

TUFTSCOPE

THE INTERDISCIPLINARY JOURNAL OF
HEALTH, ETHICS, AND POLICY



**DO PHARMA GIANTS INFLUENCE DRUG PRICES?
HOMELESS HEALTH IN PARIS
AN INTERVIEW WITH DR. DAVID WALT**

JOURNAL HISTORY

Since 2001 *TuftsScope: The Interdisciplinary Journal of Health, Ethics, & Policy* has provided an academic forum for discussion of pertinent healthcare and biosocial issues in today's world. The journal addresses different aspects of healthcare, bioethics, public health, policy, and active citizenship. It is operated and edited by undergraduate students of Tufts University and is advised by an Editorial Board composed of Tufts undergraduates and faculty. Today the journal is one of the few peer reviewed undergraduate published journals in the country.

PUBLISHER AND PRINTER

TuftsScope is published by the *TuftsScope Journal* organization at Tufts University. The journal is printed by Puritan Press, NH (<http://www.puritanpress.com>).

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FUNDING

TuftsScope is funded by grants from the Tufts Community Union Senate.

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Website: www.tuftsscopejournal.org
Address: Available on back cover.
ISSN: 1534-7397

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Cover Image: In this issue, *TuftScope* discusses a wide variety of topics, including the effect of large pharmaceutical companies on drug prices.

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LETTER FROM THE EDITORS

An Epilogue

Dear Reader,

Our Spring 2015 issue marks the conclusion of a very exciting year in which *TuftScope* has broadened its scope to include articles from a variety of fields and topics, and has worked with a multitude of student organizations to foster greater on-campus health awareness. In this issue, we aim to continue to propagate discussion and consolidate seemingly different viewpoints surrounding healthcare.

In this issue, we are particularly proud to present a much wider array of cross-disciplinary topics that range from scientific analyses to critical editorials. In our “Opposing Viewpoints,” Lushna Mehra and Joseph St. Pierre debate the use of social media as a platform for ALS awareness. Prachi Sharma adds a new economic perspective to our journal by synthesizing the literature about the economic roots and solutions of the obesity epidemic in the United States. Evan Balmuth goes abroad and details the plight of the homeless in Paris, who have been reported with higher rates of tuberculosis. Lena Chatterjee, however, brings our focus back home by commenting critically on the Tufts Center for the Study of Drug Development’s funding. Finally, we would like to thank Dr. David Walt, scientific founder of Illumina and Quanterix, for speaking with editorial board member Caroline Russell-Troutman about his entrepreneurial work in diagnostics in our feature interview.

On a personal note, this final issue of the year is also the final issue for us as Editors-in-Chief and as Tufts undergraduates. We both joined the staff our freshman year, and have since seen the journal grow in size, win awards for collaborating with numerous organizations, and produce papers that fuel innovative discussions on health. We would like to specifically thank our senior editorial staff members, Allison Kuperman, Ayal Pierce, and Rohan Rao, for their tireless work over the past four years. We are grateful for the vast hours Allison has spent in designing our journal, Ayal’s help in updating our website, and Rohan’s effort in obtaining submissions that have allowed us to publish pieces with perspectives from outside of Tufts. As always, we are very appreciative of our entire staff for their continuous effort in helping us create and maintain our reputable journal.

We leave *TuftScope* in the very capable hands of our new editorial board, and wish them nothing but the best for the years to come. If you are interested in joining or contributing to *TuftScope* for our next fall issue, please e-mail us at TuftScope@gmail.com.

We hope you enjoy this issue!

Sincerely,

Prachi Sharma & Joseph St. Pierre
Editors-in-Chief

Selections From Our News Analysis Weblog

FDA Approves Zarxio, Its First Biosimilar Drug

Prachi Sharma

The Food and Drug Administration (F.D.A.) has recently approved Zarxio, a biosimilar drug produced by Sandoz, to prevent infections in cancer patients who are receiving chemotherapy. While Zarxio had already been approved in Europe, its approval in the United States is unprecedented as there was no regulatory system in place to bring biosimilar drugs to the market. This approval is vital as it allows increased access to these alternative drugs that are potentially much cheaper than those that are currently available.

Biosimilar drugs utilize biologic drugs, which are made from living cells instead of chemicals like typical pharmaceuticals. Biologics are known for being extraordinarily expensive due to the lack of competition that has resulted from their patent protection. When first developed, these drugs were so complex that the development of generic versions was unfathomable. However, over the years, pharmaceutical companies have developed similar copies of these biologics and have sought approval from the F.D.A. Thus, these low-cost alternatives, which are approximately a third cheaper than brand name biologic drugs, will create newfound competition and potentially allow for some reduction in cost of older cancer care drugs. Furthermore, it is estimated that if the 11 biosimilars that are currently in development are approved, the United States may save approximately \$250 billion in drug costs. There are still many challenges: the naming process of biosimilars as generics or brands is being debated; also, doctors may need to prescribe biosimilars because they cannot be automatically substituted for brand name drugs yet. Regardless, the FDA's approval marks a new age for the pharmaceutical industry in the United States.

Deadly CRE Germs Linked to Hard-to-Clean Medical Scopes

Kathryn Gibb

CRE, or Carbapenem-resistant Enterbacteriaceae, is a family of germs that can develop into antibiotic-resistant bacteria. Recently, the U.C.L.A. Medical Center discovered that these germs were transmitted to patients via improperly sterilized duodenoscopes. These medical scopes are used in procedures to diagnose and treat diseases. The devices have many small crevices that make them easy to house leftover body fluids and germs, while making them difficult to clean. When not properly disinfected, the scopes have the potential to transmit the dangerous CRE bacteria. Antibiotic-resistant bacteria can make infections impossible to treat, oftentimes resulting in death. Although the U.C.L.A. Medical Center claimed that the scopes were cleaned according

to the manufacturing company's standards, two of the seven duodenoscopes used at the hospital had been suspected to transmit the germs to patients. The hospital has agreed to clean the scopes in a way that "goes above and beyond the manufacturer and national standards," according to a statement issued by the U.C.L.A. Health System. While the F.D.A. has the power to remove these scopes from the market, currently there aren't any alternatives to these devices. Rather than potentially creating a greater public health problem by removing the scopes from the market, it appears they will remain in use. For now, the scopes will be cleaned thoroughly to prevent the further spread of this infection.

Cow Immune System Inspires Potential New Therapies

Steven Hefter

Scientists at The Scripps Research Institute (TSRI) have found a potentially life-altering remedy for people who suffer from hormone deficiencies. The research, which has recently been published in the journal *Proceedings of the National Academy of Sciences*, supports the hypothesis that human antibodies and hormones can be combined, a process that also occurs in cows. Humans with low hormone deficiencies need an outside source of human growth hormone (hGH) that usually comes in the form of an injection. The problem is that the body rapidly breaks down hGH, meaning that daily injections may be needed to maintain the levels of hGH needed. As expected, this worsens a person's quality of life. On the other hand, antibodies can remain in the body for weeks. The researchers noticed something interesting about the bovine antibody structure from a 2013 study published by TSRI scientists; it has a round base with a long amino-acid chain pointing outwards. At the end of this chain there is a "knob region" that supposedly binds to pathogens. The scientists wanted to see if they could switch the knob region with DNA from a human hormone, such as hGH. To do so, they used recombinant DNA technology to unite hGH with the bovine antibody. Since this combination was stable, the researchers tried to expand and not use any cow DNA in the next experiment. They used Herceptin®, an anti-cancer antibody, as the antibody in this stage. The hGH-antibody treatment worked better in rat models than did the hGH treatment alone, thus supporting the hypothesis that a hormone-antibody mixture can aid growth in humans. TSRI Research Associate Tao Liu, who is the co-author with Yong Zhang at Calibr of a paper detailing this research, believes that this method can even be used to provide insulin to treat Type 2 Diabetes. The future is exciting for the theory of an antibody-hormone complex.

A Scientific Tale of Two Dresses

Jessica Newfield

Is the famous dress blue and black, or white and gold? “A Scientific Tale of Two Dresses,” produced by CNN, provides the scientific explanation for our inability to decide on the true colors of the dress that has been captivating the online community. Cones, or eye structures in our retinas, perceive colors in different ways depending on our genes. They detect the various blue, green, and red wavelengths in the images that we see.

After that information is processed, the cones and our brain integrate the wavelengths perceived to make other colors. The colors in this blue/black, or white/gold dress hit the threshold of color perceived by our cones that differ from person to person. The paradox concerning the dress is that “each of us makes slightly different unconscious assumptions” about which light to filter out when we look at the dress. Dr. Emily Chew, an ophthalmologist at the National Institutes of Health, suggests that this dress could help pave the way for furthering our knowledge on how we understand and perceive color.

Cannabis: A New Frontier in Therapeutics

Prachi Sharma

McGill University Health Center organized a symposium as a part of the 2015 American Association for the Advancement of Science Annual Meeting. In this conference, medical and healthcare professionals debated the therapeutic potential of medical cannabis, or marijuana, and gave an overview of current research on the subject. Some experts used personal anecdotes to assert that there is a real need for medical cannabis for patients with severe chronic pain, but also emphasized that prescriptions should be patient-centered, as not every patient will benefit from treatment. Another theme that emerged in the forum was the importance of integrating research and education for patients, physicians, and policy-makers alike. Incorporating scientific research into policy was therefore proposed. Other experts spoke in detail about their research, and stated that while there is currently little evidence that supports cannabis as a therapeutic agent, medicines based on tetrahydrocannabinol (THC) have been approved. This component is the psychoactive ingredient of cannabis. Furthermore, research has found that tetrahydrocannabivarin (THCV), a non-psychoactive component of cannabis, actually produces anti-schizophrenic effects in a preclinical model of schizophrenia, thereby illustrating that there may in fact be some therapeutic properties of cannabis. Additionally, research is currently being done on the short and long-term neuropsychiatric effects of cannabis use, and current findings have illustrated that there is no significant cognitive decline in recreational marijuana users, though its effect on brain development of teenagers and children has yet to be studied thoroughly. Ultimately, the symposium was an interesting forum that brought forth multiple perspectives from the scientific community on this controversial issue.

Diet, Nutrition Essential for Mental Health

Kathryn Gibb

Nutritional supplements may be part of new prevention and treatment plans for mental disorders. A recent article published in *The Lancet Psychiatry* claims that both diet and nutrition are important determinants of mental health status. In fact, Dr. Jerome Sarris, a researcher at the University of Melbourne, claims that nutrition is as important to one’s mental health as it is to other aspects of physical health. Certain nutrients such as omega-3’s, B vitamins, iron, zinc, magnesium, and vitamin D have been proven to have a connection to mental health. Dr. Sarris states that nutritional supplements may be prescribed in the future to help manage mental disorders. In addition, the International Society for Nutritional Psychiatry Research states that there are other studies that show the connection between consumption of the aforementioned nutrients and the development of depression or other mental health disorders during critical life stages. For example, there is a confirmed relationship between “unhealthy dietary patterns” and a lower mental health status in adolescents and children. This is important news for public health advocates in that promoting a healthier diet could potentially prevent the development of certain mental disorders.

Ground-Breaking Lung Cancer Breath Test in Clinical Trial

Catie Donlon

Researchers at the University of Leicester and at the hospitals in Leicester have been working with Cambridge-based Owlstone Nanotech Ltd. to develop a new device to detect lung cancer at earlier stages. Currently lung cancer affects hundreds of thousands of people in the United States alone every year. It holds a position in the lowest five-year survival rates of all cancers, and has a poor general prognosis due to the fact that doctors are unable to detect it until its more advanced stages. Currently doctors diagnosis lung cancer using expensive methods such as chest X-rays, CT scans and bronchoscopy. However this new Lung Cancer Indicator Detection program uses a breath test to provide a cheaper, smaller, and non-invasive method of diagnosing lung cancer in a General Practitioner’s office. It works by measuring the volatile organic compounds on a patient’s breath. This device is now in clinical trials at Glenfield Hospital and its results are expected by early 2016. These efforts and this test could allow for earlier detection of lung cancer, leading to more effective treatment. This would raise the rate for early detection of lung cancer from 14.5% to 25% and could ultimately save over 10,000 lives.

References for News Briefs may be found online at

Tuftscope.Blogspot.com

FEATURE INTERVIEW

A Discussion with Dr. David Walt, Scientific Founder of Illumina, Inc

Caroline Russell-Troutman



PHOTO OF DR. DAVID WALT

Dr. David Walt holds a multitude of accomplishments in academia and entrepreneurship alike. He is both the Robinson Professor of Chemistry at Tufts and a Howard Hughes Medical Institute Professor. In 1998, he founded Illumina, Inc., a company that has developed groundbreaking new sequencing and genotyping methods for genetic analysis. Walt also founded Quanterix in 2007, a company that uses an ultra-sensitive single molecule assay to aid in early detection of disease. In addition to his academic and entrepreneurial achievements, Dr. Walt has contributed greatly to science education. He leads the Chemistry Organized Outreach Program (CO-OP), a program that allows local high schools to use Tufts laboratory equipment so that students may learn about new techniques in chemistry and biology.

Before expanding into the private sector, you had a lot of experience in academia – can you tell me a bit about how you got into your research?

I've always been interested in the medical applications of the basic sciences and I enjoyed chemistry but I was focused on applying it to something that had meaning. Medicine was always something that was attractive to me. I had considered going into medicine early in my education but once I got involved in research, I realized that this was a way to have perhaps an even more profound impact – not necessarily on an individual basis but on a more global scale.

A lot of your technology can be applied to early diagnosis of diseases. What got you interested in diagnostics?

My lab has been involved in developing new technologies that enable both genetic diagnostics as well as something called protein diagnostics. On the genetic side, my focus was on developing tools that enabled genetic analysis, rather than diagnostics per se. It was really more to understand the underlying causes of genetic diseases and that's the technology that we enabled. On the protein side of things, our recent work is on trying to detect disease at a very early stage. We've got projects in early breast cancer diagnosis using blood as a sample for screening as well as infectious disease diagnostics to predict at a much earlier stage whether somebody is going to get an infection and how severe that infection would be. We have a method that can measure things really sensitively and what more important problem can we apply it to than to try and detect deadly diseases at the earliest stage when therapies might be able to reverse the trajectory of the disease and change the outcome?

What inspired you to take the leap from academia to starting a company?

My bias is that academics is a great place to do some of the fundamental discovery work and to develop new technologies, but if you're really going to scale it, there's no way that you have the infrastructure in an academic environment to do so. The best you'll be able to do is perhaps create a prototype but that's not enabling the technology or the discovery to be fully implemented. The private sector is built on

scaling things and developing things that are reproducible in large enough quantities to meet demand. It's kind of a shared responsibility: the academic community has to partially come up with the new ideas and technologies, but then it's industry's role to scale those and produce them in ways that are robust and capable of being produced on a wider scale.

You've talked about the importance of having an impact. Do you feel that by expanding to the private sector you've been able to help people on a wider scale than if you had stayed in academia?

Unquestionably – there are technologies derived from what we developed in my laboratory that are being used on a daily basis to assist with prenatal care, decisions about cancer therapies, a whole host of genetic diseases, as well as neurological disorders and inflammatory diseases. These technologies are helping millions of people. This would just not have been possible in a clinical environment. I'm not trying to discourage potential physicians or people interested in helping patients in a clinic, but my personal trajectory has been one where I've been able to leverage the research done in the laboratory to change the way medical care is implemented, how disease is diagnosed, and change the course of treatment.

What advice would you give to other researchers who are thinking of following a similar trajectory by expanding their research into the private sector?

If a researcher's goal is just to publish a paper in a high-profile journal, my personal opinion is that that's not a particularly high-impact end result. Even if that paper gets read, ultimately it's how your work ends up changing the world that matters. Oftentimes there's a very long, circuitous route between a basic discovery and the time that it has impact, but I think that there's obvious research that has very short-term applications and people really need to embrace the notion that they are responsible for seeing that discovery or technology through to implementation. Just expecting someone to read a paper and say, "What a great idea, I think I'll start a company" – that's not going to happen. It's really the researcher who's

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been the innovator and initiator of that work who is responsible for taking that research to the next step.

More specific to your work – after developing Illumina, Inc., what led you to then found Quanterix in 2007?

The last thing I wanted to do after founding Illumina was to start another company, but in 2006 we made a discovery that led to our ability to detect proteins at extremely low levels in biological samples. I felt a responsibility to take that technology and make sure it got developed to the point where it would be used for the best purposes. It was a situation where I knew that if I didn't take responsibility for seeing to it that this technology got developed, it probably wouldn't see the light of day other than through publications.

Beyond educating college students, I see you also have an interest in an early science education for K-12 students through your work with CO-OP. Can you tell me a bit more about that project?

For the last ten years, we've had a pretty substantial effort towards taking cutting-edge technologies into high schools. We're really showing students the value and excitement of discovery. These are open-ended projects; there is no obvious answer at the beginning of the experiment. They're designed to stimulate inquiry and show students how science is really done. If you've taken chemistry courses both in high school and college, many of those experiments are either designed to teach you a technique – for example, in Organic Chemistry class you're learning a technique like crystallization – or you're following a recipe that is destined to give you a well-predicted result. That's not what scientists do; they design their own experiments and they don't know the answer to them. We're trying to provide that experience for primarily high school students that would not have access to the kinds of tools we're bringing to the school without this program.

Finally, what are you working on right now and what kind of projects do you see yourself developing in the future?

We have a very diverse group of projects ranging from fundamental science involving single molecule enzymology to nanoparticle catalysis, and then more applied projects where we're trying to identify markers in the bloodstream that will enable women to be diagnosed with breast cancer at a very early stage, ideally 3-5 year before any kind of imaging technology would be able to pick it up. We have another project – maybe the easiest way to describe it is trying to understand some of the ways in which we think life began on the planet. It's kind of an origin of life type of study. So, we have highly diverse projects, some of which are very fundamental, and other that are using our technology to apply them to clinical problems. Frankly, I don't know where the next technology or invention is going to come from. It could come from a fundamental project, or it could come from an applied project. I don't have a crystal ball to be able to say which one's going to lead to the next thing that we begin to consider commercializing, but we're always looking and prepared to notice an unusual observation that eventually leads to a new capability.

RESEARCH HIGHLIGHTS:

Review of Jian Ling Decoction Efficacy for Treating Hypertension Shows Inconclusive but Potentially Promising Results

Caroline Russell-Troutman

Hypertension is a massive public health issue today. It leads to increased risk for cardiovascular and renal disease, and is currently ranked as a leading risk factor for mortality globally despite being largely preventable. It is thus vital to develop effective treatments for hypertension to relieve symptoms early. In East Asia, practitioners of traditional Chinese medicine often prescribe Jian Ling Decoction (JLD), a mixture of eight common herbs, to treat essential hypertension.

