACK OF relevant high-quality scientific research has often been given as a reason^{1,2} to explain why a large number of health care practices are termed *alternative*. However, the fact that it required congressional intervention^{3,4} for the National Institutes of Health (NIH) to earmark 0.02% (\$2 million) of its \$10.7 billion 1992 budget to evaluate practices used by more than 35% of the US population suggests that issues beyond the scientific were involved. Nonscientific factors have played a major role in limiting scientific exploration of these areas, have discouraged potential investigators, and have dictated greater profitability elsewhere. This article examines current definitions of alternative medicine and proposes a new one, outlining those factors, sociological (academic), political, regulatory, and economic, that must be considered when exploring this field.

Definitions of Alternative Medicine

Despite increasing use of alternative medicine,⁵ the creation of the NIH Office of Alternative Medicine (OAM), and increasing health insurance coverage for alternative therapies, no clear definition of alternative medicine has been established. When definitions have been proposed, they included either ad hoc lists of practices felt to be alternative^{6,7} or categorical criteria that are changing rapidly⁸ and, therefore, do not allow for a lasting definition of alternative medicine.

Lists of alternative medical practices are disparate^{6,7} and encompass complex traditional health care systems, eg, Chinese (traditional Chinese medicine), East Indian (Ayurveda), Native American,^{9,10} as well as their integrated and complementary components practiced as distinct entities (eg, medicinal herbs, acupuncture, dietary principles, and spiritual practices). These lists also include a wide variety of discrete modalities and products more difficult to categorize. Furthermore, among the proponents of practices such as hypnosis, osteopathy, and chiropractic (which have been taught in degree-granting institutions for more than a century), there is little consensus as to whether these modalities are alternative or mainstream.

Alternative medicine also has been defined as what is not taught in medical schools or not covered by insurance.⁸ These definitions also have drawbacks because their reference criteria are changing rapidly and are not consistent across the country. For example, in the 75 US medical schools that offer courses in alternative medicine, the curriculum varies widely.¹¹ Health insurance coverage for alternative practices also varies widely among insurers and regionally. Most important, these definitions do not provide a rationale for the term *alternative medicine* to encompass such diverse practices.

Commonalities Among Traditional Health Care Systems

Comprehensive traditional health care systems and their components form much of what is generally understood in the

United States as alternative medicine. Other alternative practices or products not originating in a traditional health care system also represent a substantial but less coherent grouping.

Traditional health care systems represent philosophical approaches to managing health and disease that differ substantially from those of Western biomedicine.^{9,10,12-14} The question of what is common to these traditional systems has been largely overlooked, but spirituality is an integral part of each. As this trait is often directly related to the dominant religion or philosophical system of the originating culture, it is taken for granted within the context of health care. For example, the ancient Chinese health care system was influenced by several spiritual schools, in particular Taoism.¹² Ayurveda, a traditional medical system of India, reflects the traditional Hindu world view.¹³ Similarly, Tibetan physicians practice Buddhist meditation as an integral part of their medical training.¹⁴

In many traditional medical systems, the primary explanation for biological phenomena is based on the existence of a "vital force," an elusive entity designated *Qi* in China, *Ki* in Korea and Japan, *prana* in India, and *vital force* in Western traditions (eg, homeopathy). The terms *energy* and *energy medicine* are also used with increasing frequency. However, given the scientific definition of energy, this designation is misleading, as nothing is known of the nature of this hypothetical entity.

Also common to traditional health care systems is the belief in a unity underlying all diversity, implying holism (or wholism), that nothing can be considered in isolation.¹²⁻¹⁵ In the realm of health, these principles lead to considering the person as an indivisible whole, rather than as dissected anatomic parts. Thus, diagnoses and treatments are based primarily on concepts of organ functions, although not necessarily directly correlated to the actual organ entities or their anatomic locations. In addition, it is believed that health maintenance depends on a proper interaction with the environment. Hence, therapeutic interventions include stimuli (eg, sound, color, and taste) for any of the 5 senses, as these allow the individual to interrelate with his or her environment. Similarly, means of communication with the "invisible" environment (eg, meditation or prayer) form an important part of the therapeutic approach.¹²⁻¹⁵

Conceptual Differences and Commonalities Between Biomedicine and Traditional Health Care

The characteristics common to traditional (alternative) systems of health (vital force, spirituality, and holism) also seem to distinguish them from biomedicine. Biomedicine is founded in part on materialism (in contrast to the vital force explanation). Materialism in this context refers to the theory that "physical matter is the only or fundamental reality, and that all beings and processes and phenomena are manifestations or results of matter."¹⁶ While biomedicine does not necessarily reject religion or spirituality, it does not routinely incorporate these aspects into diagnosis and treatment (unlike traditional systems). Consistent with this philosophical theory, biomedicine considers biological entities more or less as equal to the sum of their anatomic parts (a view opposite to holism) and endeavors to elucidate molecular, physiological, and patho-

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logical mechanisms believed to form the basis of biological processes. Allopathic medical treatment often logically consists of interventions chosen to interfere with identified pathological molecular processes.

As it has not been scientifically demonstrated that "physical matter is the only reality," materialism, therefore, is akin to a religion, ie, "a system of beliefs held to with ardor and faith."¹⁵ Western allopathic medicine would, therefore, have the same fundamental quality as traditional systems of health: it reflects the dominant philosophical belief system of the society in which it developed.

Proposed Definition of Alternative Medicine

I propose that *alternative medicine* be defined as a broad set of health care practices (ie, already available to the public) that are not readily integrated into the dominant health care model, because they pose challenges to diverse societal beliefs and practices (cultural, economic, scientific, medical, and educational). This definition brings into focus factors that may play a major role in the a priori acceptance or rejection of various alternative health care practices by any society. Unlike criteria of current definitions, those of the proposed definition would not be expected to change significantly without significant societal changes.

