Use of machine learning to predict pulmonary exacerbations

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Cystic Fibrosis

Pathophysiology

Sinusitis

Chronic Pulmonary Infection

Bronchiectasis

Salty sweat

Cirrhosis

Pancreatic Insufficiency

Diabetes

Intestinal Obstruction

Male Infertility
Cystic Fibrosis

Pathophysiology

- Sinusitis
- Chronic Pulmonary Infection
- Bronchiectasis
- Salty sweat
- Cirrhosis
- Pancreatic Insufficiency
- Diabetes
- Intestinal Obstruction
- Male Infertility

Failure to maintain airway surface liquid

Cystic Fibrosis

Pathophysiology

Cystic Fibrosis
Transmembrane Regulator

Cirrhosis
Pancreatic Insufficiency
Diabetes
Intestinal Obstruction
Male Infertility

Chronic Pulmonary Infection

Bronchiectasis

Salty sweat

Sinusitis

Failure to maintain airway surface liquid

Progressive Inflammatory Lung Damage

Obstruction

Infection

Inflammation
Why bother with Home Monitoring?

Current Problems with CF care

The Promise of Home Monitoring
Why bother with Home Monitoring?

Current Problems with CF care

Why am I in clinic if I’m well?

Clinic only when you need to

The Promise of Home Monitoring
Why bother with Home Monitoring?

Current Problems with CF care

**Why am I in clinic if I’m well?**

**Am I about to become ill?**

Clinic only when you need to

Predicting Exacerbations

The Promise of Home Monitoring
Why bother with Home Monitoring?

Current Problems with CF care

Why am I in clinic if I’m well?  
Clinic only when you need to

Am I about to become ill?  
Predicting Exacerbations

What’s the point of treatment?  
Physiological feedback

The Promise of Home Monitoring
Why bother with Home Monitoring?

Current Problems with CF care

Why am I in clinic if I’m well?
Am I about to become ill?
What’s the point of treatment?
Cross-infection

Clinic only when you need to
Predicting Exacerbations
Physiological feedback
Minimising risk

The Promise of Home Monitoring
Pilot Telemed Study (TeleCF)

Evaluation of novel biomarkers
- Daily sputum Sample
- 15 Adults with CF
- 6 months study
- Daily monitoring
- PC-based upload

Symptom diary

Activity tracker
- Peak Flow FEV₁
- Pulse ox
- Weight
- Body composition

Completed Dec 2013

Papworth Hospital 2011-13

SBRI

Health Enterprise East

C/w Kevin Auton
Pilot Telemed Study

1. Complex data sets
2. Enthusiasm for home monitoring
3. Much larger study required
4. Sensor connectivity critical
Symptom scores

- iv antibiotics
- FEV1
- Biomarker A
- Oxygen sats
- Heart rate
- Weight
- Activity

Multi-dimensional phenotyping

- Siderophore
- Caseinase
- Swimming
- Gela-nase
- Twitching
- Hypermimutator

Pilot Telemed Study

Emem Ukor, Louise Ellison, Martin Welch
Pilot Telemed Study

Symptom scores

iv antibiotics

FEV1

Biomarker A

Oxygen sats

Heart rate

Weight

Activity

Genotype-phenotype correlation (GWAS)

Josie Bryant, Julian Parkhill (Sanger)
Pilot Telemed Study

iv antibiotics

Symptom scores

FEV1

Biomarker A

Oxygen sats

Heart rate

Weight

Activity

Systems genetics (a functional wiring diagram)

Aaron Weimann, Oli Stegle (EBI)
Pilot Telemed Study

iv antibiotics

Symptom scores

Biomarker discovery: Metabolic fingerprinting

Josie Bryant, Karen Brown
150 Adults with CF
7 adult CF centres
6 months study
Daily monitoring
Smartphone upload

Funded by:

Cystic Fibrosis Trust
Cambridge Centre for Lung Infection
SMARTCARE 1

Multi-centre feasibility study

Evaluation of novel biomarkers
Microbial Genetics

Daily sputum Sample
Home freezer

Symptom diary

Activity tracker

Peak Flow $\text{FEV}_1$

Pulse oximeter

Weight
Body composition

Microbial Genetics
• Completed April 2017
  Lock down data October 2017

• 147 subjects enrolled
  4 deaths
  10 withdrew within first month
  15 withdrew between Month 1-6

135 subjects >4 months data
What SMARTCARE 1 hoped to achieve:

1. **Test the system**
   - Do the sensors work?
   - Does the data upload?
   - Does the software work?