Recent trials have suggested that JLD may effectively relieve hypertension symptoms, but these trials are small and their results are often unclear or inconclusive. A recent study published in the *British Journal of Medicine* (BMJ) has compiled a comprehensive review of many trials to better evaluate the overall efficacy of JLD as a hypertension treatment.

This study reviewed ten randomized controlled trials with 655 participants total. Trials were only included in this review if they focused on patients who met the diagnostic criteria for essential hypertension, and if they tested the effects of JLD against the effects of another drug for hypertension treatment. JLD produced no serious side effects in patients in any of these trials.

After compiling the results of all these trials, researchers found some evidence to suggest that JLD can greatly reduce systolic and diastolic blood pressure in hypertensive patients, but this result was only significant in trials where JLD was combined with an existing hypertension treatment in the experimental group. Trial results also suggested that JLD may improve long term quality of life in hypertensive patients. Overall, though results were inconclusive, there is some evidence that JLD may ameliorate certain hypertension symptoms and future studies are needed to explore these findings further.

This study was not without limitations. The trials looked at were varied in their methods and scope, and they often had small sample sizes. The number of trials reviewed was also fairly small. This review is still important, however, as it paves the way for further research into the potential efficacy of JLD and explores the vital issue of treating hypertension globally.

BMJOpen. 2015;5:e006502doi:10.1136/bmjopen-2014-006502

Was the ALS Ice Bucket Challenge an Ethical Venture?

Joseph argues that the funds raised and participant choice legitimates the movement, but **Lushna** asserts that the egoism and media-driven elements of the challenge mars its validity as a model for charity.

The opinions expressed in these articles do not necessarily reflect those of the authors.



Image Source: <https://flic.kr/p/oC6mFg>

YES

Prior to 2014, the majority of funding for research covering the documentation, analysis, and possible treatment of Amyotrophic Lateral Sclerosis (ALS) was covered largely through grants funded by the National Institutes of Health (NIH).¹ However, last summer brought the ALS Ice Bucket Challenge, and with it, a surge in awareness and funding. As a quick summation, the challenge involved dumping a bucket of water on to one's head before "nominating" friends and family, who then had 24 hours to do the same or make a donation towards ALS-oriented charities. This ritual was video-recorded and almost always uploaded to a social media website. Fiscally, the movement was a smashing success, raising almost 100 million dollars towards the DC-based ALS Association (ALSA), the disease's major charity and advocating base— 35 times the revenue received between July and August of 2013^{1,2} alone, with nondomestic organizations like ALS Canada and the Irish Motor Neurone Disease Association accruing similar, though perhaps less dramatic, amounts.^{1,2}

This phenomenon also represents a massive milestone within the sphere of philanthropy, serving as perhaps the most dramatic advancement of media-driven charity yet, with critics and proponents alike using the movement and its aftermath as a conduit for their opinions. These critic concerns – specifically those focused on fund allocation and participant self-image— are all serious views whose impact will have lasting effects on how future media-driven charity movements, as well as the Ice Bucket Challenge itself, will be viewed. However, upon addressing such concerns, I posit the ultimate results of the challenge far outweigh any of the following grievances.

The first concern to be discussed focuses on the money raised by the challenge. As previously mentioned, the Ice Bucket Challenge was a huge fiscal success. This spike in funding ensured the continuation and improvement of existing projects, but it was the potential to branch into new undertakings— many of which were not fiscally viable prior to the challenge's advent— which truly revolutionized the field of ALS research. One such example was the the fiscal de-risking of current approaches – especially clinical trials of prototype drugs— to understanding and treating the disease. Prior to 2014, the majority of ALS-oriented research centered around two disease-linked loci – SOD1 and C9ORF72 – and their respective projects.¹ NIH and ALSA funding backed the development of possible treatments, notably an SOD1 antisense oligonucleotide treatment designed to silence a disease-causing SOD1 mutation by ISIS pharmaceuticals.^{3,4} However, with bolstered funding, advocates hope to align private research with large pharmaceutical investment to drive forward new stage 1 clinical trials, with research hopefuls citing the stage 1 clinical trial for the aforementioned SOD1 treatment as a model for future endeavors.^{1,4}

Another example features the use of novel approaches, like the use of whole genome sequencing across a large population to better document the genetic causes and environmental risk factors contributing to the disease. It should be clarified that though a correlation exists between two genetic loci and ALS, a definitive cause has yet to be confirmed. Prior to the Ice Bucket Challenge, large scale studies like the one just discussed were largely unviable due to the great cost per individual (ALSA proponents cite whole genome sequencing costs at approximately US \$1200 per person).¹

Herein lies the critique: that the impact and magnitude of the Ice Bucket Challenge represents a massive misallocation of resources. According to ALSA figures, roughly 2 out of every 100,000 people in the United States are afflicted by ALS, with a similarly yearly death rate.⁵ Comparatively, heart disease— the

Continued on page 12

Joseph St.Pierre is co-Editor-in-Chief of *TuftScope*.

NO

Participation in the ALS Ice Bucket Challenge required participants to dump a bucket of ice water over their heads to increase awareness about ALS. The movement went viral, blowing through social media like wildfire. Despite the fact that this was probably all over your Facebook newsfeeds between the months of July and August, if I were to ask you what the letters ALS stand for, would you be able to tell me? Could you confidently say that it was for Amyotrophic Lateral Sclerosis, or Lou Gehrig's disease, which leads to the breakdown of motor neurons and loss of muscle control?¹ From the sheer amount of people that made the mistake of calling it the "ALS Challenge" in their videos, I grew to understand that it was not truly the cause that they were supporting.

This lack of understanding and true support for ALS became evident, as I would log onto Facebook every day just to see who had the most outrageous Ice Bucket Challenge of them all. Who dumped the most water on themselves? From what height? What were they wearing? It appeared to become a sort of mindless participation in this viral phenomenon in order to be seen as 'part of the trend' and to be socially relevant. You had to outdo the person who tagged you and get everyone talking about *your* video. Even better was the way in which most people worded the challenge: "You have 24 hours to participate in the Ice Bucket Challenge or donate \$100 to the ALS charity of your choice."

OR? So really, making this video was a way to circumvent donating to the cause whose awareness is trying to be increased. But then again, there were those individuals who chose both to do the Ice Bucket Challenge and donate some money. They got to appear 'cool' (literally) by participating in the latest trend, while also appearing charitable by donating as well. This behavior, known colloquially as *slacktivism*,² served mainly to boost the egos and satisfaction of the participants of the challenge as opposed to focusing on the cause itself or the effect the contribution could have on advancing ALS research. Such trends can be likened to the "Livestrong" yellow silicon bracelet trend, where many people bought the bracelet just because others had it and did not necessarily know that its goal was to raise money for those affected by cancer.

Certain elements regarding the video-recorded aspects of the challenge were also questionable. For one, the challenge required a considerable amount of water. This water was then simply poured on oneself and let fall to the ground. For all the people who let the water fall to the ground without using it for another cause, which was the case for most if not all videos I viewed, the valuable resource was wasted. While many people are privileged to have running water, the challenge became little more than a display of privilege. For example,

"This behavior, known colloquially as *slacktivism*, served mainly to boost the egos and satisfaction of the participants of the challenge..."

California and much of the Midwest has been subject to severe drought for the past three years.⁴ The waste of water was like laughing in the state's face, not to mention the faces of other countries with limited water supplies. Along with the scrutiny of using up our natural resources, the ALS Association (ALSA) received so much attention that it was scrutinized on almost every aspect. Online controversy over the association's use of embryonic stem cells began, with multiple pro-life groups sparking the debate as to whether ALSA was indeed the best charity to receive funds.³ Again, energy and funds which could have otherwise been forwarded towards the cause were lost in participants' attempts to maximize self-image through searching for the "best charity." Though the purpose of the ice bucket challenge was mainly as a fundraiser, the blind desire to be a part of the trend without necessarily knowing about the cause being represented was a prevalent problem.

The egotistic aspect that the whole phenomenon took on almost made it seem like the challenge was not even about something as serious as a neurodegenerative disease, but was more a fun and whimsical thing to do with friends the next time you hung out. Getting to waste all that water was a great plus too, right? The situation grew absurd to the point that the "Ice Bucket Challenge" Halloween costumes were offered for sale by the merchant site BrandsonSale,⁵ highlighting the incredible disconnect between the challenge and the cause it supported. The Ice Bucket Challenge was pulled in so many directions that its detachment from ALS deemed it an acceptable target for mockery. Next time you participate in a viral trend, perhaps understanding its reason and aims will help maintain a healthier balance between the more fun aspects of the movement and the serious nature of the cause.

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YES

perennial leading cause of death in the United States—claimed 611,105 lives in 2013 alone.⁶ Therefore multiple critics argue viral movements distract from a more utilitarian allocation of funds.

Many media-based critiques draw from a viral infographic generated by Julia Belluz of Vox comparing charity funding for various diseases relative to the deaths said diseases cause, which illustrates fundraising giants like Komen Race for the Cure and the ALS Ice Bucket Challenge (erroneously posted as having raised 22.9 million USD; ALSA announced it had raised \$94.3 million in charitable funds a mere seven days after Belluz's article was published²) with funds-to-death ratios dwarfing those of Heart Disease and Chronic Obstructive Pulmonary Disorder (COPD).⁷ However, analysis of this figure reveals an incomplete, unfairly-cropped, and perhaps erroneous image of the current state of health-oriented philanthropy. First, in an attempt to draw parallels to the ice bucket challenge, the figure seems to regard a single public charity movement as representative of total charitable revenue, confusing funds raised in a single public movement with the total income for a given cause. Second, the figure fails to adjust for public funding. NIH categorical spending reports reveal \$1.224 billion being forwarded towards heart disease relative to breast cancer's \$ 715 million and ALS' \$48 million,⁸ and while this piece does not seek to justify NIH fund allocation, it is clear disease subsidies are contingent on variables besides dealing with social visibility.

Finally, to dissent charitable movements like the Ice Bucket Challenge on the grounds of low relative need is to ignore participant choice and passion. Consider a 2010 literature compilation by Bekkers and Wiepking, which focused on factors driving charitable giving. The summation outlined eight research-identified mechanisms influencing philanthropy: need, degree of solicitation, costs and benefits, altruism, reputation, psychological costs and benefits, values, and efficacy. Under this model, even if factors like perceived altruism and costs to the benefactor were to be controlled, an allocation of funds based on need alone would require solicitation (visibility of the charity), reputation based on social culture, personal values, and efficacy of giving to be equal. Of course, holding all such variables – particularly personal values and social reputation— constant is impossible, and almost implies the penalization of more visible charities to allow for the expansion of less visible charities with greater perceived need. The aforementioned compilation also discusses the concept of self-image, a subtheme of reputation, as a major impetus not only for charitable preference, but whether a benefactor will give at all. Citing a 1972 study by Schwartz, the authors discuss the concept of personal norms, how they contribute to social norms, and vice-versa. If the social norm is to donate, then frequency of giving increases.⁹

Unfortunately, it is this idea of self-image (and charitable solicitation, to a lesser extent) as a major impetus for charitable giving which leads to the third and final objection: that the challenge was focused more on participant visibility than the actual cause. Jacob Davidson of *Time*, himself having lost a father to ALS, lambasted the culture the challenge represented, questioning how much awareness for ALS was actually raised. However, he did concede he could not argue against the beneficial nature of the funds raised. “In an age where hashtag activism and information-free awareness campaigns are becoming more and more common, we should be very conscious of how to make viral trends as useful as possible,” he wrote on the topic, hinting the problem with the Ice Bucket Challenge concerned a lack of public knowledge as to what they were funding as opposed the actual fundraising aspect.¹⁰ Will Oremus and Arielle Pardes of *Slate* and *Vice*, respectively, voiced similar online concerns.^{11,12} This is perhaps the more disturbing of the two issues. If the models held by the Bekkers compilation are to viewed as valid,⁹ “information-free” (or even information-poor) charity campaigns driven primarily by social-image are particularly threatening in that they limit other variables—leaving potential benefactors at the mercy of the next fad.

Consequently, such concerns are indeed valid, though somewhat overblown. Regarding critic concerns over the lack of awareness raised, consider a *Forbes* report revealing English Wikipedia hits for “ALS” spiking from 163,000 to 2.89 million in the month of August 2014, with similar success for the corresponding German, Spanish, and French pages.¹³ Is it not reasonable to assume at least a fraction of such hits account for participant self-education? Even the money raised can speak for itself, as donations to specific organizations like ALSA require at least some research on the part of the benefactor, even if only to determine a means of donation.

Perhaps, however, the ultimate reason this concern—or the previous dissent, for that matter— falls flat is that it fails to account for participant choice. Decrying the participation in a event judged to be relatively low risk, charitable, with positive social impact— regardless of however selfish or ignorant one's motives might be— insults the not only participant judgement, but maligns the funds raised. While experts (and non-experts) will always have an opinion as to how a responsible populace should spend its time or allocate its funds, the reality with regards to charity is people will almost always make their own specific choices based as to what they think is best for themselves and their environment. And if such ignorant bumbling does indeed end up raising \$100 million towards the research and treatment of a life-threatening disease, however rare, perhaps there are greater issues to critique.

References for this articles can be found at
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Digital Health Devices Are Transforming How We View Health

Samantha Fine

More now than ever, mobile tools are being used to monitor our health. Digital health devices can now track heart rate, blood-oxygen levels, miles walked, stairs climbed, sleep cycles and the list goes on. The popularity of mobile health tools is growing, and production of apps and watches such as the Fitbit or the Nikefuel band are predicted to triple in the next two years.¹ Besides fitness monitoring devices, mobile apps also have a practical appeal for health professionals and those with serious health issues. Many health care professionals now use personal digital assistants (PDAs)², which have greatly improved clinical practices. For diabetics, many new apps can now monitor glucose readings and provide healthy food recipes. Mobile tools can be life changing; however, as health technology becomes more integrated into the daily lifestyle, the reliance on mobile tools is increasing, transforming the way society views health.

There is a great appeal to digital health tools in that one can learn more about personal habits and exercise trends. Author of the *Fortune* article “Fitness trackers: a narcissist’s dream” Ryan Holmes explains his fascination with using health apps. He tracks his run using Strava, a website that can log running routes. Then he will use RFLKT, a cycling app that tracks personal records and speed when he goes for a bike ride. At night, he uses a Sleep Cycle app to learn about his sleeping habits. Health apps satiate desires for self-knowledge and self-improvement. By constantly tracking and monitoring one’s body, people like Ryan are creating a “quantified self,”³ using logged miles and calories burned to define how the day was spent. There is an addictive and slightly narcissistic quality to see how much exercise was done for the day. One can share their progress with others on Facebook or twitter and create new health goals. There is a growing pressure to put a number on health. Digital health devices are changing the way to view health, creating another outlet to share personal information and measure one’s lifestyle.

Various apps are not only altering the lives of adults like Ryan, but those of children as well. Childhood obesity has doubled in children and quadrupled in adolescents in the past thirty years.⁴ Obesity can lead to increased health risks such as type 2 diabetes, stroke, several types of cancer, and heart disease.⁵ Kurbo Health, a new app invented by Stanford University’s pediatric obesity program, is helping

parents, pediatricians and children learn about healthy and safe weight loss. The app is based on a traffic light diet, where instead of counting calories for foods eaten throughout the day, one uses green, yellow and red colors to represent food. Healthy foods like fruits and vegetables are green. Breads are yellow, and fried foods and candy are red. The goal of the app is to reduce the red foods.⁶ Joanna Strober, the CEO and co-founder of Kurbo Health states that “at the beginning, [the kids] might not be that motivated, but once they start realizing it can work, they are pretty likely to continue”. Kurbo Health began in May 2013, and already 85% of children who use the app have reduced their BMI. Furthermore, apps like Kurbo allow for children to take control of their health,

making parents and pediatricians feel less pressure to hover and be overbearing. Health technology is allowing children to monitor their weight in a safe way, creating another intervention to combat prevalent health issues.

From MyFitnessPal to Fooducate, there are a growing amount of health apps available for smart phones; however, with health wearables such as Fitbit, Nikefuel band, and the upcoming Apple Watch, digitalized health is becoming more immersed in daily

lives. The Apple Watch, which will be released in April 2015, can be connected to one’s calendar, contacts, and schedule - and can make phone calls. It has a built-in heart rate sensory, measures all the ways one moves (walking, running, etc), and can track when one stands up. Over time, the Apple Watch learns about one’s personal activity and then suggests realistic achievable exercise goals. With its Taptic Engine, one can even send their personal heartbeat to another Apple Watch wearer. Unlike mobile devices, devices like the Apple Watch are something that are constantly worn. Health devices are creating “a new chapter in the relationship people have with technology.”⁷ Wearable health tools allow technology to be integrated at an intimate level. The Apple Watch will not only provide quantitative data, but with the suggested goals and progress reports, it also provides qualitative advice on how to improve one’s life. While technology normally inhibits face to face connection, wearable devices like the Apple Watch can create greater human connection with other users. Health

“With health wearables such as Fitbit, Nikefuel band, and the upcoming Apple Watch, digitalized health is becoming more immersed in daily lives.”

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technology is now being designed to be worn and to be truly personal, demonstrating how our reliance on technology has grown in the past decade.

Now with the expanding market of health devices, technology will further be integrated in everyday life. Digital health devices like the Apple Watch, Fitbit, and Nikefuel band only represent the beginnings of the health technology movement. In 2014 alone, 17 million fitness bands and smart watches were sold and by 2017, the number is predicted to triple.⁸ With increase in investment and production of apps and devices, companies - with permission of their users - now have massive amounts of biological data, learning more about their users for future product development, and wearable devices such as the Apple Watch create a realm for marketing that has never existed before. Major digital health trends to look out for in the upcoming years include fitness trackers to wear on the ear, sweat sensor strips to track electrolyte balance and hydration level, and even prescription-only health apps.⁹ Digital health devices are entrenching on every aspect of personal life, clearly demonstrating how technology is influencing the way society views health. There is a greater demand for lifestyle choices to be logged, calculated and coordinated with mobile health apps. Perhaps the line between digital overdependence and personal independence is starting to blur, which proposes the lingering question of whether a limit should exist with usage of technological health tools.

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RESEARCH HIGHLIGHTS:

New Device Implanted in Coronary Sinus May Improve Symptoms of Refractory Angina

Caroline Russell-Troutman

A recent study published in the *New England Journal of Medicine* (NEJM) has investigated the efficacy of a new device designed to relieve refractory angina in patients who suffer from coronary artery disease. The device is implanted in the coronary sinus where it increases pressure to relieve pain caused by angina.

104 patients at 11 different clinical centers participated in this study. All patients were over 18 years of age and had been diagnosed with class III or IV angina that had not improved with existing therapies. Half of the participants had the device implanted while the other half had a sham device implanted and served as the control group. This study was double blind so neither participants themselves nor the researchers (with the exception of the physicians who performed the implantations) knew which participants were in which group. Over the course of 3 years, researchers monitored patient angina by measuring cardiac wall motion and by asking participants to rate their symptoms in a questionnaire.