Applications of this definition to Western society include the following: (1) *cultural*—health care systems may have developed outside mainstream American culture and may not be consonant with our cultural values; (2) *economic*—therapies similar to conventional pharmacological approaches (ie, based on the use of purified molecular species, eg, antineoplastons) can be considered alternative. These tend to be therapies that are developed by private practitioners, bypass established economic networks (eg, pharmaceutical industry, research institutions, and hospitals) and have difficulties going through the steps generally required to achieve acceptance in conventional medical practice; (3) *scientific beliefs*—there exists no scientific explanation for how some practices (for example, homeopathy and noncontact practices such as *Reiki* and *Qi gong*) could possibly work. However, the paucity of research data is most likely due to their being alternative; (4) *medical*—holistic medicine practices often focus on preventive and therapeutic enhancement of existing biological mechanisms (eg, the immune system), and do not follow the allopathic model; and (5) *educational standards*—some practices are passed on from generation to generation through oral tradition, rather than through formal training at special schools or institutions.

The proposed definition also is relevant to whether the term *alternative* or *complementary* is used. The origin of a practice may be alternative (eg, culturally or economically different), while its use can be complementary with biomedicine (or other alternative practices).

Sociological and Academic Parameters

For decades Western academia has excluded alternative medicine research and practice; this has contributed much to the paucity of data in this area. Established academic researchers have been discredited and have had difficulties when attempting to conduct alternative medicine research.^{16,17} At times, explicit threats were made by mainstream medicine to individuals and institutions that would associate with alternative medicine practitioners.¹⁸ Consequently, most alternative medicine research has been conducted outside of academia by indi-

viduals with limited research training and resources, and their investigations are often methodologically inadequate.¹² Conversely, those studies deemed methodologically sound may lack comparability and replication. For example, lack of funding, differences among individual investigators' resources, and personal research interests have limited replication of studies in homeopathy and acupuncture.^{12,20}

This atmosphere, in which academic investigators were concerned about the impact that their interest in alternative medicine might have on their good standing and their livelihood, has been particularly unfavorable to the development of high-quality academic research. This is changing, as the creation of the OAM has helped to legitimize alternative medicine evaluation and allowed these investigators to manifest openly their interest. The result has been the creation of 13 academic centers dedicated to alternative medicine assessment at major US institutions.²¹

Political, Economic, and Regulatory Parameters

The interaction of politics and science in the arena of health care, one of the most lucrative industries in the United States, has played a significant role in recent development of alternative medicine in the United States. For example, in October 1991, the US Congress instructed the NIH to create an Office of Unconventional Medical Practices,⁴ later renamed the Office of Alternative Medicine. The congressional mandate was met with a less than enthusiastic response from the NIH,²² but simultaneously with high public expectations.²⁴ Compounding the difficulties, other key governmental agencies, in particular the Food and Drug Administration (FDA), were overlooked in the mandate, although their role was necessary and complementary to that of the OAM.

Similar to other federal programs, the activities of the OAM must comply with FDA regulations and policies. Yet, FDA regulations designed for conventional drugs and devices are not always applicable for alternative medicine products. For example, regulations are designed for conventional products that require research before becoming publicly available. Considerable economic incentives usually justify corporate sponsors of new therapies to submit to the FDA's stringent and onerous regulations.²⁵ Conversely, alternative medicine products are, by definition, already available, which lessens the drive for research. In addition, there is little incentive for conducting alternative medicine research, as it seldom leads to significant economic benefit. For example, research into homeopathy or medicinal plants usually does not lead to economic advantages for sponsors, because these products are not proprietary. Similarly, lack of economic incentive (due to limited markets) also led to insufficient research in the biomedical area of rare diseases and required special governmental incentives.²⁶

There are several reasons, other than economic ones, that current regulatory criteria may be difficult to apply to alternative practices, in particular traditional practices from other cultures. For example, these practices follow different diagnostic classifications than biomedicine, and the complex substances (eg, botanical, animal products) they use cannot easily meet the criteria established for essentially pure drugs or even for conventional biologics. However, the FDA recently has begun addressing the issues posed by evaluation of alternative medicine products. Representatives from the FDA actively participated in the organization of 2 conferences that

addressed the special considerations of acupuncture¹⁹ and of botanical medicines.²⁰

Conclusion

Nonscientific factors contribute to defining the scope of alternative medicine and the context for its evaluation. Economic promise of growing markets may lead to a focus on developing profitable alternative medicine products rather than on improving health care and also may lead away from addressing issues that have prompted the public to seek alternative medicine practices. Nonscientific and scientific factors are shaping this unusually heterogeneous and potentially fruitful field and must be taken into account for a thoughtful evaluation to yield more than incremental progress.

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Physicians' Ethical Obligations Regarding Alternative Medicine

A SUBSTANTIAL proportion of patients use alternative medicine, spending an estimated \$13 billion each year.¹⁻³ Complementary and alternative medicine incorporates "all health systems, modalities, and practices other than those intrinsic to the politically dominant health system of a particular society or culture" and "includes all practices and ideas self-defined by their users as preventing or treating illness or promoting health and well-being."⁴ Under this definition, the scope of professional obligations regarding alternative medicine for clinicians who provide conventional medical care is unclear. Despite the popularity of alternative medicine, conventional medicine is arguably the politically dominant health system with a somewhat circumscribed set of practices that differ from alternative therapies. However, given the strong professional obligations clinicians have toward helping patients meet health-related goals, the scope of these obligations with respect to alternative medicine deserves discussion.