✓
SMARTCARE 1

Multi-centre feasibility study

What SMARTCARE 1 hoped to achieve:

1. Test the system
   - Do the sensors work?
   - Does the data upload?
   - Does the software work?

2. Test acceptance

   Anxiety*
   - Reassurance
   - Behavioral change
     (eg physio, new therapy)

   Hassle*
   - Informing clinical decisions
     (unavoidably)
What SMARTCARE 1 hoped to achieve:
1. Test the system
   - Do the sensors work?
   - Does the data upload?
   - Does the software work?
2. Test acceptance

![Bar chart showing the proportion of participants rating remote monitoring helpfulness.](image)
Data capture

SMARTCARE 1

Multi-centre feasibility study

Damian Sutcliffe
John Winn
What can the Smartcare1 data tell us?
Example

Current clinical data

Graphs showing C-reactive protein (mg/L) and FEV1 (% predicted) over time (days). The graphs indicate the effects of iv Antibiotics and Orkambi on the parameters.
Current clinical data

FEV\(_1\) (% predicted)

\(O_2\) saturation (%)
Example

Current clinical data

[Graph showing the relationship between wellness and cough percentages over time, with markers for iv Antibiotics and Orkambi treatment periods.]
Example

Current clinical data
SMARTCARE 1

Defining the start of a pulmonary exacerbation
SMARTCARE 1

Defining the start of a pulmonary exacerbation

- **Lung health**
- Antibiotics
- Delay in starting antibiotics
- Regular

Patient 1

Days

Damian Sutcliffe
John Winn
Defining the start of a pulmonary exacerbation

Delay in starting antibiotics

Patient 1

Patient 2

Lung health

Antibiotics

Days

Regular

Quick

Damian Sutcliffe
John Winn
Defining the start of a pulmonary exacerbation

- Antibiotics
  - Regular
  - Quick
  - Slow

Patient 1

Patient 2

Patient 3

Lung health

Delay in starting antibiotics

Days

Damian Sutcliffe
John Winn
Defining the start of a pulmonary exacerbation

Aligning deteriorations using machine learning

Patient 1

Patient 2

Patient 3

Lung health

Antibiotics

Days

Damian Sutcliffe
John Winn
SMARTCARE 1

Defining the start of a pulmonary exacerbation

Average responses

Aligned to antibiotics

Aligned to deteriorations

Antibiotics

Days

*
SMARTCARE 1

Defining the start of a pulmonary exacerbation

Aligned to antibiotics
Aligned to deteriorations

Lung Function

Cough

Weight

Activity

Days

Damian Sutcliffe
John Winn
Can we use **machine learning** to understand (and then predict) acute pulmonary exacerbations?
Building a graphical model of a CF pulmonary Exacerbation

Model based on existing (prior) knowledge

ML-based graphical model (to understand biological processes)

Unsupervised machine learning
SMARTCARE 1

Using graphical model for predicting exacerbations

Supervised machine learning

ML-based graphical model

Predictive algorithm

90% 10%

Damian Sutcliffe
John Winn
Home monitoring

Where we’re aiming:

Patient empowerment
Transform Outpatient Clinics:

Clinic when you need it

Better information to judge clinical trajectories

Advanced warning of exacerbations
Home monitoring

Transform Outpatient Clinics:

Now

Call from patient

- Routine clinic review
- Emergency clinic

Where we’re aiming:
Home monitoring

Transform Outpatient Clinics:

Now

Call from patient

Future?

Algorithm alert

Home monitoring

- Routine clinic review
- Emergency clinic
- Video clinic
Home monitoring

Changing clinical care delivery:

2016: **10,500** individuals with CF

Population increasing by ~250 individuals/year

Where we’re aiming:

Bigger CF Centres in the future?
Home monitoring

Where we’re aiming:

Transform Outpatient Clinics:
Changing clinical care delivery:

Enrich CF Patient Registry:

High frequency data  Annual data

Home monitoring  Patient Registry
Home monitoring

Where we’re aiming:

Transform Outpatient Clinics:

Changing clinical care delivery:

Enrich CF Patient Registry:

Novel trial design:

- Adult CF patients
  n = 10 each group

- Remote monitoring
  FEV1, O₂ Sats, Activity, Temp

- Sputum
  Quantitative micro Cytokines

- Blood
  Inflammatory markers Functional assays

2 weeks
Treatment
Placebo
Washout
Placebo
Treatment

I-BET
Placebo
2 weeks
Placebo
2 weeks
Washout

I-BET

Functional assays

Blood

Sputum

Remote monitoring
FEV1, O₂ Sats, Activity, Temp

Adult CF patients
n = 10 each group
Home monitoring

Where we’re aiming:

Transform Outpatient Clinics:
Changing clinical care delivery:
Enrich CF Patient Registry:
Novel trial design:
Novel sensor development:
Home monitoring in Cystic Fibrosis

Transform clinical service delivery
- Video clinic
- Video triage
- Clinic when you need it

Continue machine learning analysis
- Trial novel sensors
- Develop predictive algorithms

Data Science
Home monitoring in Cystic Fibrosis

**Smartcare1**

*Project management*
Judy Ryan  Emem Ukor

*Smartcare Steering committee*
Caroline Elston  Di Bilton
Dan Peckham  Andy Jones
Nick Bell  Thom Daniels
Chris Orchard

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Louise Ellison

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**CCLi**
Cambridge Centre for Lung Infection

Charlie Haworth & Adult CF team

**Microsoft Research**

John Winn

**Cystic Fibrosis Trust**

Janet Allen