Results showed significant improvement in at least one angina class in 71% of the treatment group compared to only 42% of the control group. 35% of treatment group participants further reported improvement in 2 or more angina classes compared to 15% of control group participants. Thus, the implantation of this device was associated with greater relief from angina-related symptoms.

As heart disease rates and life expectancies for patients with coronary heart disease rise in the Western world, rates of refractory angina rise as well. It is thus vital to develop improved therapies for the symptoms of angina, since many current treatments are not very effective. However, despite its clinical importance, this study was not without limitations. The study relied heavily on patient self-report and the number of participants was relatively small (n = 104). Further studies are needed to confirm the efficacy of the device and to understand its applications on a wider scale, but for now this coronary sinus implantation device shows promise as an effective treatment for refractory angina.

N Engl J Med. 2015; 372:519-527. doi: 10.1056/NEJMoa1402556.

Teixobactin: A Powerful New Weapon in the Arms Race against Antibiotic-Resistant Bacteria

Caitlin Keenan

INTRODUCTION

The discovery of a new, “resistance-resistant” antibiotic, dubbed “teixobactin” was recently reported by a research group at Northeastern University.¹ The paper appeared in the journal *Nature* on January 7, 2015, listing Professor Kim Lewis as the lead author.¹ Teixobactin was identified in a screen for antimicrobial compounds produced by “uncultured” soil microorganisms, bacteria that are difficult to grow in standard laboratory cultures (you read that correctly: to combat bacteria, we turn to other bacteria for help).² In subsequent experiments, teixobactin exhibited antimicrobial activity against a wide panel of human pathogens.¹ Amazingly, none of the pathogens tested appeared to develop resistance to the new molecule.¹

THE SUPERBUG PROBLEM

In the 1930s, the advent of the antibiotics penicillin and streptomycin drastically improved our ability to treat human disease.¹ To date, all effective antibiotics have been isolated as natural products from soil bacteria.¹ Unfortunately, only about 1% of soil bacteria grow easily under lab conditions.² The “over-mining” of this limited resource, coupled with the widespread misuse of the drugs, has led to the evolution of antibiotic resistance, which persists as a major problem.² Antibiotics are difficult to develop because they must be able to penetrate the bacterial cell wall.² In fact, no synthetic candidates have been successfully developed into drugs; we have exclusively depended on natural products that have evolved over time to outwit pathogenic bacteria.¹ There is a constant need for new compounds to combat the ever-evolving strains that afflict humans.

THE SUPER SOLUTION

Professor Lewis’s lab, in collaboration with other labs and pharmaceutical companies in Germany and the United Kingdom, developed and implemented a method to culture the 99% of bacteria that do not typically grow under laboratory conditions.² They used the iChip, a tool that allows the bacteria to feel “right at home” in the lab.¹ Soil samples were diluted to a concentration that resulted in approximately

one bacterial cell in each channel of the iChip.¹ Then, the device was covered with two semi-permeable membranes and placed back in the soil, allowing the exchange of growth factors and nutrients.¹ Colonies were then isolated from this setup and grown *in vivo*. Ten thousand isolate extracts were screened for antimicrobial compounds by plating them with *Streptococcus aureus*.¹ The screen identified a compound produced by a new species of beta-proteobacteria, called *Eleftheria terrae*, as a hit.¹

EXAMINING THE HIT

A computer analysis revealed that *E. terrae* is a gram-negative bacterium belonging to a new genus related to *Aquabacteria* genus.¹ Prior to this study, that genus was not known to produce antibiotics.¹ A 1,242 Da fragment was isolated as the effective compound from the screen. NMR and Marky’s analysis revealed that the compound, teixobactin, is a depsipeptide, meaning it has an ester group replacing an amide group at one point along its peptide backbone.¹ Its amino acid sequence includes enduracididine, methylphenylalanine, and 4 D-amino acids, which are all unusual features.¹

“No synthetic candidates have been successfully developed into drugs; we have exclusively depended on natural products that have evolved over time to outwit pathogenic bacteria.”

RESISTANCE AGAINST RESISTANCE

Teixobactin exhibited excellent anti-microbial activity and, remarkably, bacteria could not be induced to develop resistance to it *in vitro*.¹ It was effective against *Mycobacterium tuberculosis*, which is highly resistant to antibiotics, at an MIC (minimum inhibitory concentration) of 0.125 µg/mL.¹ It also targeted *Clostridium difficile* and *Bacillus anthracis* with MICs of 5 and 20 ng/mL, respectively.¹ Additionally, it killed late exponential-phase *S. aureus* more effectively than vancomycin, the antibiotic that is normally used to treat *S. aureus* and that has major resistance problems.¹

In an experiment to test the potential for evolution of resistance against teixobactin, *S. aureus* cells were incubated with the compound at sub-MIC levels for 27 days. As

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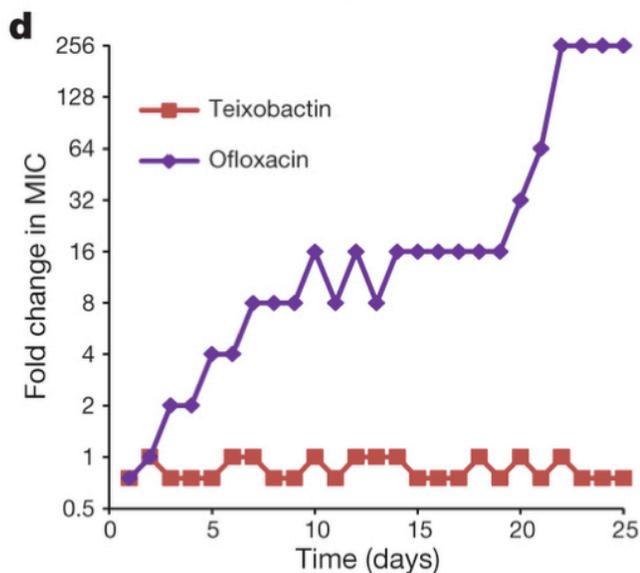


Figure 1. *S. aureus* bacteria were incubated with teixobactin and ofloxacin at sub-MIC concentrations through serial passages for 27 days. While ofloxacin required increased concentrations to maintain effectiveness against *S. aureus*, teixobactin remained effective at its initial concentration.¹

Figure 1 shows, the cells did not develop resistance to teixobactin, in stark contrast to their acquisition of resistance to ofloxacin, another antibiotic.¹

One possible explanation for this trend could, unfortunately, be nonspecific toxicity: teixobactin could effectively kill bacterial cells in a resistance-proof manner but also kill normal, healthy mammalian cells, rendering it useless as a drug. However, the data showed that teixobactin was not toxic to mammalian cells at concentrations as high as 100 µg/mL.¹ It also did not bind DNA or cause hemolysis (the rupturing of red blood cells).¹ It exhibited excellent therapeutic properties: it was stable and retained its potency in serum, and mice injected with the compound maintained serum levels above the MIC for 4 hours after injection.¹ In one striking experiment, mice were infected with MRSA (methicillin-resistant *S. aureus*) at a concentration that should have led to death in 90% of the test subjects.¹ One hour after injection, the mice were treated with doses of teixobactin varying from 1 to 20 mg per kilogram of body weight. Strikingly, all of the treated mice survived.¹

MECHANISM

So how does this wonder drug work at the molecular level? A series of careful pathway analysis tests indicate that it binds and inhibits several precursor molecules called lipids I, II, and III, in the biosynthetic pathway of peptidoglycan, the material used to build the bacterial cell wall.¹ Vancomycin operates via a similar mechanism, but teixobactin is unique because it binds to multiple precursors in the pathway as opposed to only inhibiting one step.¹

CONCLUSION

Professor Lewis is optimistic about teixobactin's ability to contend with antibiotic resistance. He points out that it took 30 years for resistance to vancomycin to evolve, and teixobactin operates via a similar mechanism.¹ Also, because the drug's target is not a protein, it will be more difficult for bacteria to develop resistance to (they cannot simply mutate the amino acid sequence of the protein to evade drug binding).¹ Interestingly, *E. terrae*, the bacteria that produces teixobactin, is protected from its own "poison" because it has an outer cell membrane that the secreted compound cannot penetrate.¹ If it had some kind of poison-degradation pathway to protect itself, the genes coding for those enzymes could be "stolen" by other bacteria, allowing them to acquire resistance.¹ Since this is not the case – the cell membrane is the protective barrier – it will be harder for bacteria to acquire resistance.¹ The research group enthusiastically expressed their belief that there are more compounds just as potent as teixobactin to be discovered among the overlooked treasure trove of uncultured soil bacteria.

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On the Frontier of Neuroprosthetics

Adam Kaminski

Imagine building a mechanical brain of silicon, gold tracks, and electrodes. What if this machine were a surrogate central nervous system (CNS) constructed of materials and devices designed to imitate their neural counterparts? While this thought borders science fiction, the field of neuroprosthetics, a discipline combining neuroscience, bioengineering, and neural prostheses, is contributing to its fruition in reality. Exploring the intricacies of such neural structures and the innovation of such engineers, however, might be better appreciated having placed neuroprosthetics in its far-reaching historical context.

Neuroprostheses are the latest culmination of a strategy that has been adopted by myriad of cultures throughout history. The first recorded mention of prosthetics comes from the Rigveda, a sacred Hindu text written around 1500–1200 BCE, in which the warrior queen Vishpala receives a “leg of iron” having lost one of hers in battle. From antiquity, notably from the Egyptian, Roman, and Greek civilizations, up until the present day, replacing biological parts has been a steadfast technique in the medical arsenal.¹ Beginning in the 20th century, however, the field of medicine began to see the production of useful and therapeutic implants such as heart pacemakers and cochlear implants followed by even more complex CNS prosthetics of the 21st century.²

Stéphanie Lacour and Grégoire Courtine, two professors of the Ecole Polytechnique Fédérale de Lausanne in Switzerland, work on the frontier of neuroprosthetics. Together, they answered a question limiting the progression of neuroprosthetics: how will scientists be able to “make innovative use of materials to design and fabricate devices that allow sustained electronic functioning in the harsh environment of the human body, without causing tissue infection and other serious adverse conditions?” - a question posed by the American Society of Mechanical Engineers.³ Their research led them to the design of multifunctional implants that use both electrical and chemical signaling of the CNS, making their implants successful transmitters of neural information. Even more astounding is that their device can be installed for long periods of time without the buildup of scar tissue or eventual rejection. The prosthetic is called the e-Dura implant; it is trailblazing the path of spinal cord injury treatment, and its resemblance to the mechanical

properties of living tissue are leading the way.⁴ e-Dura marks such a distinction from other modern approaches to treating CNS-related injuries such as paralysis in its aspirations to not only heal the injuries of patients, but also to promote a level of normalcy in their lives and bodies that was previously largely unattainable.

Besides neuroprostheses, medications that either promote the growth or improve the function of nerve cells are frequently used to treat spinal cord injury patients. Drugs that mitigate pain and muscle spasticity, strengthen bladder and bowel control, and enhance sexual functioning are often also prescribed.⁵ Having said this, medications are not the only alternative to prosthetics; other technologies, such as computer adaptations, lighter and more versatile wheelchairs, electronic aids, and robot gait training sessions, devised for retraining the ability to walk, are available for people with impaired brain or spinal cord functioning.⁶

Of these technologies and medications, however, prosthetics such as e-Dura offer a particularly unique and profound array of benefits, notably the chance to recover function with surrogate bionic body parts. This is possible thanks to new innovations that allow e-Dura implants to be placed beneath the CNS’s protective envelope known as the dura mater, a thick sheath that surrounds the

“The e-Dura implant... is trailblazing the path of spinal cord injury treatment, and its resemblance to the mechanical properties of living tissue are leading the way.”

brain and spinal cord. While the dura mater proved to be an impasse for neural prosthetics of the past, the mechanical properties of e-Dura are remarkably similar to those of dura mater. This prevents inflammation and rejection of the device, which was previously caused by implants rubbing against stretching nerve fibers.⁷

Because of its profound similarity to CNS tissues and nerve fibers, e-Dura implants can stay attached to the spinal cord or cortex for long periods of time, marking exciting potential for newly developed therapeutic techniques. The scope of implementation is broad; patients suffering from paralysis, Parkinson’s disease, epilepsy, decreased pain management, and spinal cord injury are all candidates for e-Dura implants, but before the extent of its scope is reached,

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e-Dura will continue extensive testing on rats. These trials have been met with great success and Lacour and Courtine have observed formerly paralyzed animals regain the ability to walk for as long as the prosthetic is implanted. Scientists are now moving toward clinical trials in humans, and hopefully anticipate commercialization as a next step.⁸

Within the CNS of a person with the e-Dura implant, the areas of injury are stimulated by electronic parts of the device; silicon substrate with cracked gold conducting tracks have the facility to bend with nerve fibers as they stretch. The electrodes are made from silicon and platinum microbeads (nanoparticles that can bind to neural targets according to the affinity of the ligand or binding agent). Neurotransmitters and other pharmacological substances can then be delivered via microchannels in the device, enabling nerve cells beneath the injured tissue to reactivate.⁹

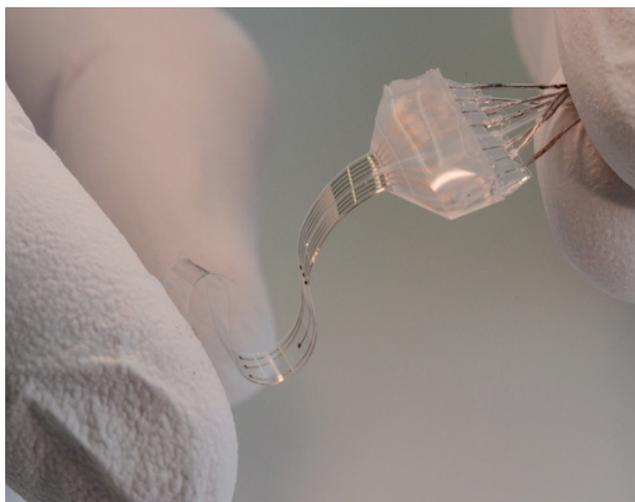


PHOTO OF E-DURA IMPLANT.

Photo Credit: bgr.com/2015/01/12/e-dura-spinal-cord-implant/

Beyond the profound and practical accomplishments of neuroprosthetics, a key feature of this relatively young field of research is its reliance on interdisciplinary work. Researchers and contributors hail from a variety of disciplines, each offering an invaluable ingredient to the conception of neural prostheses; diverse components include materials science, electronics, neuroscience, medicine, and algorithm programming.¹⁰ Taken as a composite of each foundational area of research, neuroprosthetics is an exemplar of engineering ingenuity. Designers had to create a product that was not only flexible and stretchable, but that would also have the capacity to send electrical and chemical signals in a manner comparable to and sustainable within the human brain and spinal cord. If it had not been for inspiration, innovation, and interdisciplinary manpower, this feat may not have been attainable.

The concept of prosthetics has come a long way, from conjuring images of relatively simple, external, and crutch-like implements to complex neural implants. In the next century, prosthetics will begin to take on different shapes yet again, maybe striving toward the science fiction fairytale ideal of a reconstructed brain. But whatever the direction of progress, one thing is certain: interdisciplinary research will remain vital as the field of prosthetics marches into the unknown.

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The Medicalization of Human Conditions and Health Care: A Public Health Perspective

Daryl Mangosing

“Public Health” focuses on the upstream causes of poor health, particularly those related to social and environmental factors that impact health status. However, biomedical advances in the last century have shifted the public’s health to another aspect of care: individual causes and manifestations of illness and disease.¹ This transition has led to what we call medicalization or “the process by which previously nonmedical problems become defined and treated as medical problems.”² The medicalization of human conditions releases a ripple of effects, one being whether a consumer of health care recognizes a health problem that needs to be medically addressed. These problems are generally the result of failures in biology, hygiene, and behaviors, and they are resolved through biomedical treatments delivered by providers.¹

If such is the case, two significant questions surrounding health care arise: what is the relationship between medicalization and health care spending and health policy, and is the medicalization of human conditions generally justified at the public health level? The answers to these questions, as we shall see, warrant implicative actions that shift the direction of public health interventions to a more social, community-based effort in attacking the heart of poor health. Put simply, we have to translate the knowledge gained and lessons learned from medicalization of human conditions into preventive measures that go beyond what we may think is beneficial for health not just at the individual-level but ultimately at the population-level.

Individual problems of ill health have attracted the attention of money and manpower, lending to increasing concerns of medicalization driving up health care costs in the U.S.³ It is essential then that we take a further look into these estimations. For example, a study that estimated medical spending in the U.S. of identified medicalized conditions generated the following sum: \$77.1 billion or 3.9% of total domestic expenditures on health care costs.⁴ Although it is a relatively minor portion of national health care expenditures, such an amount implies a substantial cost to private and public sectors as well as consumers.⁴ Whether this spending is inappropriate depends on the economic, social, and political dimensions of health care. Conversely, one can look to managed care, a major type of health insurance, as another major driver

of U.S. health care. Conditions that are covered by health insurance fuel medicalization whereas the lack of coverage may slow it down; for example, Medicare and other medical insurance plans decided to consider obesity a reimbursable illness while some insurance plans do not cover certain conditions such as infertility.² Furthermore, the only way to get human services paid for/reimbursed is to define a condition as a medical problem, thereby creating an incentive to medicalize more problems.² The medicalization of human conditions therefore influences health care spending indefinitely, with increasing costs yielding unknown results.

Policymakers have focused on increasing financial and geographic access to personal health services because of the assumption that health status problems are fixed by medical care. As the health problems of vulnerable populations became more medicalized, public policy started expanding access to individualized medical care.¹ This approach may broadly help to achieve some public health goals, but key social and economic causes of health vulnerability and disparities lose attention. For instance, Medicaid provides a funding umbrella through which states finance expanded services and social supports that extend beyond

medical treatment but services only become available or accessible after an individual is diagnosed with the health problem.¹ On top of health care spending, the political drivers behind it have relied on medicalization to address health vulnerabilities by increasing access, but again, policy may lose sight of the root of the problem.

When looking at patterns of health, patient/doctor ratios, the availability of tools for the job, and numbers of hospital beds may bear little relation to improvements in public health, and even disease and disability continues to directly result from medical intervention.³ Medicalization can also negatively affect how populations manage health problems in the following ways: the creation of ill-informed demand, enforcement of the belief that one has to spend more on

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medical services to secure a healthier population, and dependence on a system for medical help from womb to grave.³ Disease prevention then looks like a reliance on authoritative systems that give insufficient consideration for empowering people themselves to take responsibility for their health, giving people no choice but to support the system.