Alternative medicine and conventional medicine share some important goals, which provide some support for a limited professional obligation toward alternative medicine. Nevertheless, fundamental differences in these approaches raise questions about cultural relativism. While these questions are challenging, using a principle-based analysis,⁵ we describe the scope of the professional obligations of clinicians who typically practice conventional medicine toward alternative medicine. We do not directly address the full range of ethical issues, including the professional responsibilities for alternative medicine practitioners, despite the obvious implications for patients.⁶ Therefore, our arguments are relevant only in those situations in which alternative medicine practitioners hold the interests of patients foremost and alternative medicine is practiced with integrity and honesty. For clarity, we use "clinician" to refer to those who provide conventional medicine and "practitioner" to those who render alternative medicine.

Comparing Modalities

Conventional modalities (such as surgery and drug therapy) rely on the scientific method whereas alternative medicine modalities (such as acupuncture and therapeutic touch) do

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not.⁷ However, there are considerable similarities among conventional medicine and some forms of alternative medicine. For example, alternative dietary supplements may be a pill or capsule and dietary therapy is an established element of the conventional treatment of heart disease.

Similarly, while the definition of alternative medicine alone sets it apart from conventional medicine, their core health-related goals may not differ radically. Bratman⁸ describes 4 values espoused by alternative medicine practitioners: "(1) Use of natural remedies rather than artificial drugs, (2) Getting to the root of problems rather than treating symptoms . . . , (3) Treating the person instead of attacking the disease, and (4) Preventing illness rather than treating it after the fact, and promoting wellness rather than the mere absence of disease." Conventional clinicians share similar values. For instance, a recent international project⁹ specified 4 goals of medicine: "(1) The prevention of disease and injury and the promotion and maintenance of health," "(2) The relief of pain and suffering caused by maladies," "(3) The care and cure of those with a malady, and the care of those who cannot be cured," and "(4) The avoidance of premature death and the pursuit of peaceful death."

The concordance of these values is tangible in the current national dialogue about death and dying in which both alternative medicine and conventional medicine now hold that death is not necessarily a negative outcome and palliative care is considered an appropriate option. Both approaches also endorse attention to healing as well as curing, particularly for chronic illnesses in which a cure is often not possible. Shared health-related goals and values such as these lend some support for a limited professional obligation toward alternative medicine that is consistent with a professional obligation toward helping patients achieve these goals. Nonetheless, this obligation is certainly limited to steps that have been proven to be safe and effective, but it may be further limited by the range of practices that fall within the domain of conventional medicine.

Distinct Cultures of Healing

Despite shared values and goals, alternative medicine and conventional medicine differ in important ways. First, many alternative medicine modalities are derived from cultures other than the Western one in which conventional medicine was developed, and many of the practitioners subscribe to a different worldview.¹⁰ Second, by definition, alternative medicine represents a different approach to healing. Third, users of alternative medicine tend to perceive these modalities, in comparison to conventional ones, in greater concordance with their views toward health care.¹¹ Thus, there seems to be distinct cultures of healing, which is somewhat analogous to situations that conventional medicine encounters in other cultures. For instance, what constitutes appropriate research in developing countries? Should patients be told about a diagnosis of cancer? Should advance directives be discussed with patients whose culture proscribes these discussions? How should clinicians respond to requests for female circumcision?¹² In each of these cases, just as when clinicians encounter alternative medicine, it is essential to determine an appropriate response. When is a laissez-faire approach acceptable? When is there an obligation to intervene on behalf of patients? In making such determinations, it is essential to be vigilant in ensuring that these determinations are not clouded by hegemonic concerns about social status, market share, unfamiliarity, or prejudice.

Bounds of Professional Obligations

The spectrum of possible responses to alternative medicine is quite broad, ranging from an obligation to stifle harmful practices to mere acceptance of nonharmful modalities, to encouraging the use of beneficial interventions. Obviously, none of these singular approaches is adequate or appropriate in all cases. Rather, given the diversity of modalities embraced by a broad definition of alternative medicine and medical uncertainties regarding safety and efficacy, each approach is at times correct. The patient, the illness, and the alternative modality shape the appropriate set of obligations in a particular case. This obligation is refined and justified by attending to a set of inherent ethical principles of the medical profession: respect for persons, nonmaleficence, beneficence, and justice.

Respect for Persons.—The ethical obligation of respect for persons, or autonomy, finds application in now well-established expectations of shared medical decision making and informed consent. Such expectations have been endorsed not only on ethical grounds, but also on prudential grounds such as enhanced compliance. Respect for persons also helps prescribe appropriate behavior in the setting of cultural relativism.¹² A thorough respect for persons permits patients to reject unwanted interventions and to make choices that are consonant with their values.

Given the ready availability of information about alternative medicine, many patients may be quite familiar with particular modalities. While a knowledge gap between clinicians and patients regarding alternative medicine modalities may exist, it does not necessarily follow that respect for patients in making decisions regarding alternative therapies excuses conventional clinicians from playing any role whatsoever. Rather, clinicians have an obligation to discuss treatment alternatives with their patients and should be frank about their level of understanding of nonconventional interventions. Even without previous knowledge of particular modalities, clinicians can help patients focus their inquiry and thereby enhance their decision making. For instance, clinicians should ensure that patients have received information about safety (including potency, bioavailability, and drug interactions) as well as efficacy.

Respecting persons also includes making recommendations and using persuasion to help them reach accepted health-related goals. The efficacy, acceptability, and safety of conventional and alternative medicine approaches for treating a particular disorder are critical in determining the precise role in a given situation.¹³ For example, it is less appropriate for professionals to exert strong influence on patients' decision making regarding alternative medicine for diseases in which there is no clearly effective conventional treatment (eg, fibromyalgia), whereas such influence is appropriate when there are known effective therapies for a life-threatening disease (eg, a treatable bacterial infection).