The medicalization of human conditions have spurred the “individualization of social problems,” making social or environmental interventions either ignored or secondary, and reinforces technical fixes for complex problems.² One complex problem in which medicalization may be at odds with public health is alcoholism: is it truly a disease or is it just deviant social behavior? Not a single cause of alcoholism has been established or likely will be as patterns of alcohol abuse vary individually and are influenced by social structure and external events.⁵ Another surprising proposition is that prevention itself has become a key driver of over-medicalization.⁶ Certain diseases and conditions have a long lead-time, leading people to opt for treatment that possibly lengthens their “disease survival” without lengthening their lifespan.⁶ If screening was not enough to halt disease progression, physicians may intervene earlier or screen for “pre-disease” (e.g. pre-hypertension) that may or may not pay dividends in the end.⁶ In all truthfulness nonetheless, the medicalization of certain conditions and behaviors may surely benefit certain individuals more so than others. These others then unfortunately miss the intended benefits.

In summary, several conclusions can be inferred from what we know regarding medicalization and its effect on health care: medicalization influences health care spending indefinitely, policy has focused on increasing health access, prevention may have promoted reliance on authoritative systems, and medicalization may benefit some more than others. What remains common among these assumptions is the neutral yield of both benefits and losses, thereby calling for further research and analysis of such data. However, the implication raised here is to return to the public health view of upstream causes of health. This means policy action in income security, education, housing, nutrition/food security, and the environment to improve health among all populations, especially among socially disadvantaged groups.¹ Accompanying this step is the transition from medicalization to “healthization” – lifestyle and behavioral causes and interventions – turning health into the moral rather than the moral into health.² Doing so creates efficacious communities and stronger families, which serve as mediating institutions that can screen out the individual and social effects of disease.⁵ Put simply, the key could be a form of strong community self-help.³ The medicalization of human conditions is not an inherently negative asset of health care, but rather, it is a way for us to improve our understanding of disease processes so that we may delve into deeper solutions that attack the root of the problem. In this case, the starting point is the holistic, societal unit of the individual: the community.

References for this article can be found at

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RESEARCH HIGHLIGHTS:

Visual Impairment Associated with Higher Rates of Suicidal Thoughts and Attempts in South Korea

Caroline Russell-Troutman

Though we generally consider mental illness to be caused entirely by dysfunction within the brain, damage to other parts of the body can strongly influence the development of mental illness. Studies have shown that visual impairment, for example, can lead to a greater incidence of depression and even suicide. A study recently published in the *British Journal of Ophthalmology* has further investigated the effect of visual acuity on suicide and depression in South Korea.

Researchers used medical information provided by the Korea National Health and Nutrition Examination Survey to examine visual acuity, depressive symptoms, and suicidal thoughts and/or attempts in 28,919 Korean participants aged 19 years or older. Visual acuity was measured via an eye chart and suicide/depressive symptoms were ascertained through a mental health questionnaire. Statistical analyses showed that lower visual acuity was significantly linked with suicidal thoughts and attempts. A severe loss of vision to the point of total or near-total blindness was associated with a 2-3 fold greater risk of suicide compared to participants with normal vision. However, researchers found no link between visual acuity and depression. Importantly, researchers also found that less than 30% of participants who had attempted suicide and less than 10% of participants with suicidal thoughts had sought counseling for these issues.

It is presently unclear whether the results of this study are generalizable to people of other nationalities and cultures, and further testing is needed to confirm these results in alternate populations. Despite this, the present study has important implications for the treatment of patients with poor visual acuity. Though many programs and technologies exist to improve the day-to-day lives of blind or visually impaired individuals on a practical level, treatments often do not focus on the mental and emotional toll that comes with loss of vision. Researchers of the present study have encouraged ophthalmologists to prioritize patient mental health and encourage those suffering from visual impairments to seek counseling if needed.

Br J Ophthalmol doi:10.1136/bjophthalmol-2014-306518

Decision Making in the Delivery Room: Extreme Prematurity, Severe Anoxic Injury, and Trisomies 13 and 18

Jordan Wang

Physicians in intensive care nurseries frequently encounter ethical dilemmas concerning the withholding and withdrawing of life sustaining treatment in infants characterized by extreme conditions. Three common cases in which physicians are deeply divided occur when newborns present with extreme prematurity, severe anoxic injury, and trisomies 13 and 18. Effectively confronting these ethical crises requires a certain degree of familiarity with the themes inherently unique to each condition in addition to the themes that are shared by all. This paper reviews the existing literature in order to provide physicians with the pertinent information necessary for making ethically competent decisions in these critical life-or-death situations.

Physicians practicing in intensive care nurseries routinely encounter dilemmas concerning the withholding and withdrawing of life sustaining treatment in infants characterized by extreme conditions. Such controversy highlights an area of deep disagreement and raises fundamental questions regarding proper and ethical standards of care. Three common cases in which physicians are deeply divided occur when newborns present with (1) extreme prematurity, (2) severe anoxic injury, and (3) trisomies 13 and 18. These particular scenarios call for consideration of not only the shared themes but also of the special features unique to each in order to effectively make informed end-of-life decisions. Criteria presently used in decisions to withhold and withdraw life support vary between physicians as well as institutions. A comprehensive analysis of current practice in these three clinical cases will be highly beneficial for the future development of specific recommendations and guidelines. For physicians charged with making these difficult and often complex decisions, a comparative review of the significant themes will help to ameliorate the burdens they will confront in clinical practice.

SHARED THEMES

Future Quality of Life

For infants with poor prognoses, treatment decisions regularly concern the future quality of life that they are predicted to have.¹⁻³ It is ethically important to address the best interest of the child when considering withholding and withdrawing life sustaining treatment. For extremely premature infants, great weight has been placed on the predicted quality of life by neonatologists making these decisions in the delivery room.^{4,5} However, attitudes may differ when interpreting which particular factors define an acceptable quality of life. Physicians express great discomfort when judging which conditions are supposedly acceptable,⁶ especially in cases where decisions may result in a life of severe disability.^{7,8} Although poorly diagnosed infants who receive treatment may survive for longer periods than what is deemed to be the norm, a significant proportion are subjected to the continued use of substantial inpatient hospital care and bed days.⁹ It may

therefore be justifiable to withdraw life support given a predicted low level of future well-being even though the life of a disabled infant would still be worth living.¹⁰

Futility and Unnecessary Suffering

Treatment should neither be initiated nor continued if judged to be futile and of no significant health benefit to the infant. It is ethical for physicians to decline the provision of care on the basis of the best interest of the child.¹¹ In delivery room decisions for extremely premature newborns, initiating resuscitation is often viewed as futile.^{4,12} For decisions of withdrawing care, the mounting burden from neonatal complications should additionally be considered alongside the perceived futility of the treatment.¹³

Infants should not be forced to bear unnecessary pain and discomfort when treatment is most likely to deliver little or no health improvements. Concerns regarding unnecessary suffering are frequently held by neonatologists in the delivery room and are cited as the reason for withholding and withdrawing treatment.^{1,2,5} This is particularly significant for infants diagnosed with trisomies 13 and 18, where ongoing treatment and the subjection to major surgeries are unlikely to be of any great benefit.^{14,15} Decisions should effectively weigh the relevant costs of treatment together with its benefits.

Certainty of Prediction

Medical prognoses in infants are rarely seen as fixed and certain. The process for developing these predictions differs dramatically between physicians in terms of which factors are relevant and how much influence each possesses. It is therefore much more likely that prognoses in these cases are uncertain. Such difficulties in prognostication for the future conditions of infants are the result of limitations in science, inherent differences between parents in raising their children, and extent of impact that family and environment will inevitably have on developmental outcomes.⁶ While it is best to

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make treatment decisions early, physiological instability may act as a significant roadblock in the development of an accurate prognosis.^{7,8} In cases with such uncertainty, it may be best to first initiate resuscitation, especially for extremely premature infants.¹⁶ However, these difficult decisions should not be made by the physician alone but with the inclusion of the parents in the decision making process.

Parental Wishes and Shared Decision Making

For these controversial cases, the wishes of the parents are often considered in the treatment of their child. Decisions to resuscitate extremely premature newborns in the delivery room are frequently influenced by parental wishes.^{4,5,16-21} If preference of the parents is unknown to the physician, then resuscitation serves as the standard course of treatment.^{12,16} Most neonatologists would still continue to resuscitate the newborn if they believed it to be clearly beneficial despite parental wishes to withhold this care.¹² However, this represents a rare phenomenon since parents generally look to save the life of their child at all costs.^{6,22} For infants diagnosed with trisomies 13 and 18, parental preference is the primary reason for the initiation of resuscitation as long as ongoing treatment is likely to produce significant health benefits without the cause of suffering.^{14,23} Parental wishes possess immense power and influence in determining the future course of treatment.

A shared decision making process creates outcomes agreeable to both the parents and physician which also represents the child's best interest. Joint decision making is vital to combining the parental wishes with the clinical knowledge of physicians.²⁴ Consensus between parties during the course of treatment is essential since complaints are often due to a lack of such agreement rather than differences in ethical opinion.^{13,25} How this dialogue about end-of-life decisions is introduced to parents is of great importance. It must effectively address issues of parental autonomy and the best interests of the child.²⁶ Educating parents on various outcomes and offering a range of treatment options may be the best approach.^{6,27} For parents deciding to continue either with their diagnosed pregnancy or with treatment of their severely ill child, physicians should support and actively engage them by discussing all of the relevant issues associated with their particular decision.¹⁵

Fear of Litigation

The fear of potential litigation being brought by dissatisfied parents is widely believed to play a prominent role in the

decision making process of physicians. However, litigation concerns were found to have little impact on delivery room decisions for the treatment of extremely premature newborns.^{4,5} In spite of this, parental litigiousness may still have some influence in specific situations where neonatologists are told to do everything possible for infants with dismal prognoses.²¹ In cases of trisomies 13 and 18, a significant proportion of physicians were willing to initiate resuscitation if parents demanded it out of fear of lawsuits.^{23,27} Concerns about litigation may therefore have a role in decision making when poor prognoses are paired with parental demands to provide aggressive treatment.

Self-Fulfilling Prophecies

Self-fulfilling prophecies are commonly associated with conditions characterized by poor prognoses. It is especially significant in cases of extreme prematurity where many physicians possess irrational negative associations— either outdated or non-evidence based— with low gestational age.²⁸ These particular attitudes negatively influence survival rates since less rigorous infants may be allowed to die without the full provision of heroic interventions.²⁰ The predictions of poor prognoses due to having previously poor results are self-fulfilling if the decisions to withhold and withdraw life sustaining treatment are made on the basis of these predictions alone.^{29,30} Withdrawing life support because of a predicted low chance of survival artificially increases the measured mortality rate.¹¹ This self-fulfilling prophecy is an inevitable and continuous cycle in cases associated with extreme prognostic uncertainty.

“Withdrawing life support because of a predicted low chance of survival artificially increases the measured mortality rate. This self-fulfilling prophecy is an inevitable and continuous cycle in cases associated with extreme prognostic uncertainty.”

IN CASES OF EXTREME PREMATURITY

The Unbearable Situation

The ‘Unbearable Situation’ represents one of the select scenarios for which The Royal College of Paediatrics and Child Health (RCPCH) in the United Kingdom judges it to be both ethical and legal to withhold and withdraw life sustaining treatment in infants.³¹ In cases of progressive and irreversible illness, further treatment may be refused if it is believed to be greater than what can be tolerated by the infant. Regardless of current medical opinion considering it to be beneficial to the future health of the child, treatment can be withheld.

This particular situation can be used to describe particular cases of extremely premature infants. Although treatment may prove to be effective, its costs in terms of pain and suffering to the child may be interpreted as being too high. A common example in the intensive care nursery is neonates born with severely chronic lung disease and comorbidities who are not responding well to maximum ventilatory support.³² Such

complications of extreme prematurity are often cited as the reason for withdrawing life sustaining treatment in the neonatal unit.³³

Accuracy of Gestational Age

Predictions for the gestational age of premature infants have frequently been proven to be incorrect.^{30,34–38} Such inaccuracies may extend beyond just 1 or 2 weeks, with errors as large as 3 weeks being reported.³⁷ Estimating the gestational age in extremely premature births remains a more difficult task. The positive predictive values for such estimates are significantly lower for preterm deliveries than those that are full term.³⁸

The potential inaccuracy of a gestational age should be accounted for in decisions to withhold resuscitation in the delivery room.³⁹ Although estimates may offer some much needed structure for neonatologists being forced to make these burdensome decisions,⁴⁰ it is increasingly difficult to form accurate predictions for infants who are extremely premature.⁴¹ Any policies for decision making based strictly on gestational age alone should therefore be avoided on such grounds.⁴² Each case is inherently unique, and thus, treatment decisions must additionally consider other clinically relevant factors.

Significance of Birth Weight

Birth weight rather than gestational age represents the best objective variable for predicting outcomes in extremely premature infants.^{39,41} Although it cannot be precisely estimated antenatally, birth weight can be measured with greater accuracy than gestational age. It is therefore better equipped for prognostic purposes. Birth weight is regularly used in hospital statistics and investigational studies. For centers that selectively provide neonatal intensive care, it serves as the primary criterion in their decisions to either initiate or withhold care.¹⁷

Birth weight influences delivery room decisions due to the prognostic power it has on health risks and outcomes. The resuscitation of extremely premature infants with higher birth weight is associated with better prognosis for survival and reduced risk of neurological impairment.^{16,43} Each incremental increase of 100 grams correlates with a risk reduction equivalent to a 1 week increase in gestational age.⁴³ Since its prognostic value is highest during the first days of life for these newborns,⁴⁴ birth weight appears particularly useful when prompt decisions in the delivery room must be made.

Additional Clinical Factors

Decisions to withhold and withdraw life sustaining treatment in extremely premature infants should be based on the synthesis of all available clinical factors and neither on gestational age nor birth weight alone. Exposure to antenatal corticosteroids, female sex, and singleton birth are each

individually associated with reduced risks for death and neurodevelopmental impairment.^{43,45} The severity of illness continues to play an important prognostic role up until the fourth day of life.⁴⁴ However, other easily attainable measures in the delivery room such as Apgar score and heart rate may not be prognostically valuable in such premature infants.⁴

Due to the substantial differences between intensive care nurseries in both policy and standards of care, not all treatments provided are equivalent. Physician decisions should therefore account for the specific morbidity and mortality risks of their particular institution and also of its geographic region.³⁹ Neonatal caregivers may be unaware of the actual outcomes for extremely premature infants and be more likely to resuscitate if presented with these statistics.²⁸ Proactively making relevant clinical information readily accessible to physicians will help to improve the decision making process and clinical outcomes.

IN CASES OF SEVERE ANOXIC INJURY

The No-Purpose Situation

The ‘No-Purpose Situation’ describes a second case where withholding and withdrawing life support in infants are considered to be ethical and legal.³¹ When treatment allows for survival, but with an unreasonable degree of physical or mental impairment, it is not in the best interest of the child to receive this care and subsequently bear the outcome. Treatment should therefore be withheld and withdrawn if there is an expectation for extremely poor conditions

without any likely foreseeable and substantial improvement.

Infants with severe anoxic injury illustrate this scenario due to the associated physical and mental impairments that lack the potential for any significant improvements.³² It is improbable that severe hypoxic damage to the brain will heal in its entirety, which is often the reason for such a poor prognosis. Withdrawing treatment to prevent a future life with severe disability accounts for the majority of neonatal deaths in encephalopathic newborns.⁴⁶

Window of Opportunity

The ‘Window of Opportunity’ describes the short period when decisions to withdraw life sustaining treatment should be made.⁸ It represents an early phase of critical illness and instability when withdrawing treatment would most likely result in death. However, it is also characterized by a high degree of prognostic uncertainty. Although the subsequent phase of physiological improvement may be accompanied with greater prognostic certainty, there is also an increased risk that the infant is no longer dependent on life support. Survival with extremely severe disability is therefore much greater.

Clinicians acknowledge that this window–applicable in the first 2 to 4 days of life– creates a sense of urgency to

“Proactively making relevant clinical information readily accessible to physicians will help to improve the decision making process and clinical outcomes.”

discuss the withdrawal of treatment with parents.⁶ Unfortunately, this conflicts with the concurrent desire to not rush parents or force them into making a hasty decision. Two critical time periods vital to making these pivotal decisions exist.⁴⁷ From 0 to 6 hours after birth, the decision to withhold strategies for neuroprotection must be made. The following period until 72 hours after birth is when the condition of the infant must further be assessed for the consideration of withdrawing life support.

Due to the time restrictions, early prognostic testing should be followed when high pre-test probability of impairment exists.⁷ To aid this task, early clinical and laboratory measures are available which are successful in predicting severe adverse outcomes.⁴⁸ A timely assessment may result in greater time for deliberation in the early phase and increased chances of treatment withdrawal resulting in death.

Heading Significance of MRI and EEG

Imaging studies are commonly used to help with outcome prediction in infants with brain injury caused by severe oxygen deprivation. Cerebral magnetic resonance (MR) biomarkers, including lactate, lactate/N-acetyl-aspartate (Lac/NAA), and N-acetyl-aspartate/choline (NAA/Cho), are effective in predicting neurodevelopmental outcome in neonates with encephalopathy.^{49,50} However, serious limitations in previous studies have forced these results to be considered insufficient as the lone basis for withdrawing treatment from these infants.⁵¹ Neonatologists reiterate this sentiment through their lack of confidence in the ability of MRI studies to provide any additional clinical information in encephalopathic newborns.⁵²

The practice of using EEG, particularly amplitude-integrated techniques, in the evaluation and prognostication of such infant conditions is also commonplace. Such studies appear promising in the detection of differences in future neurologic outcome for neonates with encephalopathy.^{50,53,54} However, its combined use alongside MRI leads to significant increases in outcome sensitivity and prognostic reliability.^{55,56} Neonatologists already view the results of both methods to be more clinically important than either patient history or clinical examination in birth asphyxiated newborns.⁶

Additional Clinical Factors

Although the pairing of MR biomarkers with electrophysiological studies may result in increased prognostic accuracy, other clinically available evidence is necessary for a thorough assessment in decisions to withdraw life support in encephalopathic newborns.⁵¹ The inclusion of evoked potential studies—both somatosensory and visual—and Sarnat scores with the use of MRI and EEG independently improves prognostication of neurologic outcomes in such infants.^{50,57–59} Additionally, chemical predictors can aid in the assessment of severity for birth asphyxia. Lowered pH, elevated base deficit, and elevated lactate blood levels are helpful in predicting outcomes.^{50,60,61} Measurement of S100B protein may also have predictive power in identifying which asphyxiated infants are at increased risk for long-term neurologic abnormalities or even neonatal death.^{62–64}

Prognostically useful measures are available without the need for additional expensive imaging and neurologic monitoring. Measures of depression at birth, resuscitation and the response, and postnatal clinical status may be the earliest methods for outcome prediction.⁴⁷ Of such clinical measures, the three most significant and easily accessible within 4 hours of birth are chest compressions, age at onset of respiration, and base deficit.⁴⁸ The use of each additional measurement accounted for significant improvements in the prediction of severe adverse outcomes, with the combination of all three factors providing the most accurate results.