More difficulty arises in determining the appropriate role of clinicians when there are alternative medicine approaches for conditions in which conventional therapies have some efficacy although treatment is not completely satisfactory. For example, while conventional medicine offers both disease modifying and symptomatic treatments of rheumatoid arthritis, it would be advantageous if complementary approaches could diminish the need for the use of drugs that have deleterious adverse effects (eg, steroids). Such situations are difficult because of insufficient information regarding the safety, much

the efficacy, of using alternative medicine in combination with conventional medicine. This uncertainty makes truly informed decision making difficult at best and hazardous at worst. Nevertheless, clinicians should be prepared to give patients available and appropriate information about the safety and efficacy of conventional therapies in treating their illnesses, encouraging them to seek similar, reliable information about alternative medicine.

Nonmaleficence.—Not harming patients unnecessarily in the process of providing care is a well-recognized ethical principle. Although clinicians may not be prescribing or providing alternative medicine, the obligation for nonmaleficence still plays an important role. In short, it is incumbent on clinicians to elicit information about patients' use of alternative medicine modalities.¹³ Such information is part of taking a comprehensive medical history since use of alternative medicine might be having some influence on patients' complaints and also may guide decisions about appropriate treatment. This is critical since some alternative medicine therapies are known to be harmful.¹⁴ In addition, there may be harmful interactions between conventional and alternative medicine therapies. For example, conventional antidepressants act on the same neurotransmitters within the central nervous system as does St John's wort.¹⁵ Thus, a medical history that includes information about a patient's use of alternative medicine is critical in avoiding harm.

Beneficence.—Clinicians have a clear obligation to help patients achieve legitimate goals of medicine such as promoting health, prolonging meaningful life, and attenuating suffering. Accordingly, effective interventions obviously should be considered in determining a plan of care for patients. Therefore, a limited obligation does exist on the part of clinicians to make patients aware of safe and effective alternative medicine modalities. Unfortunately, although efforts now are under way to provide systematic data regarding some forms of alternative medicine, few systematic data are currently available to help clinicians and patients make important decisions in this regard.¹⁶

In the face of popular enthusiasm about alternative medicine, physicians may feel pressured to learn to prescribe beneficial alternative medicine modalities. While learning such interventions may be beyond the scope of clinicians' professional obligations,¹⁷ should individual clinicians elect such training, the training itself must be adequate and appropriate. Efforts are under way to provide this sort of training.¹⁸⁻²⁰ As with conventional medicine, physicians should not adopt interventions until they have sufficient experience to use interventions safely and effectively.

Accordingly, there is room for appropriate referral and consultation with alternative medicine practitioners. This includes referral and consultation when there is both an increased likelihood that the patient will benefit from the interaction and that the practitioner is experienced as well as accredited or licensed.

Justice.—A central concern of justice in health care relates to fairness. Fairness suggests that patients have fair access to alternative medicine therapies as well as conventional therapies that are known to be safe, effective, and appropriate for their conditions. Nevertheless, because little clinical research has evaluated alternative medicine, few data support claims for fair access to these therapies. This predicament, similar to that encountered in caring for children and pregnant women

(groups for whom a relative paucity of data regarding safety and efficacy of conventional therapies to guide treatment decisions)²¹ suggests the need for research efforts in this area. Given the broad use of alternative medicine, as well as the possibility that some modalities will prove to be beneficial, clinicians ought to endorse legitimate efforts aimed at the careful evaluation of conventional and alternative interventions so that they will be better positioned to help guide medical decision making.²² Despite this argument, some skeptical clinicians may still object, claiming that investigating these approaches wastes scarce research dollars and encourages patients to invest their money in sources of false hope.²⁴ Nevertheless, if this research is conducted properly, the extent to which alternative medicine therapies meet patients' expectations will be clear. Armed with these data, harmful or useless practices could be abandoned and clinicians would be better positioned to help their patients make informed decisions to reach essential health-related goals.

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Investigating Alternative Medicine Therapies in Randomized Controlled Trials

BECAUSE ALTERNATIVE medicine therapies are used by a significant number of Americans^{1,2} and people worldwide,³ there is an urgent need for their efficacy to be evaluated formally. The most stringent evaluation would take place within the "gold standard" for clinical research: the randomized controlled clinical trial (RCT). However, alternative medicine comprises a large and heterogeneous group of treatments,⁴ many of which are procedures that are not readily testable under blinded conditions and for which the choice of appropriate control conditions is by no means straightforward. Furthermore, alternative medicine therapies may also possess a theoretical basis, may stem from a cultural tradition that is seemingly antithetical to a quantitative, biomedical framework,^{4,7} or may possess little foundational research on which to base a controlled evaluation. In this article, we discuss a number of key methodological issues that arise in the controlled evaluation of one widely used alternative medicine procedure—acupuncture for the treatment of cocaine addiction, and we offer some suggestions for how these issues may be addressed.

Basis for Undertaking a Controlled Trial

An important principle governing the justification for conducting an RCT⁸ is that a condition of genuine clinical uncertainty, or "equipoise,"⁹ exists among clinical experts regarding the relative benefits of the trial's treatments. However, the application of this principle entails a community of colleagues sharing basic assumptions and a common knowledge base, with consensus views founded on empirical investigations. These conditions may not be satisfied with respect to considerations of alternative medicine, which typically involve heterogeneous groups comprising incommensurate cultural and evaluative frameworks and, more often than not, a paucity of systematically derived data. Even within the biomedical community, alternative medicine generates considerable controversy.¹⁰ The application of traditional concepts of "clinical equipoise" to alternative medicine is therefore an unsettled question, much in need of elucidation and a statement of general principles. Lacking this, investigators of an alternative medicine treatment must negotiate the justification to conduct the trial, as well as criteria for informed consent, on a case-by-case basis. Relevant to this discussion is whether the alternative medicine treatment is being compared with a conventional treatment as an alternative, as a supplement, or, where no effective conventional treatment is available, with an inactive control condition, along with whatever preliminary evidence concerning safety and efficacy is available.

Auricular acupuncture for the treatment of cocaine addiction demonstrates how a confluence of circumstances, within both Western medicine and alternative medicine, creates a context within which the evaluation of an alternative treatment can generate broad support. Among the circumstances

that support a formal investigation of acupuncture for the treatment of cocaine addiction are (1) Cocaine addiction is a serious public health problem. (2) There is a lack of effective conventional treatments for the disorder. (3) There is widespread provision of acupuncture for cocaine addiction. Currently more than 300 clinics in the United States offer acupuncture as part of their addiction treatment programs.¹¹ (4) Preliminary studies investigating the effectiveness of acupuncture in the addictions have reported positive results.¹²

Is the Treatment to Be Evaluated Codified and Accepted?

Because alternative therapies do not possess well-established clinical practice guidelines,⁷ wide variations may exist in the treatment provided for a given disorder. This raises the issue of whether the experimental treatment is regarded as representative of common practice in the field, and, if so, whether the treatment has been standardized for the trial's diagnostic category. The credibility of the study will depend in part on whether before a trial is undertaken, a consensus has been reached that the treatment being tested is the most appropriate for the target disorder. This consensus can be inferred either by expert opinion, or, where it exists, through standards of practice guidelines. In addition, like conventional treatments, alternative treatments are most cogently investigated in trials that pose well-defined questions with respect to specific diagnostic categories based on validated assessment instruments. Auricular acupuncture for treating cocaine addiction satisfies these conditions insofar as the experimental treatment is codified in the widely used protocol established by the National Acupuncture Detoxification Association and can be delivered to patients meeting *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*¹³ criteria for cocaine abuse or dependence by practitioners trained by the acupuncture association.¹⁴

Identification of Objective Outcomes

Similar to any treatment, alternative medicine therapies are prone to expectancy effects and other influences that may lead to biased self-reports of outcomes.⁴ For this reason, and in view of the possibility of selection bias as well as the need to enhance the credibility of alternative medicine research, it is important that objective measures be included in alternative medicine studies whenever possible. For example, an RCT designed to test the efficacy of acupuncture in treating cocaine addiction could address this straightforwardly by obtaining urine toxicology screens 2 or 3 times a week. Identifying objective outcomes of other alternative medicine therapies or other target disorders may present a greater challenge.

Devising Adequate Controls

The development of control conditions for alternative medicine therapies poses a number of problems, such as the mechanism of action is usually not well understood, the treatment is typically a procedure that involves some degree of interaction between patient and treatment provider, and the development of controls for procedures is significantly more complex than for pharmacotherapies.¹⁵ Yet, given the controversy and

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right skepticism concerning alternative medicine. In clinical trials, the use of well-designed controls in their evaluation is an important factor in establishing the credibility of the trial and, therefore, the treatment being evaluated. For auricular acupuncture, controls for both needle-insertion effects and nonspecific effects, such as relaxation, may be required. Controlling for needle insertion, a "ritual" that might elicit a placebo response in drug users independent of any acupuncture-specific mechanism,¹⁶ involves inserting needles into so-called "sham" points, which are presumed to be ineffective for the target disorder. This simple statement belies numerous complexities. Traditional Chinese medicine does not include the concept of a "placebo," and the organismic model that underlies traditional acupuncture theory does not embody a concept of an "inert" treatment.¹⁷ Furthermore, within a Western framework, there is no biochemical "marker" of an active auricular treatment, nor is there one that would differentiate an active from a control treatment. Hence, unknown relative levels of therapeutic activity between active and control conditions constitutes a potentially serious impediment to the interpretation of findings in acupuncture research.¹⁸

Key issues to consider when devising a needle insertion control include ensuring the comparability of control and active treatment with regard to any aversive effects that may affect dropout or subjective response to treatment¹⁹ (eg, pain or discomfort caused by the treatment), and identifying a theoretical and empirical basis for regarding the control treatment as less active than the experimental treatment. In addition, there would ideally be an objective method for determining specifically where the needles are to be inserted within the hypothesized "active" and control regions. In seeking guidance on these issues, the extant literature should be approached critically. For example, in preliminary studies, we found that (1) a commonly used control in auricular acupuncture studies, insertion of needles proximate to active points, though no more painful than active sites, is probably too active to be a suitable control^{20,21}; (2) needling of regions on the ear helix, in points relatively removed from the active sites and that are not indicated for the treatment of addiction, is rated least active and least preferred by patients who use cocaine compared with 3 other auricular needle configurations and, therefore, may represent a more appropriate control²²; and (3) "active" auricular sites can be differentiated from control sites on the basis of their electrical resistance characteristics.²³ However, some commercially available "electrical point finders," used to select points for needle insertion, may be unreliable due to circuit design problems and pressure artifacts.²³ The development of adequate needle-insertion controls is an area still much in need of further research. Consideration should also be given to controlling for nonspecific effects of the treatment context that may affect the target disorder. In the case of addiction, this may include controlling for the effects of relaxation induced by sitting quietly for 40 minutes daily to receive the acupuncture treatment, because relaxation has been associated with reduced drug craving.^{24,25} Control conditions should possess the nonspecific elements of the acupuncture treatment context, including credible rationale, equivalent time demands, and similar patient-staff contact. We note that standard care comparison groups do not usually contain these elements. Precisely what aspects of the experimental treatment such groups control for should be carefully considered in determining their suitability in an RCT.