IN CASES OF TRISOMIES 13 AND 18

The No-Chance Situation

The 'No-Chance Situation' offers a third set of circumstances where it is believed to be ethical and legal to either withhold and withdraw life support in infants.³¹ This scenario applies when the treatment of severe illness would only serve to delay a foreseeable death without delivering any substantial or even potential improvement in the quality of life. Such treatment also would be unable to significantly reduce the suffering of the child.

Infants born with congenital anomalies such as trisomies 13 and 18 demonstrate this scenario and its inherent complications.³² The initiation or continuance of life sustaining treatment in these cases may only postpone an inevitable death without providing considerable relief from constant pain or discomfort. Resuscitation is believed to be against the best interest of these infants as evidenced by current practices of withholding care in the delivery room.^{5,20,33}

Prenatal Diagnosis and Maternal Age

The ability to detect pregnancies with trisomies 13 and 18 has helped to reduce their live birth prevalence.⁶⁵ Trisomies 13 and 18 can be predicted antenatally in 40% to 44% of cases.^{66–68} The majority of diagnoses are identified using chromosome analysis after abnormalities are observed in ultrasound studies during the second trimester.⁶⁹ These low rates suggest that improved efficiency in prenatal screening practices is greatly needed. Following a positive diagnosis for pregnancy with trisomy 13, corresponding rates of termination were 69% and 86%, while trisomy 18 had rates of 82% and 89% respectively.^{68–70} A small but significant proportion of parents may agree to initial screening procedures but then decline following offers to terminate their pregnancies.

The risk for pregnancies being diagnosed with trisomies 13 and 18 increases with maternal age and even exponentially after the age of 30 years.⁷¹ The higher frequency of such pregnancies may be the result of a concurrent increase in the percentage of mothers over 35 years.⁶⁵ The mean maternal age for positive diagnoses is reported to be 35 years⁶⁹ with mothers over the age of 35 years accounting for 47% and 67% of cases with trisomies 13 and 18 respectively.⁷² An advanced maternal age should prompt further prenatal testing, which is proven to be an effective strategy for improving the frequency of antenatal diagnoses.⁶⁹

Comorbid Conditions and Birth Defects

Infants with trisomies 13 and 18 are frequently affected by multiple, severe comorbidities, often occurring at rates over 100 times those of unaffected infants.⁷³ Cardiac and central nervous system malformations account for the majority of such birth defects, while tracheo-esophageal fistulas, cleft lips, and abdominal wall and limb defects represent other common abnormalities.^{66–68,73,74} The presence of multiple defects significantly complicates the conditions of these infants.

Due to the severe comorbidities linked to both of these genetic syndromes, the chances of proper bodily functioning and the continuance of such are extremely unlikely. The majority of deaths are a direct result of either cardiopulmonary or multiorgan failure with contributing factors commonly associated with congenital heart defects and pulmonary hypertension.^{67,75} Central apnea is additionally frequently observed as the mode of death in many cases.^{66,68} Such extremely poor conditions of health are inherent to trisomies 13 and 18.

Shortened Life Expectancy

The average life expectancy of these affected infants is severely shortened. Median survival for trisomies 13 and 18 are reported to be between 2.5 to 10 days^{66,69,76,77} and 3 to 14.5 days^{68,69,76,77} respectively. Although trends for increased survival do exist at 1 week and 1 month after surviving the initial 48 hours, survival is extremely unlikely beyond 1 year of life.^{65,77} The prognoses for both conditions remain particularly poor.

In most cases, death occurs prior to discharge with only a small proportion of newborns surviving the neonatal period and leaving the neonatal intensive care unit.^{67,73} With the provision of intensive treatment via intubation, surgical operations, and mechanical ventilation, survival rates can be improved.^{75,78} However, these rates substantially drop beyond 1 year, and the results are limited from a lack of consideration for the degree of impairment and the quality of life. Although some infants are eventually discharged to home care, a significant proportion is also discharged to long-term skilled nursing facilities and similar institutions.⁷³ Even if infants diagnosed with trisomies 13 and 18 manage to survive longer than expected, their lives still remain greatly affected by their conditions.

CONCLUSION

For infants with extreme prematurity, severe anoxic injury, and trisomies 13 and 18, physicians are deeply divided on the delivery of care when facing issues of withholding and withdrawing life support. It is therefore extremely important to acknowledge the applicable themes that influence decision making. Significant differences exist between the perspectives of parents and physicians, which can be ameliorated through effective shared decision making processes that emphasize clear communication, recognition of family values, and respect for autonomy. Staying current with the most recent clinical studies, prognostic assessments, outcome statistics, and survival figures in addition to the associated ethical concepts will help to reduce the burden of making these difficult

life and death decisions. In the absence of specific universal guidelines, it remains the responsibility of national pediatric associations to periodically provide the most up-to-date and relevant information. The best solution is for physicians to be proactively armed in anticipation of encountering these controversial cases. Only then, will they be sufficiently equipped to effectively navigate the intricacies involved in withholding and withdrawing life sustaining treatment for these infants.

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Cancer Immunotherapy: A Frontier of Prevention and Treatment

Palak Khanna

Cancer immunotherapy is an exciting and highly promising avenue of research for the prevention and treatment of multiple cancer types. After decades of domination in cancer studies by radiation, chemotherapy, and surgery – the three traditional defenses against cancer since the early 1800's, cancer immunotherapy has recently emerged into the limelight with the potential to deliver more comprehensive cancer treatment by targeting localized regions of the body and destroying specific cancer cells while minimizing adverse side effects.

WHAT IS CANCER IMMUNOTHERAPY AND HOW IS IT DIFFERENT FROM RADIATION OR CHEMOTHERAPY?

Immunotherapy refers to treatment for disease that is spearheaded by the patient's own immune system. The immune system acts as the human body's shield against viruses, bacteria, and other foreign substances that are not recognizable, and that could be deleterious to organs or organ systems. If the immune system is unable to effectively ward off disease, immunotherapy, in general, serves to 1) activate the immune system to attack harmful substances it cannot recognize, or 2) strengthen the existing response by providing man-made immune system proteins to help the system carry its normal function.¹ Cancer immunotherapy deals specifically with the immune system's response to cancer – that is: uncontrollable cell proliferation, development of tumors, and the consequences of tumor formation which risk normal function of nearby organs and impair the function of many body processes [blood flow, digestion/absorption, and respiration, to name a few, and depending on cancer type and advancement]. Chemotherapy differs from immunotherapy in that the immune system is suppressed and man-made chemical drugs are introduced into the bloodstream to poison cancer cells and reduce the growth of tumors. Radiation therapy, similarly, does not involve stimulation of the patient's immune system, but rather delivers high energy radioactive particles to damage and destroy cancer cell DNA.

WHAT IS THE IMMUNE SYSTEM'S NATURAL RESPONSE TO CANCER PRIOR TO ANY INTERVENTION?

The immune system is able to differentiate between normal cells and foreign substances via protein identification tags [glycoproteins] on the external surface of cells. As foreign substances, most viruses and bacteria do not carry protein tags on their external surfaces or display incorrect tags, making them easily vulnerable to destruction by the immune system. Cancer cells, by contrast, have fewer clear differences because they are born within the body as opposed to being introduced into the body from the external environment.

Cancer cells are born when mutations arise within normal cell DNA in regions responsible for proper cell growth and maintenance. These mutations prevent cells from recognizing signals to terminate cell division and proliferate uncontrollably as a result. Given the similarities, the immune system has a harder time pinpointing cancer cells and destroying them. Often times, cancer cells also secrete substances that prevent the immune system from taking action.²

WHAT DOES CANCER IMMUNOTHERAPY DO TO FIX THIS?

Monoclonal antibodies and cancer vaccines are two types of cancer immunotherapy that researchers are currently working with to address the existing problems.³

Monoclonal antibodies are synthetic proteins that mimic the proteins in the immune system responsible for recognizing and destroying cell types that either lack identification tags, or carry incorrect tags. Since cancer cells are especially difficult to target by the immune system, researchers are first tasked with isolating cancer cells and observing their external surfaces. If tags exist, these tags are mapped in order to produce a specific antibody that will recognize it as foreign. Depending on the type of cancer, the region where mutations arise, and even the individual, the external surface of the cell may differ. Thus, researchers are tasked with painstakingly crafting monoclonal antibodies specific to the cancer and the cell type. When injected into the patient, these monoclonal antibodies are oftentimes attached to chemotherapy drugs [chemolabeled antibodies] or delivered with radiation [radiolabeled antibodies] to form complexes called conjugated monoclonal antibodies. The addition of chemotherapy or radiation strengthens the immune response and protects normal cells that would otherwise be damaged by delivering the poisonous chemicals or radiation solely to cancer cells. Conjugated monoclonal antibodies have proved to be more useful than general monoclonal antibodies, suggesting that the combination of a variety of treatment methods is beneficial.⁴

Cancer vaccines are both preventative and treatment measures against cancer. Preventative cancer vaccines serve to prepare the immune system for potential attack by introducing benign strains of specific viruses that cause cancer.⁵ These are also known as vector-based cancer vaccines since they introduce specific virus strains to stimulate the production of an immune response.⁶ The injection of these benign viruses is meant to activate the production of T-cells and antibodies by the immune system ahead of time in case of

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future cancer onset. Cell based cancer vaccines are another type of vaccines injected after cancer diagnosis. Although not successful thus far, the concept behind cell based cancer vaccines are to combine cancer cells and other immune cells cultured from the patient to deliver a personalized vaccine that reduces the likelihood of rejection and strengthens the immune response.⁷ Preventative cancer vaccines have proven to be more successful than cancer vaccines administered after diagnosis. The development of the cancer vaccine against the Human Papilloma Virus (HPV) linked to onset of cervical, anal, and throat cancers is a notable example of a preventative cancer vaccine.

WHY HAS CANCER IMMUNOTHERAPY SUDDENLY BECOME A HOT TOPIC FOR RESEARCH? WHAT ARE THE LIMITATIONS?

Chemotherapy, radiation, and surgery are not cancer treatments that specifically target cancer cells without destroying healthy cells in the meantime. Thus, a combination of these traditional therapies and cancer immunotherapy seems most promising for the future. Cancer immunotherapy is the hope for more directed cancer prevention and treatment.

However, as exhilarating as this field of research is, there are many limitations that need to be addressed. Nowadays, prevention and early detection are the mantras when it comes to cancer. Monoclonal antibodies and cancer vaccines may be most effective in these circumstances. However, the majority of cancer diagnoses around the world today are made long after the cancer has first erupted. Moreover, cell based cancer vaccines which may be revolutionary for cancer treatment regardless of cancer type or level of development are not yet proven and administered on a widespread level. Monoclonal antibodies, even with attachment of drugs, may not be effective for treatment since cancer cells mutate as a result of chemotherapy and radiation treatment. If the target is no longer the same as a result of mutation, then the antibody is useless.⁸ In addition, if the cancer is not localized to a particular region, enough of the antibodies must be produced to reach all the affected cells. Yet at present, the issue of sustaining an immune response is not guaranteed. This means that once some antibodies are introduced, that the immune system may not respond by generating similar antibodies. Monitoring the patient and frequently injecting antibodies might be necessary, and if doses are missed, then the consequences of such an action need to be determined. Many monoclonal antibodies are commercially available, yet not in sufficient quantities or proven for success.⁹ Most of the general public is likely unaware of the existence of these antibodies or even additional vaccines, for that matter, since they tend to be extremely expensive. Thus, in the coming years, as much as continued research in the field of cancer immunotherapy will matter, providing access to information and affordable treatment for all who need it will be most important.

References for this article can be found at

TuftScopeJournal.org

RESEARCH HIGHLIGHTS:

Simian Virus 40 May Be Carcinogenic Virus Linked to Osteosarcoma

Caroline Russell-Troutman

Osteosarcoma is a rare bone tumor, mainly affecting children. Little is known about its etiology, though some studies have suggested that it may be associated with the presence of simian virus 40 (SV40). SV40 is a virus that contaminated some polio vaccines between 1955 and 1963, infecting millions of people and altering their B and T cells. Some adults infected by the 1950's vaccine contamination may have unknowingly infected their children through contact since then. In past studies, SV40 has been found within various bone tumors, including osteosarcoma, and, though there have been conflicting results, many scientists believe that SV40 could be a carcinogenic virus. A study recently published in *Cancer* further examined this potential link between osteosarcoma and SV40.

Researchers in the present study acquired serum samples from 55 patients with osteosarcoma and from 114 healthy control subjects. 78 patients with breast cancer and 64 with undifferentiated nasopharyngeal carcinoma (UNPC) also gave serum samples to control for a possible association between SV40 and cancer in general. The median age of all participants was 18. Researchers used ELISA, an assay that indirectly measured the presence of SV40 antigens, to test these sera for SV40. Results showed a 44 percent prevalence of SV40 in osteosarcoma serum samples, which was significantly different from the 17 percent prevalence seen in healthy controls, the 15 percent prevalence seen in breast cancer patients, and the 25 percent prevalence in patients with UNPC. There was a statistically significant prevalence of SV40 associated with osteosarcoma, while no other participant group showed a significant prevalence of SV40.

These results provide strong support for a potential association between SV40 and osteosarcoma, though it remains unclear exactly how SV40 may act as a carcinogenic virus. More studies are needed to answer this and to further support the link between this virus and osteosarcoma. If SV40 is truly involved in osteosarcoma development, these results may pave the way for antiviral therapies to treat these rare tumors. Further investigation of the role of SV40 may also enable researchers to more fully understand the pathology of osteosarcoma itself.

Cancer. 2015; 121:708-715. DOI: 10.1002/cncr.29137

Optogenetics: A Way of the Future

Rohan Rao

It is easy to assume that, this far into our existence, humans have conquered most realms of the physical world and gained a tight grasp of the world around us. We tend to get complacent with our current level of understanding. Frequently, however, we are thrust to higher levels of knowledge by leaps and bounds. Such sporadic progress can occur in any scientific field, be it chemistry, particle physics, or immunology. In the last decade, one particular field, optogenetics, has demonstrated a great degree of progress and generated plenty of excitement.

Optogenetic technology "...allows [for] targeted, fast control of precisely defined events in biological systems as complex as freely moving mammal."¹ Essentially, these techniques incorporate a combination of genetic knowledge and optical procedures to either excite or inhibit specific physiological events. With light as the stimulus, scientists are able to exert a degree of control on mechanisms that could only previously be regulated somatically. Optogenetics offers more than just the ability to control physiological processes, though. By inserting opsin genes into cells and activating them, researchers can also investigate the exact mechanisms of [ideally] any type of cell.³ This could shed a very insightful light onto the inner workings of the body.

This field of study has particular importance to Tufts University, as the Department of Biology is working to hire a new optogeneticist.

The idea of using light to stimulate cellular mechanisms is not necessarily a new one; it was actually first conceived in the 1970's. Francis Crick, one of the fathers of modern-day genetics, was a visionary in this field. In 1979, he speculated that one of the biggest roadblocks to the progression of neuroscience was the inability to precisely manipulate individual cells without globally affecting an entire region.¹ The main tools used at that time in neuroscience, electrodes and drugs, were either not precise enough or too slow, respectively, to allow for such precise control.

As the idea was years ahead of its time, Crick's contemporaries found no plausibility in such a technique. It was not until the emergence of a 2015 report highlighting a microbial opsin gene 2005 did the scientific community begin to fully comprehend the potential of optogenetics. Opsins are photoreceptors that change conformation in response to light and can activate cellular pathways to bring about a wide net of

physiological changes.³ In the report, researchers successfully introduced the gene for an opsin into a cell's genome and transformed neurons to be responsive to photo signals. The most common method of introducing these microbial opsin genes into animal cell tissue was through viral vectors.²

More specifically, opsin genes can affect tissue in one of two ways. One class of opsin genes contains DNA to produce proteins that manipulate ion levels in cells, such as ion pumps or ion channels.² These proteins can act in an excitatory or inhibitory fashion, depending on the ions involved and the direction of ion flow. These particular opsin genes are found natively in microbes.²

“Optogenetics could have searing implications for future treatments of diseases and health conditions, as well as the potential to launch the medical field to unprecedented heights.”

On the other hand, vertebrates are host to opsin genes that work in a slightly different manner. Vertebrate opsin proteins can act as G protein-coupled receptors.² When the receptor is excited by photons, it activates a second messenger system within the cell, although itself not in

contact with the cytoplasm. This phosphorylating cascade can activate enzymes within the cell to stimulate or inhibit gene transcription and protein translation.

There are still plenty of hurdles to cross before optogenetic techniques are used universally. One article cited that, "... it has not been possible to deliver causal, temporal precise gain or loss of function," in neural or other somatic tissue. In particular, many scientists hope to be able to perform optogenetic techniques on animals while conscious. This is not an unrealistic goal of optogenetics, but will require its own leaps and bounds to achieve. However, steps are continually being taken in the right direction. In all, optogenetics could have searing implications for future treatments of diseases and health conditions, as well as the potential to launch the medical field to unprecedented heights.

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Tufts Study on Drug Development Costs: How Our Pharmaceutical Company-Funded Center Can Influence Drug Prices

Lena Chatterjee

The Tufts name is brandished on widely acclaimed academic establishments from Boston proper to Talloires, France, including internationally renowned graduate schools and our very own undergraduate university. However, a different Tufts institution has recently been making headlines in the health community.

The Tufts Center for the Study of Drug Development (CSDD) is an academic, non-profit independent group that researches issues affecting pharmaceutical development. The CSDD is unique in how it applies a holistic approach to its studies, including not only economic and scientific factors, but also looking into political and legal concerns, as well. The CSDD gathers data from a variety of “pharmaceutical and biotechnology companies” but never releases specific information about which companies this includes. Moreover, the funding for the CSDD also comes from these pharmaceutical and biotechnology companies in the form of grants, which make up at least 40% of the Center’s total funding. Commissioned projects, which also receive grants, are not included in this 40%.¹ On the Corporate Sponsorship page of its official website, the CSDD publicizes that it is “highly regarded and cited by companies, regulatory authorities, governments, and academic leaders worldwide. Tufts CSDD has a unique and influential voice on issues dealing with pharmaceutical biopharmaceutical innovation.”²

With its influential voice, the CSDD released the findings of a study on November 18, 2014, with a news title stating that the “cost to develop and win marketing approval for a new drug is \$2.6 billion.”³ This figure was high enough to raise not only eyebrows but also red flags across the health community. Most estimations about the full cost of researching, developing, and winning approval of a drug had been in the hundred millions, and few had passed \$1 billion. The CSDD had released a similar study in 2003, and their final estimate was \$802 million. Accounting for inflation, \$2.6 billion is still a 145% increase over a single decade. The Center attributed this significant increase to higher research and development (R&D) costs, as well as higher failure rates.⁴ The \$2.6 billion figure has been broken down into \$1.4 billion due to average out-of-pocket costs, \$1.2 billion “time costs,” which are the

profits that a company foregoes during R&D, and a final \$312 million investment for post approval R&D.⁵

Initial R&D is such a nuanced part of the drug development process that it is always hard to accurately calculate figures, but \$2.6 billion is much higher than anyone can understand. Even at first glance, there were a few points of concern. First, the study seemed to use data almost exclusively from New Molecular Entities (NMEs). NMEs are drugs in which the active ingredients use compounds and mechanisms that have never been approved by the FDA. On the other hand,

a large majority of drugs that are submitted for approval are “copycat drugs,” which utilize previously approved active ingredients. NMEs require much more R&D and are therefore much more expensive to get approved.⁶ Additionally, the study seemed to ignore grants entirely, despite the fact that many drug development studies receive grant funding at some point in their development life cycle. Since 2003, the

“Initial R&D is such a nuanced part of the drug development process that it is always hard to accurately calculate figures, but \$2.6 billion is much higher than anyone can understand.”

NIH alone has given grants of at least \$26 billion per year towards drug development.⁷

Though many in the health community questioned why and how this \$2.6 billion figure came about, there were few answers to be found due to the fact that the CSDD has refused to release their methodology for the study. Since the study has not been submitted to any peer-reviewed journals, there has been no confirmation that their methods were just. Additionally, though the findings of the study have been made public, there has been no public release of the study itself. This is strange considering Kenneth Kaitin, the director of the CSDD, has acknowledged that “this is a controversial study in that it has a tremendous political and industry impact.”⁸

Kaitin’s words cannot be stressed enough. This study, indeed, has many implications in the pharmaceutical world. When determining how to price a drug once it gains approval and is made available for retail, the cost of drug development is strongly considered. Thus, if the cost of developing a drug has increased as greatly as the study claims, then the pricing of pharmaceuticals will also see a significant increase.

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New Product Revenue – 2002 Approved drugs

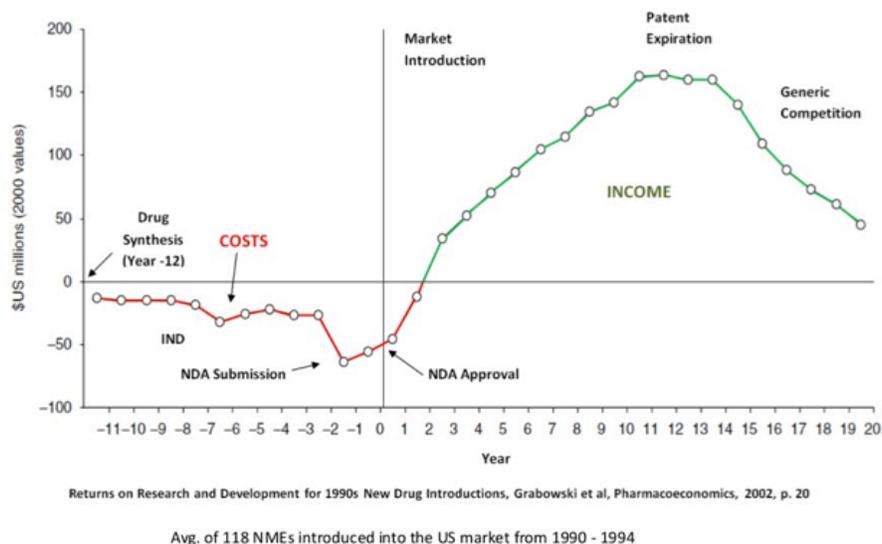


Figure 1. This graph, taken from an IT member of a pharmaceutical company, shows the initial costs invested in a drug compared to the income it eventually generates. This is an average of 118 New Molecular Entities, which typically incur more research and development costs than normal “copycat drugs.” The income still far outweighs the costs.¹²

Though it makes economic sense that the price of a product will increase as the cost of production increases, it is important to keep in mind that pharmaceutical companies already reap huge profits (Figure 1). The findings of this study can easily influence the pricing of any drugs that will be approved in the future, but there is a particular implication on an area of healthcare that is already highly expensive and yields few alternative options: cancer treatment.

One group that has been particularly vocal is the Union for Affordable Cancer Treatment (UACT). The UACT recently wrote a letter to President Anthony Monaco in which they questioned the sources of funding for the study and the secretive nature of the data. They also pointed to areas of the study that can be particularly harmful if it is applied to cancer treatment. For one, the patient trial size and cost per patient have never been specified, but cancer trials normally involve far less patients than the standard drug trial size, incurring less overall costs. The letter also calls into question the lack of consideration of grant funding, which becomes even more relevant in cancer studies. Not only does the NIH National Cancer Institution reward more than \$5 billion per year for cancer research, but the Orphan Drug Tax Credit is also awarded to many cancer treatment trials, which covers 50% of clinical trial costs. Most importantly, the letter asks the questions that every cancer patient needs to know: “How does the study data relate to the facts for drugs for cancer? How does the Tufts study deal with these differences? Should we consider the study even relevant to products for cancer?”⁹

As the looming concern in the health industry has grown, there has been more pressure on the CSDD to release

the details of the study. However, the CSDD has remained minimally cooperative, holding only one news release with a slide show and a backgrounder. Both of these only included general information about the data such as the fact that 106 drugs that began human testing anywhere from 1995-2007 were used in the study.¹⁰ Though it seems that the CSDD is trying to extend an olive branch with these releases, they are instead further publicizing the \$2.6 billion without answers to any of the numerous concerns that have been reiterated by articles and health advocacy groups since the first release.

Overall, the CSDD has shown a pattern of questionable actions. Though this study on the cost of drug development does not show a clear disregard of scientific integrity, its enigmatic findings raise considerable concern. The subsequent evasion of clear answers and an obscure release of data further diminish the credence of the study. After all, it is hard to trust the center’s ability to be unbiased when the companies funding the CSDD are those that stand to profit from the extravagant results they are claiming. That being said, there has yet to be clear evidence that the CSDD performed any wrongdoing when it executed its study, and it is still possible that these results are valid. However, the lack of public release of the study’s methodology and the Center’s avoidance of getting verification from a peer-reviewed journal in the scientific community does not bode well for its credibility. Therefore, it is imperative that the CSDD publicly releases and verifies their study. This is not only important for the center’s reputation but also for consumers around the world. The influence of this study extends globally and can affect all people regardless of nation, class and race. Moreover, it stands to have the

strongest impact on those that are already disadvantaged in the health community. As healthcare providers, patients, advocates, and consumers continue to seek answers from the CSDD, it is imperative that Tufts students themselves become part of the conversation. As Tufts students, our voice is valued when speaking out against our own institution's actions. Tufts prides itself on teaching its students values such as global leadership and active citizenship. Considering these values, we must reflect on how our own institution's actions can influence a global market, we must question the impact of this research being performed by our very own, and we must continue to pressure the CSDD to fully release their findings. After all, without all the data, how is one to disagree with a company that self proclaims "no other entity does what we do?"¹¹

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RESEARCH HIGHLIGHTS:

Optimism for Methadone Treatment to Reduce Drug-Related HIV Incidence in Kenya

Caroline Russell-Troutman

Kenya has recently experienced an upsurge in HIV prevalence related to drug injection with HIV rates being as high as 50% among injected-drug users in Nairobi. Up until now, heroin addiction treatments in Kenya have generally been based on detoxification and have had only short-term effects. In 2014, health officials adopted opioid substitution treatments (OST) in the hopes of reducing drug-related HIV rates, making Kenya the third Sub-Saharan African country to do so. Part of OST involves the use of methadone to treat heroin addiction. There is already strong evidence to suggest that methadone treatment as part of OST successfully reduces opioid-related HIV incidence, but there has been little research on how OST may be implemented in a new social context. A study published in the *British Medical Journal* (BMJ) has investigated how methadone treatment is expected to impact HIV transmission in Kenya.

Researchers used existing data on HIV incidence in Kenya to develop a mathematical model of sexual transmission of HIV among injected-drug users. In addition, researchers interviewed 109 Kenyan injected-drug users. Participants were predominantly male, had a mean age of 41, and 97% of them injected drugs on a daily basis. 28% of these participants reported themselves to be HIV positive, though no formal drug tests were administered. After the interviews, researchers coded the participants' responses into several thematic categories. Overall, participants expressed a desire to recover from their addiction, optimism towards recovery through methadone treatment, but also caution and concern about how this treatment would be implemented.

In general, researchers predicted that, at a treatment coverage of 10%, OST may only reduce HIV incidence by 5-10% over the next five years. However, if coverage could be increased to 40%, researchers expect a 20% reduction in HIV incidence. Methadone is likely to be seen as symbol of hope for treating drug addiction among Kenyans, and despite high sexual transmissions among injected-drug users, researchers predict that widespread implementation of methadone treatment will be an effective strategy for reducing HIV infection rates. However, the true effects of OST remain to be seen in the coming years and continuing modeling studies will further assess the efficacy of OST in this new social context.

BMJ Open 2015;5:e007198. doi:10.1136/bmjopen-2014-007198

The Economics of Obesity

Prachi Sharma

INTRODUCTION

The rising prevalence of obesity in the United States has spurred a vast amount of popular and political interest, and has consequently caused the obesity epidemic to become a major policy focus for lawmakers. While obesity is very clearly a public health issue, economic theories and concepts can explain much of the rise of obesity in the United States. Furthermore, economic models have been proposed to explain the factors that lead to obesity, and lend insight into potential methods to promote obesity prevention. However, the question of whether obesity necessitates a government intervention is a source of contention between economists. This paper attempts to consolidate and analyze the current literature exploring the economic causes and consequences of obesity, and discusses whether government intervention is necessary and effective in curbing the obesity epidemic.

UTILITY MAXIMIZATION MODELS AS AN EXPLANATION FOR OBESOGENIC BEHAVIORS

The economic concepts of utility maximization and tradeoffs are essential in modeling incentives and explaining behaviors that potentially cause obesity. Mavromaras (2008) finds that this model explains individual choices, and thus explains how and why people turn to obesogenic behaviors. The utility maximization model illustrates the concept that people will consume combinations of bundles of goods that will provide them with the most utility, or happiness. Thus, health can be treated as a good which individuals can consume more or less of in order to gain, or lose, utility. Mavromaras (2008) cites a common example of a health related tradeoff from Viscusi (1993): some individuals tend to accept health-jeopardizing jobs for higher pay. In this case, individuals gain more utility from higher pay than from having a safer job. While Viscusi (1993) discusses the values individuals place on their lives in regards to certain health and safety risks, a relevant example that more effectively illustrates the tradeoffs resulting in obesity is when an individual drives to get to their home and family more quickly, instead of riding a bike, because there is more utility gained from arriving home earlier.¹ Furthermore, extrapolating from Viscusi's (1993) findings on the valuation of life, measuring the value individuals place on participating in risky obesogenic behaviors can determine how policymakers might promote healthier behaviors that equal or surpass the value of participating in obesogenic behaviors. However, Viscusi's (1993) valuation analysis of labor risks on health provides examples that are more concrete to individuals than obesity, which can have multifaceted, abstract effects. Thus, due to the multitude of behaviors that could indirectly or directly cause obesity, valuation methods could be better focused on measuring the

value individuals place on being thin. In the case of obesity, economists might assess individuals' demands for being thin by assessing how much individuals would be willing to pay to avoid obesity. This value reveals information about an individual's utility function that provides insight into the role and prevalence of obesity-inducing behaviors. Essentially, Mavromaras (2008) summarizes, "In the case of voluntary and well-informed choices, the economics framework will say that, given the personal circumstances of each individual, their choice will reveal whether they value the utility they gain from the (obesogenic) behavior more than they value the utility they lose from the increase obesity that behavior generates".¹

However, the degree to which people base their decisions on the utility model has been debated. Mavromaras (2008) acknowledges that people do not consciously consider obesity in making every decision, which thereby illustrates that the choices individuals make often have nothing to do directly with obesity-inducing behavior. Therefore, the degree to which people actually actively base their decisions on gaining utility from preventing in obesity is limited. Furthermore, the model is based on the idea that individuals make well-informed decisions, which is not always the case. Mavromaras (2008) does not acknowledge the fact that many disadvantaged individuals may not have the ability to make fully informed healthy decisions. For example, health literacy is, as defined by the U.S. Department of Health and Human Services, "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions".² This information includes knowledge of interpreting healthy behaviors, as well as having the knowledge of obtaining proper healthcare. In the United States, according to the National Adult Health Literacy Survey, 14 percent of adults have "Below Basic" health literacy, and those individuals were found more likely to report having poor health.² Thus, individuals may not be maximizing their utility because of insufficient knowledge of their health status or the health risks of their activities.

ECONOMIC FACTORS OF OBESITY

The utility maximization model describes consumption choices on the individual level and can thereby explain why individuals make behavioral choices that induce obesity. Rashad *et al.* (2005) further substantiates this idea described by Mavromaras (2005) by finding that the rapid increase in obesity in the United States has stemmed from economic

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changes that have induced unhealthy behavioral changes. For example, Philipson and Posner (2008) find that technological changes, such as agricultural innovation, have fueled an increase in productivity, thereby reducing food prices, and ultimately reducing “the cost of consuming calories.”³ This “neoclassical theory of obesity,” as described by Philipson and Posner (1999), builds further on the concept of utility and reflects Mavromaras’s (2008) paper as an explanation of time trends and the historical development of obesity through the past decades. Essentially, as technology has improved, production has increased and food has become cheaper. As food becomes cheaper, individuals are more inclined to consume increased amounts of the cheaper food products. Thus, Philipson and Posner find that “fast food is a consequence of technological change, rather than an independent explanation of obesity,” and deviate from the popular belief that the exponential growth in fast food restaurants has led to the rise in obesity solely.⁴

Cutler *et al.* (2003) however argue that Philipson and Posner (1999) only explain long run changes and do not explain the continued current rise in obesity, as there has not been any major technological change since the 1980’s. Rather, though Cutler and his co-authors still focus on the same notion that technology is important, they explain that technology has continued to make food “cheaper” in the sense that it is timesaving. For example, microwaveable meals are cheaper in the number of minutes it takes to make a meal, and are thereby often more valuable to individuals.⁵ The utility maximization model can explain this behavior in that individuals value their time more than preparing time-consuming healthy meals. This notion is important in explaining the current trends in obesity because people have been leading increasingly busy and stressful lives, and thus tend to value free time more heavily than other “goods.”⁵

In addition to describing the direct effects of technological advancements on the food industry and food consumption, Rashad *et al.* (2005) also note that the growth in suburban regions, which has resulted from economic growth, has contributed in part to the obesity epidemic. Using research measuring the extent of urban sprawl from Smart Growth America, the authors found that urban areas that “offer more transportation choices, are more compact, and have a variety of stores and activity centers within reach have lower rates of obesity.”⁶ This indicates the individuals in these centers have more healthy (exercise-inducing) choices in the way they increase their utility. Chen *et al.* (2012) however scrutinizes specific aspects of these urban centers and estimates the effect of the locations of fast food restaurants to individuals in urban areas. Though the authors find some evidence of a relationship between obesity and the proximity to fast food, the

authors also find that policies aimed at reducing the access to fast food in urban areas may have only a limited effect.⁷ These studies illustrate that heterogeneity accounts for variation in obesity trends.

Both Cutler *et al.* (2003) and Philipson and Posner (2008) also note the difference in obesity trends due to the heterogeneity of the U.S. population, while Mavromaras (1993) simply attributes the overall growth in obesity to the continuous economic growth that has increased individual incomes. Describing the income effect, he states individuals consume more of what they value as their incomes increase. However, both Cutler *et al.* (2003) and Philipson and Posner (2008) describe the relationship between income and weight more specifically: essentially, individuals at lower income levels tend

to be overweight. While income growth for the poor leads to an increase in food consumption and weight, income growth for wealthier (over-weight) individuals tends to lead to weight loss.³ This decrease in weight is likely due to the increased ability for wealthier individuals to invest in weight loss regimens.⁸ This discrepancy in income levels illustrates the necessity for establishing efficient and widespread policies that will target the right group of people. Essentially, the factors that have led, and are continuing to contribute to the obesity epidemic, reveal the complexity of obesity as both a public health and political problem.

“The factors that have led, and are continuing to contribute to the obesity epidemic, reveal the complexity of obesity as both a public health and political problem.”

ECONOMIC CONSEQUENCES OF OBESITY AND PROPOSED INTERVENTIONS

Obesity is a major concern on an individual public health scale due to its effect on heart disease and mortality. Obesity, however, also has consequences on the economic system: according to the Centers for Disease Control, the estimated annual medical costs of obesity was \$147 billion dollars in the United States in 2008, and on average the medical costs for the obese in 2008 were \$1,429 higher than individuals of normal weights.⁹ Propper (2005) notes that if the private costs of obesity diverge from its social costs, the market failure that results from this negative externality could warrant government intervention, possibly through taxes. Essentially, if the government were to create a tax, it could “reduce costs, borne by all of society in a tax-financed system, of treating the medical care that is associated with obesity.”⁸ Propper (2005) also notes that a tax, or price-based incentive, should only be utilized to change the behavior of the proportion of population with self-control problems, and only if a significant number of people fall in this category. Propper (2005), however, does not further assess this population, thus weakening his assertion and making the claim ambiguous. Zheng *et al.* (2013), however, specifically examine the effect of changes in sales and excise tax on food or beverage demand, and find that the tax change may only affect consumers if the tax change is an excise tax, as consumers are often inattentive to sales tax. The authors however, do not assert whether this is an appropriate

measure or not, indicating that further studies should be conducted. Thus, these economists have reported (though tentatively) that government intervention could be necessary to offset the cost externalities of obesity.

However, not all economists accept that there are substantial economic negative externalities of obesity that justify public intervention. Bhattacharya and Sood (2011) find that these cost externalities are not a reason for government intervention, as the costs of the obese are actually subsidized by the obese themselves.¹⁰ For example, employers tend to pay obese people lower wages than thin people due to their high cost of health coverage, so there is no actual risk pooling in employer-sponsored health plans because health insurance “induces a wedge between the wages earned by obese and thin workers.”¹⁰ This notion thus counters the negative externality of the high costs imposed on the public health care and insurance system. Philipson and Posner (1999) further explain that although taxation superficially seems to reduce the externality, it ignores the fact that a reduction in mortality that would actually increase the elderly population, who “consume a disproportionate fraction of medical expenditures.” Therefore, the medical savings from a tax measure may in fact be exaggerated because of the obese people to die at younger ages. Thus, the perceived negative cost externalities of obesity may not actually be significant.