Difficulties of Blinding Procedures

Blinded conditions in an RCT control for a host of potential confounds and biases,²⁶ and they provide conservative estimates of treatment efficacy.^{27,28} However, evaluations of procedures, unlike those of pharmacotherapies, are nearly impossible to conduct under conditions in which both the patients and practitioners are blinded. Training and competency are a prerequisite to providing the treatments, and experienced practitioners will know which treatment is hypothesized to be active. Unlike pharmacotherapy studies in which the active medication and the pill placebo can be made to be identical in appearance, procedures are observably different to all of the participants in the study. Therefore, acupuncture RCTs may need to be conducted unblinded, with multiple checks on bias.

Guarding Against and Checking on Bias

Following Pocock,²⁹ at least 3 categories of participant bias that may be considered in RCTs of alternative medicine are treatment providers, patients, and staff. For any procedure, the interaction and ongoing relationship between the treatment provider and patient presents opportunities for the treatment provider to influence outcome, knowingly or unknowingly.²⁹ Several approaches to check this tendency can be implemented in RCTs of alternative medicine by imposing constraints on the patient-treatment provider interaction; monitoring these interactions by a third party; and evaluating the practitioner-patient relationship across treatment groups.³⁰ Various factors associated with study patients also represent a potential source of bias. In any RCT, the treatments must be described simply and factually to patients to ensure properly informed consent.³¹ However, this information should be communicated in a way that minimizes expectancy effects; it should neither enhance the experimental treatment nor introduce bias against the control conditions. Treatments that are regarded as credible when administered, even if they are subsequently shown to be ineffective, can result in significant improvement in the target disorder.³² Hence, for studies of alternative medicine, it is important to design the active and control treatments to be equivalently credible and to assess the credibility of the treatments.³³ One way to accomplish this is through multiple administrations of a treatment credibility assessment instrument, which permits for comparisons across groups of patient-perceived credibility of the assigned treatment.^{34,35} In any RCT, staff bias can operate on a number of different levels and must be protected against. This may be especially important in the evaluation of controversial therapies or in treatments about which participants may be thought to have strong positive or negative opinions. The use of a primary objective outcome (eg, urine toxicity screens in addiction studies) may protect against patient bias as well as staff bias influencing primary outcomes. To preclude potential staff bias from influencing patients' self-reported change, assessment interviews should be conducted by staff members blind to treatment assignment.

Conclusions

The validity and credibility of alternative medicine investigations will be enhanced by using research designs that embody the highest standards for demonstration of efficacy: the randomized clinical trial. However, controlled evaluation of alternative medicine therapies may require its practitioners to undertake a fundamental conceptual shift from a view of patients as requiring individualized treatment that may vary.

at each on to one in which trial participants are regarded as members of an equivalence class, defined by the diagnosis, who all will be given a standard prescribed treatment. Although in this article we have urged the use of RCTs for evaluating alternative medicine therapies and have discussed some of the problems that arise in this endeavor, we recognize that this approach may be viewed by others as irretrievably distorting the content of those treatments. This complex issue, comprising a wide range of opinions concerning the cultural relativity of methodological principles, has yet to be resolved.

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Complementary Medicine and the Cochrane Collaboration

EVERY YEAR, millions of US consumers spend billions of dollars on alternative and complementary medical treatments.¹ A similar trend exists in the United Kingdom and Australia.^{2,4} As people increasingly use these treatments, questions arise from consumers, clinicians, payers, and policymakers as to the effectiveness of these interventions.

The Cochrane Complementary Medicine Field

To meet the increasing demand for evidence-based complementary medicine (CM), a CM Field, funded by the National Institutes of Health Office of Alternative Medicine, was established within the Cochrane Collaboration⁵ in 1996. The

goal of the Cochrane Collaboration is to produce, maintain, and disseminate systematic reviews on all topics in health care. The CM Field focuses on CM topics. Two major products of the Cochrane Collaboration are a database of systematic reviews and the Cochrane Controlled Trials Registry, the largest registry of its kind.⁶ Both databases are updated quarterly with information added regularly by the CM Field.

The systematic review is a method par excellence for synthesizing evidence on a given topic, and policy agencies are increasing use of it to summarize evidence.⁷ Cochrane reviews are more transparent than other reviews,⁸ so that conclusions are replicable and methods are explicit. Systematic reviews are valuable even when the results are inconclusive because reviews point out where knowledge gaps exist.

Search Strategies to Retrieve Randomized Trials of CM

Since the CM Field has been functioning, a great deal of effort has focused on laying the groundwork for reviews by con-

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structuring a database of randomized controlled trials (RCTs) on CM topics. Capturing all relevant trials in MEDLINE has yielded surprising challenges. The scope of practices defined as complementary within the CM Field is broader than those captured in a MEDLINE search of the term *alternative medicine*. For example, Chinese movement therapies such as Qigong and Tai Chi are considered complementary therapies by the Field's standards, but are not accessed by a hierarchical MEDLINE search of the term *alternative medicine*. Similarly, herbal remedies may be described by MEDLINE as plant extracts rather than by any alternative medicine term. To aid MEDLINE searching, a 250-line MEDLINE search strategy has been written and is available for public use.⁹

Assessments of MEDLINE sensitivity (the proportion of RCTs identified by a MEDLINE search relative to a "gold standard" of the known number of RCTs) have demonstrated that on average, MEDLINE searches yield only half of all known trials on a given topic, with CM topics usually scoring below average (eg, 17% for homeopathy, 31% for *Ginkgo biloba*, and 58% for acupuncture).¹⁰ The first reason for low MEDLINE sensitivity may be that articles are appearing in journals not indexed by MEDLINE. This is true for acupuncture¹¹ and vitamin C for the common cold.¹² Of approximately 16 000 serial medical journals worldwide, MEDLINE references about 3700 (23%).¹⁰ Of the 695 CM journals worldwide identified by the Office of Alternative Medicine and the National Library of Medicine, MEDLINE indexes 69 (10%). Collaborations between the National Library of Medicine, the CM Field, and the Office of Alternative Medicine should soon result in increasing the number of indexed CM journals and expanding the MEDLINE thesaurus to include more CM search terms.

To retrieve studies indexed in other databases, the CM Field is searching both standard medical databases and specialized CM databases. By mid-1998, the Cochrane CM Trials Registry contained more than 3500 RCTs, with only 33% identified by a MEDLINE search for RCTs in alternative medicine and 20% not found in MEDLINE. Periodically, the CM registry uploads its trials to the Cochrane Controlled Trials Registry, making these trials available to individuals with access to the Cochrane library. The CM Field maintains the CM registry, adds new trials, assists reviewers doing CM reviews, and proactively provides references to all 40 Cochrane Collaboration reviews and protocols that have a CM component. A second reason for low MEDLINE sensitivity is that articles exist in journals that are not indexed by any electronic database. Volunteers within the CM Field are now searching by hand approximately 40 indexed and nonindexed journals in English, German, Italian, Japanese, and Spanish and are reading every article published in these journals back to their first issues to locate every RCT.

Publication Bias

A third reason for low MEDLINE sensitivity is that studies exist that have never been fully published in any journal ("gray literature").¹⁰ Estimates from conventional medicine show that only about 50% of the RCTs that appear as conference proceedings ever materialize into published journal articles. Some observations¹³ estimate CM gray literature to be at least as plentiful. Complementary medicine gray literature includes expected sources, such as conference proceedings and dissertations, and unexpected sources such as US patents records.¹⁴

Beyond the hard-to-find trials in the gray literature lie the even harder to find studies that do not appear in print anywhere

and exist only in homeopathic company data files or researchers' file drawers.¹⁵ Gray literature plus unpublished data are collectively termed unpublished studies.¹⁶ Publication bias is "the tendency of investigators, reviewers, and editors to differentially submit or accept manuscripts for publication based on the direction or strength of the findings."¹⁶ To the extent that publication bias exists, systematic reviews that omit unpublished studies risk overestimating treatment effects. Bias has been demonstrated both in what investigators submit to journals¹⁶ and what conference abstracts editors accept.¹⁷ However, whether to include unpublished studies in reviews is still a source of debate.¹⁸ The influence of unpublished studies in CM systematic reviews is being analyzed by the CM Field as part of a review of 164 CM systematic reviews.⁹ Until the value of including CM unpublished studies can be answered more conclusively, the CM Field will continue to search for unpublished studies to help answer a frequently asked question: How much evidence exists in CM?

Examining how publication bias skews the CM evidence is important for the CM Field because some forms of publication bias may be unique to CM. One question is whether both positive and negative publication biases exist in CM. Asked another way, do CM journals tend to publish results favoring CM treatments and conventional medical journals publish results not favoring CM treatments?

Examining publication bias is not always straightforward. A study by the CM Field found that studies published in Russia and China had a disproportionately high number of statistically significant results (97% and 99%, respectively) when compared with England (75%).¹⁸ It is not yet evident whether these high proportions are due to extreme forms of publication bias or low study quality, which overestimated treatment effects.^{19,20} The CM Field is obtaining translations of these studies to examine study quality. The qualitative results will determine whether it is practical to devote efforts to the tedious task of identifying unpublished studies.

Language Bias

Moher and colleagues²¹ demonstrated that the quality of studies published in French, German, Spanish, and Italian is comparable with those published in English. The present research of the CM Field will extend methodological quality knowledge to studies from Russia and China. Egger and colleagues²² demonstrated that a language-related publication bias exists in which authors who publish in both German and English tend to report nonsignificant findings in German and significant findings in English. Preliminary observations suggest that an additional language bias may exist for CM. Regardless of whether results are significant, some CM topics are almost exclusively published initially in languages other than English. A systematic review on St John's wort for depression²³ noted that none of the trials had been originally published in English, although some were subsequently published in English. A similar experience has been reported for *Ginkgo biloba* for cerebral insufficiency,²⁴ which suggests that for certain topics in CM, there may be a language-related publication lag time—a trend not reported for conventional medicine. Trends such as this underscore the importance of the CM Field's effort to retrieve trials in languages other than English and to identify biases that may be unique to CM.

Quality Assessment of RCTs

Assessing study quality also may improve the validity of systematic reviews. The finding that low-quality studies have re-

Reviews completed
Acupuncture for asthma
Acupuncture for nicotine addiction
Balneotherapy (spa therapy) for arthritis
Cabbage leaves to reduce breast engorgement in nursing mothers
Garlic for lower-limb atherosclerosis
Homeopathy for asthma
Massage for smoking cessation
Massage for low-birth-weight infants
St John's wort for depression
Vitamin E for intermittent claudication
Vitamin C for the common cold
Reviews in progress
Acupuncture for lower back pain
Acupuncture for headache
Acupuncture for osteoarthritis
Alexander technique for asthma
Echinacea for the common cold
Evening Primrose Oil for premenstrual syndrome
Ginkgo biloba for dementia
Ginkgo biloba for intermittent claudication
Manual therapy for neck pain
Manual therapy for asthma
Marine oil supplementation for type 2 diabetes mellitus
Music therapy for dementia
Padma 28 for intermittent claudication
Pygeum africanum for benign prostatic hyperplasia
Secale cereale for benign prostatic hyperplasia
Serenoa repens for benign prostatic hyperplasia
Spinal manipulation for low back pain
Therapeutic Touch for wound healing
Yoga for epilepsy

peatedly yielded exaggerated treatment effects has been documented for conventional medicine^{19,20} and acupuncture.²⁵ Yet, methodological assessments are sometimes absent from non-Cochrane Collaboration CM systematic reviews. A summary of 29 meta-analyses of mind-body techniques, for example, demonstrated that only about half assessed study quality.²⁶ Although assessing study quality cannot compensate for fraudulent or inaccurate reporting, it can provide additional validity-related information to guide reviewers' conclusions. For CM, quality assessments will provide needed answers to another commonly asked question: How good is the quality of CM trials?