Mavromaras (2008) cites Good *et al.* (2005) as a counterexample for his analysis, as their report also seems to indicate that government intervention is not necessary because of self-limiting behavior. The authors find that the obese will respond to their own weight gain by changing their behaviors and participating in healthier behaviors because of the positive externalities of being thin (society’s perception of beauty, living longer, etc.). Liu *et al.* (2007) come to similar conclusions in their findings, in that as incomes increase individuals tend to purchase better quality, healthier foods. This trend, they claim, could reverse obesity patterns, and the authors thus strongly emphasize that “if body weight is a matter of rational individual choice, then there does not exist a public health crisis that warrant government intervention.” However, Mavromaras (2008) highly disagrees with this conclusion, criticizing it for “lacking empirical support” and being an extravagant conclusion drawn from little data. Furthermore, these studies also seem to ignore the differences in populations,³ and the fact the disadvantaged populations maybe be unable to participate in this self-limiting behavior. Thus, their conclusions about the effects of self-limiting behavior seem overstated. Instead, Mavromaras (2008) argues that research on self-limiting behavior should be used to identify the activities most likely to be affected by obesity in a self-limiting manner. These studies could thereby reveal “the underlying incentive structure” and support public programs that would most likely support and be utilized by the obese.¹

Currently, education methods are the most frequently purposed and utilized intervention programs to eliminate the information asymmetry that results from the lack of general health and nutrition knowledge. General education, and nutrition or exercise education public programs have been accepted as methods to spread awareness and knowledge

to large groups of people quickly. The hope is that with increased information, individuals will be better able to make decisions that actually maximize their utility, as mentioned by Mavromaras (2008). However, Philipson and Posner (2008) find that “the incentives created by technological change have more than offset the increased understanding of caloric intake and expenditure.” Essentially, the authors believe that the low prices and timesaving incentives that have been a result of technological innovation generally provide more utility to individuals, regardless of the amount of information they have about food consumption. Thus, they assert that the effectiveness of education programs, such as food labeling or diet advertising, “cannot be confirmed.”³ Propper (2005) substantiates this belief, stating that “if the price differentials are large or healthy products are not available, this information may have limited impact.”⁸ General education programs, however, that target general literacy for disadvantaged populations, could improve the effectiveness of nutrition programs because “uneducated persons have less of an incentive to invest in their health because their longevity and their utility from living are below average.”³ Though the authors did not elaborate on how they established this claim, Philipson and Posner (2008) assert that this population is likely aware that obesity is an adverse health condition, but this population does not value anti-obesogenic activities to the same extent as others. Ultimately, to eliminate market failures, such as information asymmetries, there are a variety of methods that are currently being implemented, though their effectiveness on reducing obesity is unclear.

Essentially, there is a multitude of proposed methods of intervention, which are built upon utility maximization, that aim to curb the obesity epidemic. The question remains, however, whether the government is justified in enacting these policies, as many economists debate the significance of the externalities of obesity.

CONCLUSION AND SUGGESTED FURTHER DIRECTION

According to the Centers for Disease Control, approximately 35.7 percent of Americans are currently obese,⁹ with this number rapidly increasing each year. As the obesity epidemic grows, so does the economic literature assessing the public health concern. A vast number of economic factors, stemming from economic growth, can partly explain the roots of obesity. The vast amount of research surrounding this field illustrates the growing problem of obesity, but also the growing problem of creating effective policy measures that address the epidemic. While individuals’ utility maximizing behaviors may be an indication of how individuals would react to certain policy measures, ranging from “sin taxes or “fat taxes” to education programs, the current literature varies over the effectiveness of these programs. Furthermore, the core of the discussion of obesity lies over whether intervention is appropriate. Obesity is very clearly a problem from a public health standpoint, but from an economic standpoint the issue becomes more controversial. While no answers have decisively been given, due to the complexity of the problem and the politics that tend to surround any major initiative, more research should be analyzed to obtain additional insights

into behavioral health economic theories. Furthermore, current research can be studied to determine the global trends of obesity in developing nations to assess if the economic growth in the United States is indicative of health trends as economies industrialize and improve. Essentially, the greater understanding policymakers can gain about the economics of obesity can better aid them in their policy making process in addressing the issue of obesity.

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RESEARCH HIGHLIGHTS:

Healthy Lung Development in Children Linked to Improved Air Quality

Caroline Russell-Troutman

Lung development throughout childhood is important for preventing the development of diseases such as asthma, and poor lung development has been associated with increased mortality and increased risk for cardiovascular dysfunction later in life. Many studies have linked problems with childhood lung development to high levels of air pollution in cities. To further understand the health effects of air quality, a study recently published in the *New England Journal of Medicine* (NEJM) has investigated how lung function in children changes with improving air quality over time.

In this longitudinal study, researchers looked at lung function data from 2,120 children who had participated in three Children's Health Study cohort studies. These data were taken over three separate periods corresponding to the three separate cohort studies: 1994–1998, 1997–2001, and 2007–2011. To assess lung function, researchers measured the maximal forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) of each child. Researchers further collected data from air-pollution monitoring stations in each of the areas where the three cohort studies had been conducted in order to determine the level of air pollution that children had been exposed to during the time range of each study.

Statistical analysis of the collected data showed that air pollution had improved overall in the studied areas since 1994. Results further showed that, across cohort studies, increases in FEV1 and FVC over time were linked to the degree to which air pollutants had decreased over the same period of time. Therefore, improvements in air quality were strongly associated with better lung development in children. However, this study is not without limitations: children in different cohort studies were not tested with the same frequency and there is no control group in which no changes in air pollution were taking place. Furthermore, this study was conducted only in southern California so its results may not be generalizable to other areas. Despite its limitations, this study contributes to an existing body of research that supports a link between reduced air pollution and healthy lung function in children.

N Engl J Med 2015; 372:905-913. DOI: 10.1056/NEJMoa1414123

Tuberculosis and Preventative Health Solutions in the Homeless Population of Paris, France

Evan Balmuth

INTRODUCTION

Paris, France: the “City of Lights,” full of berets, romance, wine and baguettes. Along the Seine, a bearded man plays an accordion, its melancholic song bellowing as couples stroll by into the dusk. Hundreds walk past the rugged musician each day, as he perfectly strikes each note despite shaky hands, rotting teeth, and a bitter cough. Once all of the tourists have gone to bed, the man retires to his sleeping bag, where he rests beneath a bridge every night alongside his coughing wife and child.

This accordion player belongs to the growing homeless population in Paris, which has increased by over 50 percent since 2001.¹ Approximately 142,000 people are without a fixed residence in Paris today, including over 30,000 children.¹ In such a large population that lacks access to many of the basic services provided to residential citizens, numerous concerns arise – yet the foremost concern is the issue of health. Among other factors, lack of medical care, unsanitary living conditions, and a prevalence of foreign pathogens render the homeless significantly more susceptible to illness. This increased susceptibility is clearly reflected in the results of recent studies, which indicate heightened rates of dermatological, psychiatric, and respiratory illnesses in the Paris homeless population.²

Perhaps most concerning in this population is a drastically heightened rate of tuberculosis (TB), a deadly and infectious respiratory illness caused by the bacterium *Mycobacterium tuberculosis*.^{3,4} If left untreated, this disease spreads quickly within unvaccinated communities – and potentially to other populations. Indeed, the World Health Organization warns that if TB is not controlled on a global level, it will kill at least 35 million people over the next 20 years.⁵ However, this epidemiology is surprising for the city of Paris, since a TB vaccine – the Bacillus Calmette–Guérin (BCG) vaccine – is distributed thoroughly in France as in most industrialized countries. Thus, this alarming state of health provokes two important questions: why does TB persist at a heightened rate in this homeless population of Paris, and how can preventative aid be implemented to address this problem? In order to evaluate these questions, an overview of the Paris homeless population’s health and medical services will be presented, followed by an analysis of potential reasons for the heightened incidence of TB, and lastly an evaluation of potential solutions to the problem.

STATE OF HEALTH AND MEDICAL SERVICES

Overall, the homeless population of Paris – consisting of adults and children without a permanent residence and including those who sleep in the street – faces serious health concerns. Approximately 14 percent of the population suffers from respiratory illnesses, 10 percent from digestive problems, 9 percent from abnormal eating behavior such as anorexia or bulimia, and 7 percent from dermatological infections.² Regarding highly infectious diseases, over 4,100 homeless Parisians suffer from a variation of hepatitis, human immunodeficiency virus (HIV), or TB. These cases total 46 percent, 61 percent, and 59 percent of the total cases in all of France.⁶ Of particular concern is the prevalence of TB, which has been difficult to define due to low surveillance, but has been estimated to rest around 220 cases per 100,000 homeless persons. This prevalence is approximately 25 times that of the national average.⁵ Clearly, the homeless population in Paris – concentrated in poor living conditions – has fostered a breeding ground for this deadly infectious disease.

TB is transmitted by airborne droplets, inhaled into the lungs where the bacteria penetrate into the alveoli and proliferate. An infection suppressed by the immune system (latent TB) can rest dormant in the lungs for an indefinite period with up to a 23 percent chance of reactivation later in life.^{7,8} Upon reactivation or initial disease manifestation, symptoms of fever, chronic productive cough, and weight loss develop rapidly. If left untreated, active TB kills approximately 50 percent of those infected.⁸

Yet unfortunately, the heightened prevalence of this grave illness in the Paris homeless population is paired with a tragic discrepancy in medical coverage. An estimated 18 percent of homeless Parisians are not covered by France’s universal healthcare system – and this rate increases to approximately 45 percent for those who sleep in the street.⁶ Yet regardless of national medical coverage, some special health services are provided for the homeless population. These provisions stem primarily from nonprofit organizations such as Médecins du Monde (Doctors of the World) and SAMU Social de Paris (Service of Urgent Medical Aid of Paris), which provide medical aid to those who cannot access national or private medical care.

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“Among other factors, lack of medical care, unsanitary living conditions, and a prevalence of foreign pathogens render the homeless significantly more susceptible to illness.”

POTENTIAL FACTORS

Related to the lack of sufficient medical coverage in the Paris homeless population are several potential factors behind its increased prevalence of TB. Firstly, the French population has insufficient TB vaccination coverage overall. In 2006, the predominant TB administration device was recalled from the French market in favor of an alternative intradermal device due to manufacturing concerns.⁹ Subsequently, stemming from a lack of training to use this new device and a decreased safety profile, TB vaccination administration decreased approximately 54 percent in France over the next year.⁹ And following this controversial transition, France suspended its obligation for TB vaccination of infants in 2007.¹⁰ These changes may have been influenced by a drastic deterioration of French opinion toward vaccinations in the last decade – approximately 60 percent of the population was in favor of vaccines in 2010, having dropped 30 percent since 2005.¹¹ However much influenced by attitudes, TB vaccine coverage of infants born after the above legislation changes is estimated to be around 76 percent in France.¹² Overall, in combination with their decreased medical coverage, the French homeless experience a particularly reduced likelihood of receiving TB vaccination compared to the rest of the French population which already experiences incomprehensive vaccination coverage.

Secondly, while France displays a low rate of TB immunization, many homeless Parisians have emigrated from nations that demonstrate drastically high incidences of TB, resulting in an influx of immigrants already carrying the disease. Indeed, in metropolitan France, the incidence of TB is approximately 15 times higher for immigrants than for French nationals – and strikingly, demographic studies have concluded that over 50 percent of the Paris homeless population is composed of immigrants.^{5, 13} Specifically, immigrants from sub-Saharan African countries have the highest incidence of TB, at approximately 19 times the national average.⁵ Studies have concluded that one third of the sub-Saharan African population is infected with latent TB, despite a vaccination coverage of approximately 75 percent in the region.⁸ Particular to this part of Africa, the heightened rate of infection despite vaccination has been linked to coinfection with HIV, as the resulting immunodeficiency may render the vaccine's action insufficient for protection against TB.⁸

A related problem in sub-Saharan Africa, also experienced globally, is that of the TB vaccine's inefficacy. As an

example stated above, one-third of the sub-Saharan population is infected with latent TB despite a 75 percent vaccination rate – and with its significant potential to reactivate later in life, latent TB constitutes the primary source of TB transmission.¹⁴ And in general, the efficacy of the TB vaccine has proven highly variable, with protection rates ranging from zero to 80 percent.¹⁵ In addition, immunization does not normally last more than 15 years, and does not protect against reactivation of latent TB.^{8, 14} Lastly, the current TB vaccine is becoming less and less efficacious in the face of proliferating mutant strains of multidrug-resistant bacteria. Since the first TB vaccination in 1921 and the first antibiotic treatment in 1944, the bacterium has adapted and evolved to evade such interventions – a vicious cycle that results in continued mutations with each new treatment introduced, leading to both insufficient immunization and antibiotic treatment.^{16, 17}

While the above potential factors of low vaccine coverage and efficacy pose problems for everyone, the Paris homeless' poor living conditions place them in a position of utmost risk. The principal danger of homeless living conditions concerns overcrowding, in *bidonvilles* (shantytowns) often seen under bridges or abandoned buildings in Paris, and in homeless shelters. In these overcrowded conditions, the already high incidence of TB infection and low vaccination protection combines with frequent and close person-to-person contact – thus, a perfect storm for TB transmission. Likewise, poor sanitation and hygiene capabilities facilitate TB transmission by supporting bacterial growth and compromising the immune



Figure 1. Section of a *bidonville* in the 19th arrondissement of Paris. This community, consisting of approximately 20 Romanian immigrant families, was constructed in an abandoned office building. A row of shanties, housing one to five individuals each, can be seen in the bottom left corner. *Photo credit: Evan Balmuth*

system.¹⁸ In sum, this at-risk, contained and concentrated homeless population of Paris rapidly transmits TB within its own isolated communities, in a perpetual cycle.

As a final consideration, the psychological perception of health is an important yet often overlooked factor. A recent survey by the French organization Insee (National Institute of Statistics and Economic Studies) concluded that 78 percent of homeless Parisians perceive themselves to be in good health, as opposed to only 69 percent of the general French population.^{6, 19} These results are surprising given the heightened incidence of disease in the homeless population, and beg the question of whether different standards of health persist among Paris homeless communities. Within a population that displays more illness and a lower quality of sanitation and hygiene, while often living in isolated *bidonvilles*, it is likely that a different perception of health and illness exists. As a result, a homeless Parisian coughing due to a TB infection may perceive himself in better health than would a non-homeless Parisian, if the homeless person lives in close

proximity to several others suffering from advanced stages of HIV, hepatitis, and other illnesses. Consequently, the coughing person may be less inclined to seek medical aid amidst such a different relative perception of health, until the infection has advanced to a deadly stage and the bacteria have already been transmitted to others. Although in-depth anthropological investigations have not been conducted on this subject in the homeless population, such studies may yield insights into a potential lack of medical aid seeking in this community that would contribute to TB transmission.

POTENTIAL SOLUTIONS

Given all of the potential factors for the increased incidence of TB in the Paris homeless population, this issue is clearly a complicated one that cannot be resolved by one simple solution. However, several preventative health actions can be taken to address the problem – and if taken together, over time TB can be virtually eliminated in the homeless population.

One important step is that of TB education. As the homeless may be unable to identify TB symptoms and may have inadequate knowledge of its graveness and transmissibility, it is important provide them with education on the characteristics of TB so that the disease can be recognized, and motivation can be instilled to seek treatment. Additionally, providing information on the availability of governmental and nonprofit care would allow the homeless to find existing treatments and preventative aid. Such education can be accomplished by conducting information sessions in neighborhoods highly affected by homelessness, and by mobile teams that can speak and distribute pamphlets in *bidonvilles* and in other affected neighborhoods.

With regards to the influx of latent TB via immigrants, the French immigration control could improve its immigrant TB screening. Currently, the process relies upon the tuberculin skin test, which demonstrates high variability in its sensitivity for TB detection.^{20,21} Additional chest radiographs, clinical examinations, and confirmatory blood chemical assays – as implemented successfully by the United States among other countries – would more efficiently and accurately identify immigrants carrying TB, in order to direct them to necessary care before TB reactivation and further spread of the disease.²⁰

In the biological domain, an improved TB vaccine that accounts for multiple mutant strains of the disease could be significantly more efficient in preventing TB infection. Today, approximately 20 TB vaccine candidates are under development, incorporating novel immunological technology and techniques to target novel TB antigens and elicit stronger, longer-lasting immune responses.²² Many vaccines, such as MVA85A, are being tested in clinical trials as booster immunizations to follow an earlier BCG TB vaccine.²² This sort of immunizing reinvigoration may be able to prevent reactivation of latent TB infections and thus halt later disease progression.

Taking into account the above steps that would effectively combat the TB problem in the Paris homeless population, some nonprofit organizations in Paris are taking multi-tiered approaches to address the issue – approaches that can

serve as models to make an important impact over time. One model is the DOT (Directly Observed Treatment) program of SAMU Social de Paris, which deploys mobile volunteer teams to accompany homeless TB patients to treatment sessions, ensuring completion of treatment and education on available care.⁴ However, this program can only accommodate a minority of patients. In contrast, Médecins du Monde has launched a TB prevention campaign with four goals: TB education via information sessions and flyers; increasing access to TB screening via partnerships with local medical laboratories and individual incitation; augmenting access to medical care in Médecins du Monde care centers and via accompaniment to hospitals; and raising awareness of the TB problem in the homeless population to other health organizations and the government.²³ Perhaps the most powerful aspects of the aforementioned models are their educative nature and mobility. In such isolated and excluded homeless communities, where health perceptions vary and medical aid is hard to reach, it is often necessary for the aid and information to find those in need via mobile teams. Such teams from SAMU Social de Paris and Médecins du Monde help not only by providing aid to individuals, but through caring for entire homeless communities in Paris by increasing disease recognition and helping the homeless attain treatment of their own accord.

CONCLUSION

The Paris homeless population struggles each day to get by amidst significantly higher rates of TB infection and other illnesses compared to the rest of the French population. However, by identifying the potential factors behind such an increased prevalence, appropriate steps can be taken to eradicate TB from this population. Furthermore, although many aspects of this problem are specific to Paris, many of the same issues and preventative health solutions can be generalized to homeless populations throughout the world. Indeed, Médecins du Monde, as implied by their name, is not limited to Paris but works around the globe combatting TB on five continents, amidst different communities and health policies. By assessing and caring for homeless populations such as the one in Paris, it may be possible to find a means for TB eradication globally. Surely, this result is long from achievement as foreign pathogens continue to pass across borders, unsanitary living conditions and low medical coverage persist, ineffective and insufficient vaccines are distributed, and homeless populations remain uneducated about TB and available care. However, TB education, more comprehensive TB screening, novel vaccine developments, and autonomy-based aid programs provide hope for the possibility of eradication. One day, homeless accordionists along the Seine and all other homeless people around the world – attaining their basic right to health – can survive to find employment and houses, nourish their families, and live successful lives.

References for this article can be found at
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Health Disparities in Pediatric Asthma: A Multidisciplinary Review

Jordan Wang

Evidence from previous literature that examines how race and ethnicity, family households, socioeconomic status, and geographic environments affect children with asthma has been extremely controversial. A comprehensive review of these findings is necessary in order to explain the current state of pediatric asthma, which will ultimately lead to potential solutions in the near future. Through the use of a multidisciplinary approach in reviewing the existing literature and the various influences of culture, significant information can be uncovered regarding the relevant effects of our current health disparities.

BACKGROUND

Asthma is one of the most common chronic illnesses in childhood. The Centers for Disease Control and Prevention estimate that 7.1 million children under the age of 18 are affected by asthma.¹ It is the third leading cause of hospitalization for those under 15 years of age² and is also one of the primary causes for absenteeism from school, accounting for an estimated 14.4 million school days annually lost by children.¹ For the United States in 2007, it was estimated that the direct health care cost and productivity loss due to asthma totaled 56 billion dollars.³ This illness is considered a critical concern for both healthcare and our society.

Asthma is a chronic inflammatory disease of the airways, which presents with recurrent yet reversible respiratory obstruction and bronchospasm. It is characterized by symptoms that include coughing, wheezing, chest tightness, and shortness of breath. Asthma is a result of a complex interaction between genetic and environmental factors.⁴ Genetic predispositions for allergies and asthma, which do not follow classic Mendelian inheritance patterns, increase risks for those who are applicable. Environmental triggers such as exposure to tobacco smoke or other allergens have been extensively studied pertaining to the onset of asthma. In addition, physiological factors such as the presence of allergies or bronchiolar hyper-responsiveness also play key roles. Many other triggers have been found to exist, further compounding the numerous complexities of this illness.

Although there has been many medical and technological advances in therapy, increasing levels of asthma prevalence, severity, and mortality still exist.⁵ In response to this escalation, few answers have been found; however, the medical community continues to seek out its causes in addition to searching for improved strategies for treatment and prevention.⁶ Continued controversy regarding which factors have contributed to these increases has led to additional in-depth studies, especially observing relationships to race and socioeconomic status.⁷ However, further research is needed to find new strategies to reduce this rise in asthma, particularly regarding its high frequency in children.

The solution may not be in the advancement medical treatment but in fully understanding the major causes

of current health disparities. Many studies have extensively examined the influences that race and ethnicity, family households, socioeconomic status, and geographic environments have on children with asthma. A review of these findings may help to explain the current climate of pediatric asthma, ultimately leading to potential solutions and therapies. By using a multidisciplinary approach to review the literature and to interpret the various influences that culture has, more information may be uncovered on the relevant health disparities.

ON RACE AND ETHNICITY

Both race and ethnicity greatly influence the health disparities of children with asthma. Studies have examined their effects on pediatric health, particularly observing Black, Hispanic, and Latino children. Many such studies have found that racial and ethnic minorities possess an inherent disadvantage for health risks concerning asthma. In a regional study of asthmatics, Black and Latino children had greater frequencies than White children of reporting limitations in physical activity and of needing urgent medical care.⁸ These results appear to support previous studies. Data from a national survey previously showed that Black children were more likely to have asthma than were White children.⁹ In addition, Black children were more than three times as likely to be hospitalized for asthma and were more than four times as likely to die from asthma when compared to White children.¹⁰ Evidence suggests that being a Black child presents as a significant disadvantage. However, one study observed that the prevalence of asthma in Hispanic children was even greater than any other racial and ethnic groups.¹¹ These studies altogether support the claim that asthma may be related to either cultural behaviors or genetic variations, both of which are heavily influenced by race and ethnicity.

A great deal of research has observed pediatric populations within Medicaid to study the effects of race and ethnicity on asthma. By utilizing this particular subset, researchers can control for similar insurance coverage and attempt to limit the influences of income. It is also beneficial that

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Medicaid insures many children of minorities.¹² Findings from a Medicaid population suggest that Black and Hispanic children were less likely than White children to receive timely follow-up visits after being seen in the emergency department for asthma.¹³ This lag may contribute to the exacerbation of future asthma attacks by increasing their severity. Black and Latino children were also found to have worse asthma conditions and decreased usages of preventive asthma medications than White children.^{14,15} This poor adherence to effective management strategies may explain the differences in hospital usage. Black children had greater use of the emergency department and inpatient services, with inadequate use of preventive care as demonstrated by fewer visits to their physicians for asthma.¹⁶ In combination, these studies suggest that the overall habits and behaviors characterized by the differences in race and ethnicity are responsible for existing health disparities.

Studies on race and ethnicity tend to provide limited results due to the difficulty of controlling for variables. Although Medicaid studies are important and offer potential evidence for the health disparities of minorities, this subgroup typically comes from lower income. A national survey showed that Black children were at greater risk for asthma than White children but only among the very poor.¹⁷ This may explain the observed patterns from Medicare studies. However, after adjusting for such socioeconomic factors and environmental exposures, other studies still found a higher prevalence of asthma in Black children compared to White children.^{18, 19, 20}

Due to the difficulty of isolating a single variable, more studies must be completed in order to clarify previous inconsistencies. New studies should adjust for any associated socioeconomic and environmental risk factors. Concerning the cultural habits and behaviors of various races and ethnicities, improved patient education may offer a potential solution. Black and Hispanic patients will benefit from increased education that reinforces the significance of structured asthma medication therapies and treatment adherence. If differential genetic susceptibility to asthma is later found to explain variations, then researchers can begin to search for gene sequences that increase such risk. Future advances in gene therapy may provide the tool to safely and effectively ameliorate any differences in susceptibility. Whatever the cause for these racial and ethnic disparities, it is clear that further studies are required to establish grounds for consistent and verified evidence.

ON FAMILY HOUSEHOLD

Family culture helps to explain the incidence of childhood health disparities. The households of children play an important role in impacting their overall health and hygiene. Family environments associated with aggression, conflict, and underprovided nurturing may increase the risk for physical

and mental health issues in children.²¹ Asthmatic children who have encountered greater levels of family conflict and dysfunction are at greater risk for increased lifetime hospitalizations and severe and poorly controlled asthma.^{22,23} Such detrimental interactions within the family can greatly influence pediatric health.

Childhood asthma has been thoroughly studied in regards to the psychological state of parents and the environments of households. Parental attitudes and behaviors particularly affect asthmatic children since these adults are the essential caregivers--typically residing over the administration of prescribed medical treatment. The onset of pediatric

asthma and its outcomes are associated with multiple family characteristics pertaining to specific emotional states and adherence to asthma management.²⁴ Distress in family households adds to the ongoing risk that children may have of developing severe asthma. Stressful environments with parents in a depressive state prevent prescribed medical treatment adherence and undermine effective asthma management behaviors. Psychological functioning of parents or caregivers has been associated with worse asthma out-

comes in children. Mothers with high depressive symptoms were 40% more likely to report that they had taken their child to the emergency department than those with low depressive symptoms.²⁵ Methods of identifying and managing unhealthy emotional states of parents may help to reduce unnecessary hospital visits and improve asthma management.

Parent-child relationships were also found to play a significant role. Healthy interactions between parents and children can lead to increased understanding of symptoms and treatment practices. Higher levels of parental criticism were associated with greater medical noncompliance, which can ultimately lead to an increased risk of severe and poorly controlled asthma.^{23,26} In further support of the damaging effects of high-conflict relationships, studies show that asthma management may be more difficult where effective communication and supervision are compromised.²⁷ Parents who were reluctant to show affection correlated with poorer asthma medication adherence.²⁸ In combination, these findings suggest that the best atmosphere for a child is characterized by strong parent-child relationships that yield low levels of both criticism and conflict with high levels of affection.

By understanding the influences that family households have on pediatric health, we can begin to address existing health disparities through potential interventions. Healthcare providers should place greater significance on the environments of their patients. With the creation of a scoring system intended to seek out characteristics that define the previously described dysfunctional atmospheres, medical professionals can better predict which children are at elevated risks for poor medical adherence and repeat hospital visits. Those receiving

“Black children were more than three times as likely to be hospitalized for asthma and were more than four times as likely to die from asthma when compared to White children.”

worse scores will benefit from specialized attention and education pertaining to effective asthma management strategies. However, it is still evident that additional studies are needed to determine the extent to which these environmental factors drive disparities in the prevalence, incidence, and outcomes of asthma and what approaches are most effective to counteract their influences on disparities.²⁹

ON SOCIOECONOMIC STATUS

Socioeconomic status remains crucial in understanding the existence of health disparities in asthmatic children. There have been many extensive reports on the function of socioeconomic status, and it has since been described as an important determinant of health.³⁰ Low incomes and little education are considered to be strong predictors of a range of physical and mental health problems. Numerous studies have attempted to examine the association between children with asthma and the income, education, and occupation of their families. Since it was suggested that socioeconomic status may influence asthma occurrence and prognosis,³¹ lower socioeconomic conditions were associated with increased asthma occurrence, severity, and hospitalization.³² When comparing socioeconomic status to the severity of childhood asthma, those considered to be in the low socioeconomic group as defined by parental education possessed increased prevalence of severe asthma.³³ This study is one of very few that distinguishes between the degrees of asthma severity in an effort to fully understand the association between childhood asthma and socioeconomic status. This is especially important since the majority of studies examines solely the prevalence of asthma and has ultimately provided conflicting results.

Poverty is an important marker of socioeconomic status in asthmatic children, ultimately impacting the frequency of visits to the hospital, physicians, and emergency rooms. Regardless of race, poverty in children is the single most predominant risk factor for hospitalization from asthma.³⁴ Poor asthmatic children visit physicians less frequently despite higher numbers of bed days and hospitalizations.³⁵ These results suggest that families in poverty may neither have adequate access to primary care physicians nor understand that their physicians are in place to help prevent the onset of severe asthma attacks. Asthmatics with increased visits to the emergency room possessed lesser knowledge of asthma control criteria in addition to asthma management skills.³⁶ This particular group of patients trended toward lower levels of socioeconomic status including education level. In counteracting this lack of information through interactive communication, health care providers can help to lower the incidence and severity of childhood asthma.

Spreading awareness of the effects of socioeconomic status on childhood health can help families of lower socioeconomic status. Some families may not have the proper means

to frequently visit physicians, so public education is a must. Families that have asthmatic children must be taught to recognize premature signs of attacks and learn how to best manage them through treatment. A disconnect may exist as to when and why families are administering asthma treatment during certain times and symptom presentations. It has been recommended that physicians focus more on educating patients on the need for treatment rather than exclusively showing them how to administer treatment alone.⁷ Families may better adhere to instructions when they fully understand the reasons as to why each step of asthma management is considered necessary.

ON GEOGRAPHIC ENVIRONMENT

Geographic settings have long been considered as a factor for current disparities in childhood health and particularly asthma. In a national study, all children regardless of race or income who lived in an urban setting were at increased risk.³⁷ Of the many locations examined in a particular study, New York City was home to one of the highest asthma mortality rates, reaching almost three times that of the entire United States in previous years.³⁸ New York hospitalization rates for asthma increased 3.8% per annum, whereas New Hampshire saw a 5.8% decrease in the same rates.³⁹ Trends for one of the largest urban centers provide clues as to how this illness is affected by living conditions. Combinations of poor housing conditions, outdoor air pollution, and harmful land uses must be examined to fully understand the distribution of childhood asthma in urban neighborhoods.⁴⁰ Only after considering all sources of potential influence in these geographic settings, can we begin to thoroughly analyze the effects of urban environments and our current climate.

Urban housing conditions are known to be grounds for poor and imperfect living quarters, particularly concerning unacceptable levels of air circulation and environmental allergens. Such allergens are fully capable of triggering asthma onset. In a report citing the former Surgeon General, David Satcher, one of the reasons given for rising levels of asthma in urban areas was that these children spend more of their time indoors, thereby increasing their exposure to poor ventilation and indoor allergens.⁶ In the absence of adequate ventilation, the buildup of dust poses as a challenge. Exposure to high concentrations of indoor allergens, such as dust mites, is a dominant risk factor for asthma in children.⁴¹ Inner-city dwellings are also known to be the home of many indoor pests. Exposures to high levels of cockroach allergens were correlated with higher frequency of asthma-related health problems, including risk of hospitalization, in inner-city children.⁴² The bedrooms of those examined in this study showed increased frequency of high levels of cockroach allergen in dust when compared to other environmental allergens. This is consistent with cockroach allergens being common to urban

“Low incomes and little education are considered to be strong predictors of a range of physical and mental health problems.”

living environments.⁴³ In addition, poor ventilation would also exacerbate any levels of tobacco smoke present in the household. A national survey showed that secondhand exposure to parental tobacco smoke was associated with increased airway hyper-responsiveness and wheezing respiratory illness in children.⁴⁴ Deteriorating or dilapidated housing is likely to exponentially compound any exposure to indoor allergens, which will trigger asthma in children.

High levels of pollution in urban environments may also cause increased prevalence of asthma. Emergency hospital admissions for children with asthma were associated with high levels of sulfur dioxide in major cities.⁴⁵ Large urban areas have reached dangerous levels of pollution for childhood health. A study by the American Lung Association found that high levels of air pollutants have disproportionately impacted urban populations, while it is also known that these particular pollutants can cause asthma exacerbation.⁴⁶ A large cohort study of children evidenced the association between traffic-related air pollution and increased physician-diagnosed asthma.⁴⁷ The prevalence of respiratory symptoms in addition to asthma has specifically been observed in relationship to traffic-related nitrogen dioxide.⁴⁸

Additional studies on the relationship of urban environments and children with asthma must be completed in order to fully determine its effects. The results of some studies are rather limited since our urban culture, particularly that of the inner city, is typically synonymous with those who are either poor, uneducated, of racial and ethnic minorities, or a combination of such. Some studies may not be able to completely control for all of these factors. However, potential solutions must be found to help mediate the urban health issues related to pediatric asthma. Cost-effective methods to increase air ventilation and decrease levels of environmental allergens are needed in order for them to be affordable to residents of urban communities. In addition, increased education about inner-city asthma may help to inform children and their families of facts that are previously unknown to them. Individualized asthma education using videotapes, activity books, and discussion with staff nurses upon hospital admission increased knowledge of warning signs for acute asthma and reduced emergency room use in inner-city children.⁴⁹ Pertaining to the dangers of pollution, stricter standards and successful solutions must be implemented. Improved household conditions, increased patient education, and enhanced environmental intervention can help to reduce the prevalence of allergen-induced asthma, especially from cockroach allergens.⁵⁰

COMMENTS

A multidisciplinary review of the influences that race and ethnicity, family households, socioeconomic status, and geographic environments have on pediatric asthma provides great insight into the current climate of health disparities. Only after taking each of these factors into consideration can we begin to fully understand the exacerbating effects that our current culture has on children with asthma. Health disparities can be effectively addressed in the near future through effective solutions that are based on the amalgamation of research concerning the relevant cultural influences.

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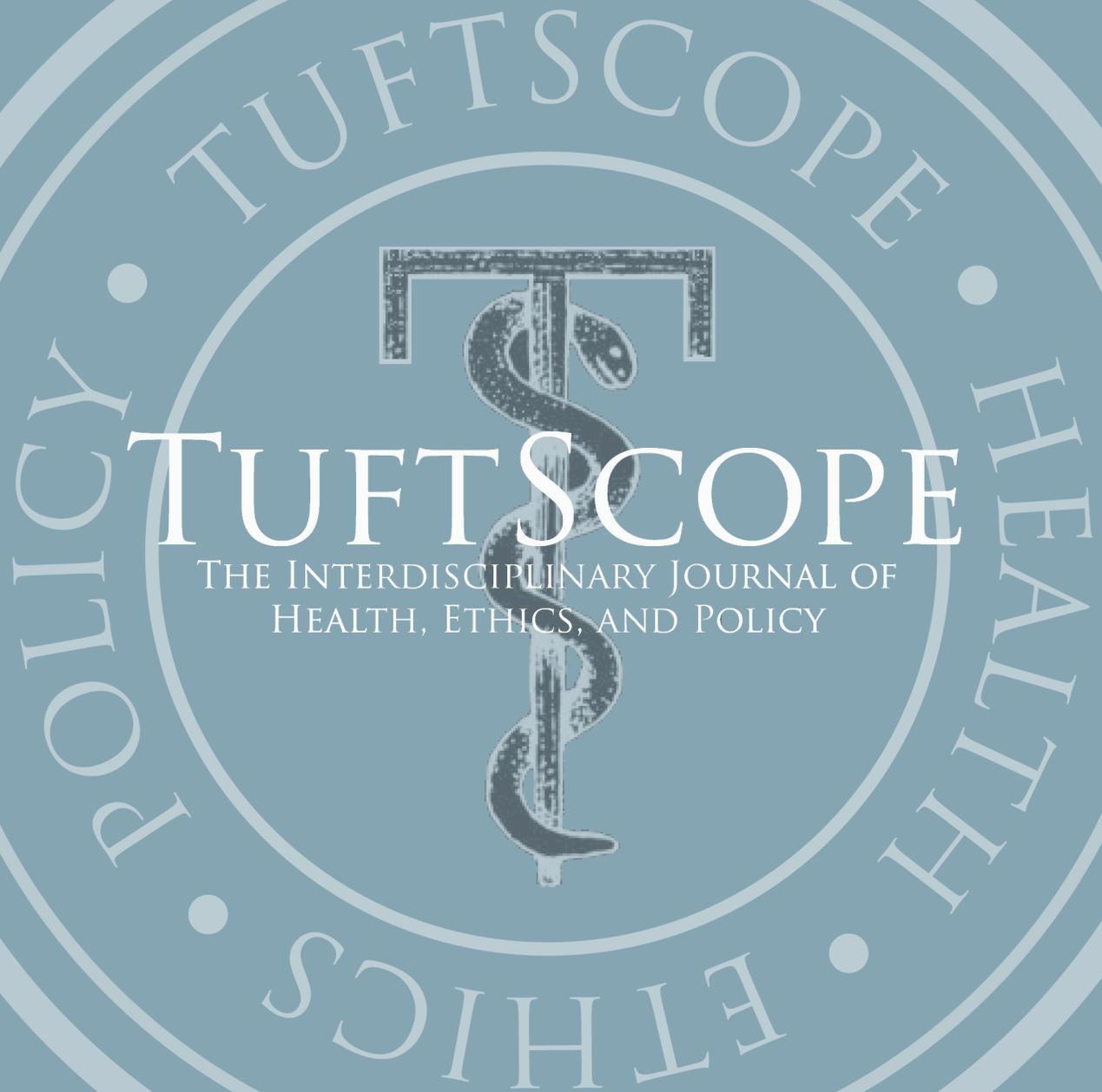
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