This quality question is usually raised as an implication that CM trials reflect lower methodological quality than conventional medicine trials. To examine this notion, Cochrane Collaboration methodologists are collaborating with members of the CM Field to compare the methodological quality of CM trials with conventional medicine trials on the same diseases. Low-quality meta-analyses for analgesic interventions have been found to be associated with more positive results than high-quality meta-analyses.²⁷ The analysis of CM reviews is to examine whether this can be replicated in low-quality vs high-quality CM reviews, and how conclusions of low-quality vs high-quality CM reviews on the same topic differ.

Reviews Completed by the CM Field

The CM Field has completed systematic reviews on acupuncture, massage, homeopathy, and herbal medicine. Nineteen reviews are in process (Table),²⁸ and the CM Field has commented on protocols of 12 planned and completed reviews.²⁹

Conclusions

Although there is no guarantee that systematic reviews will result in changing policy and practice, there is increasing evidence that policy organizations rely on systematic reviews more than they have in the past⁷ and that practitioners rely on reviews as a primary information source.³⁰ It has also been

suggested that consumers can use reviews to guide decision making.³⁰ Traditional literature reviews, however, have lacked explicit methods and have been susceptible to biases that generally tend to overestimate treatment effects.⁷ Therefore, at a time when the public is using CM treatments in record numbers and an explicit peer-reviewed and regularly updated systematic review method exists, it is imperative to apply this method to CM. The Cochrane Collaboration provides a forum of interdisciplinary cooperation in which to produce these reviews that we hope will result in improved patient care.

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Alternative choices

What it means to use nonconventional medical therapy

ALTERNATIVE MEDICINE

If you've ever taken high-dose vitamins, used an herbal remedy, or sought treatment from a chiropractor, you're among the millions all over the world who use alternative medicine to ward off illness or treat a variety of ailments.

Known by a variety of terms — *complementary, holistic, unorthodox, integrative* — alternative medicine refers to most treatment practices that are not considered conventional medicine (widely practiced or accepted by the mainstream medical community). Although the majority of medicine practiced in the United States is conventional, worldwide, approximately 70% to 90% of health care is delivered by what would be considered an alternative tradition or practice.

Incorporating hundreds of different philosophies and procedures, alternative therapies are usually ideologically based. Most of these therapies often are not backed by scientific research that measures safety or effectiveness. Some alternative

therapies have dangerous side effects. Another concern is that people who use alternative therapies in the place of conventional medical therapy may delay or lose the opportunity to benefit from scientifically based treatment.

The use of alternative medicine in the United States is growing in popularity.

According to a new study in the November 11, 1998, JAMA theme issue on alternative medicine, 4 out of 10 Americans use some form of alternative medicine. Americans visited alternative therapy practitioners 629 million times in 1997, a 47% increase over the 427 million visits made in 1990. They spent approximately \$27 billion out-of-pocket (not covered by insurance) on alternative therapies in 1997, which is about the same as estimated 1997 out-of-pocket spending for all U.S. physician services.

Additional Sources: National Institutes of Health's Office of Alternative Medicine, AMA's Reader's Guide to Alternative Health Methods, American Cancer Society



SOME TYPES OF ALTERNATIVE MEDICINE:

- **Acupuncture** — Insertion of needles into specific points in the body for therapeutic purposes; also may involve use of heat, pressure, or electromagnetic energy to stimulate anatomic acupuncture points in the body
- **Aromatherapy** — Use of essential oils extracted from flowers, leaves, stalks, fruits, and roots for therapeutic purposes
- **Chiropractic** — Based on the idea that spinal misalignments are the principal cause of disease; uses manual procedures and interventions to manipulate the spine
- **Folk medicine** — Medical treatment based on the beliefs, traditions, or customs of a particular society or ethnic/cultural group
- **Herbal medicine** — Use of various parts of plants to treat symptoms and promote health; herbs have a long history in medicine, but many herbs that have been proven to be effective years ago have been replaced by more effective synthetic compounds; the U.S. Food and Drug Administration (FDA) does not currently regulate herbal products, and herbal products can only be marketed as dietary supplements because manufacturers and distributors cannot make any specific health claims without FDA approval
- **Homeopathy** — Remedies made from plant, animal, or mineral substances that are highly diluted with the intent to stimulate the body only enough to trigger a healing response

ISSUES TO CONSIDER ABOUT ALTERNATIVE THERAPIES:

- **Safety and effectiveness** — The product or practice should not cause any harm and should provide benefit when used as intended. Specific information about the safety and effectiveness of any alternative or complementary therapy should be readily available.
- **The practitioner's expertise** — Closely examine the training, qualifications, and competence of any potential health care practitioner. Alternative medicine is not as well regulated as conventional medicine.
- **Quality of service delivery** — Determine if the delivery of service adheres to standards for medical safety and care; contact state or local regulatory agencies or health care consumer organizations; visit the practitioner's office, clinic, or hospital; and talk to people who have used the service.
- **Costs** — Many alternative therapies are not covered by health insurance, so compare the costs with those of other practitioners or through professional medical associations.
- **Consult your physician** — Discuss any type of medical therapy with your doctor. Your doctor needs to know about any conventional and alternative therapies you have used or are currently using to treat you more effectively and to prevent medication interactions.

FOR MORE INFORMATION:

- National Institutes of Health
Office of Alternative Medicine (OAM)
OAM Clearinghouse
(does not provide referrals or medical advice)
P.O. Box 8218
Silver Spring, MD 20910
888/644-6226
(8:30 a.m. to 5 p.m. ET weekdays)
888/644-6226 (TTY) or altmed.od.nih.gov

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