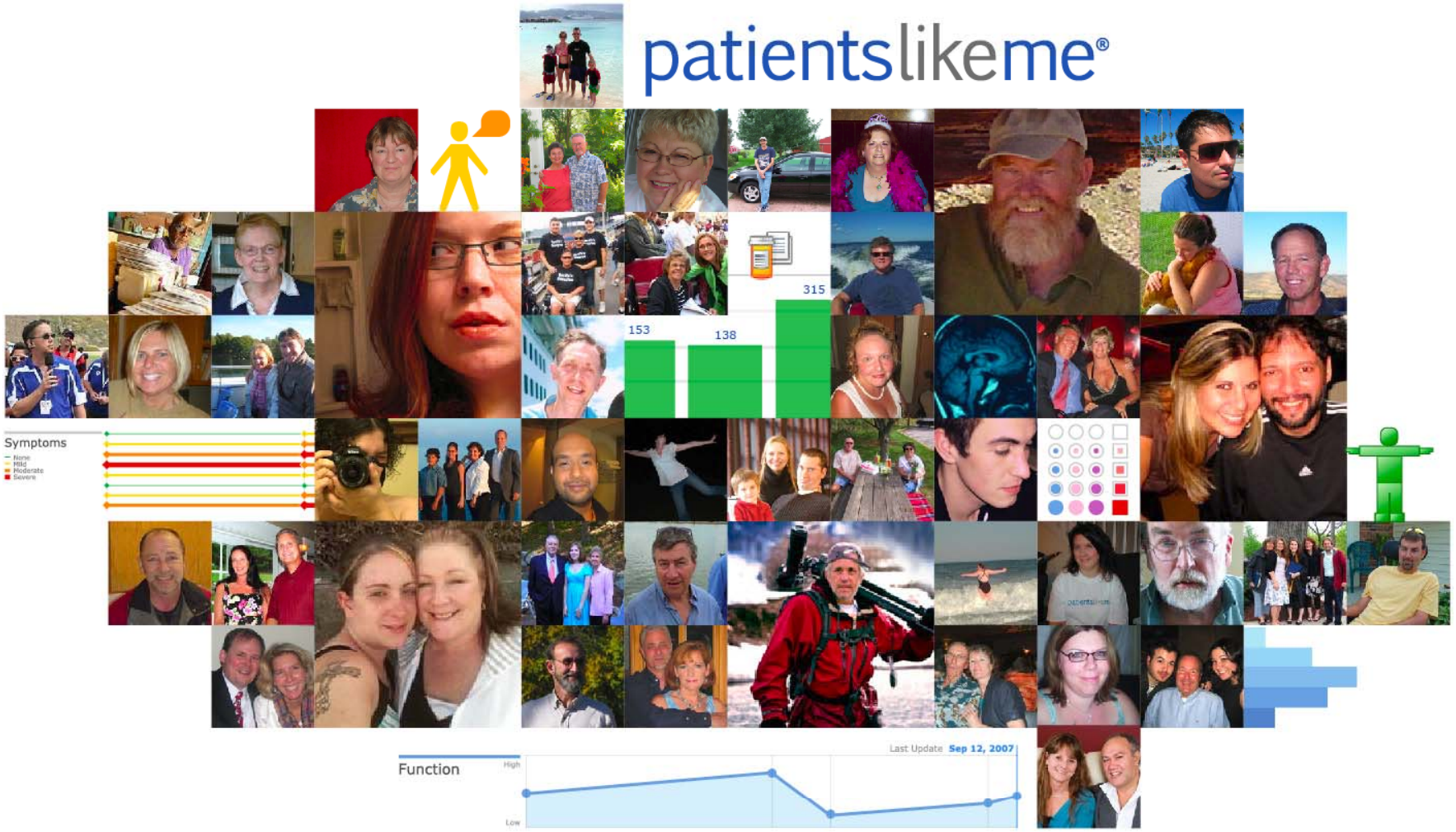


James Heywood

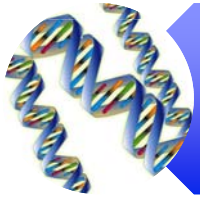
"It is far more important to know what person the disease has than what disease the person has"

– Hippocrates

"A great wind is blowing and that gives you either imagination or a headache"

– *Catherine the Great*

Empowered patient

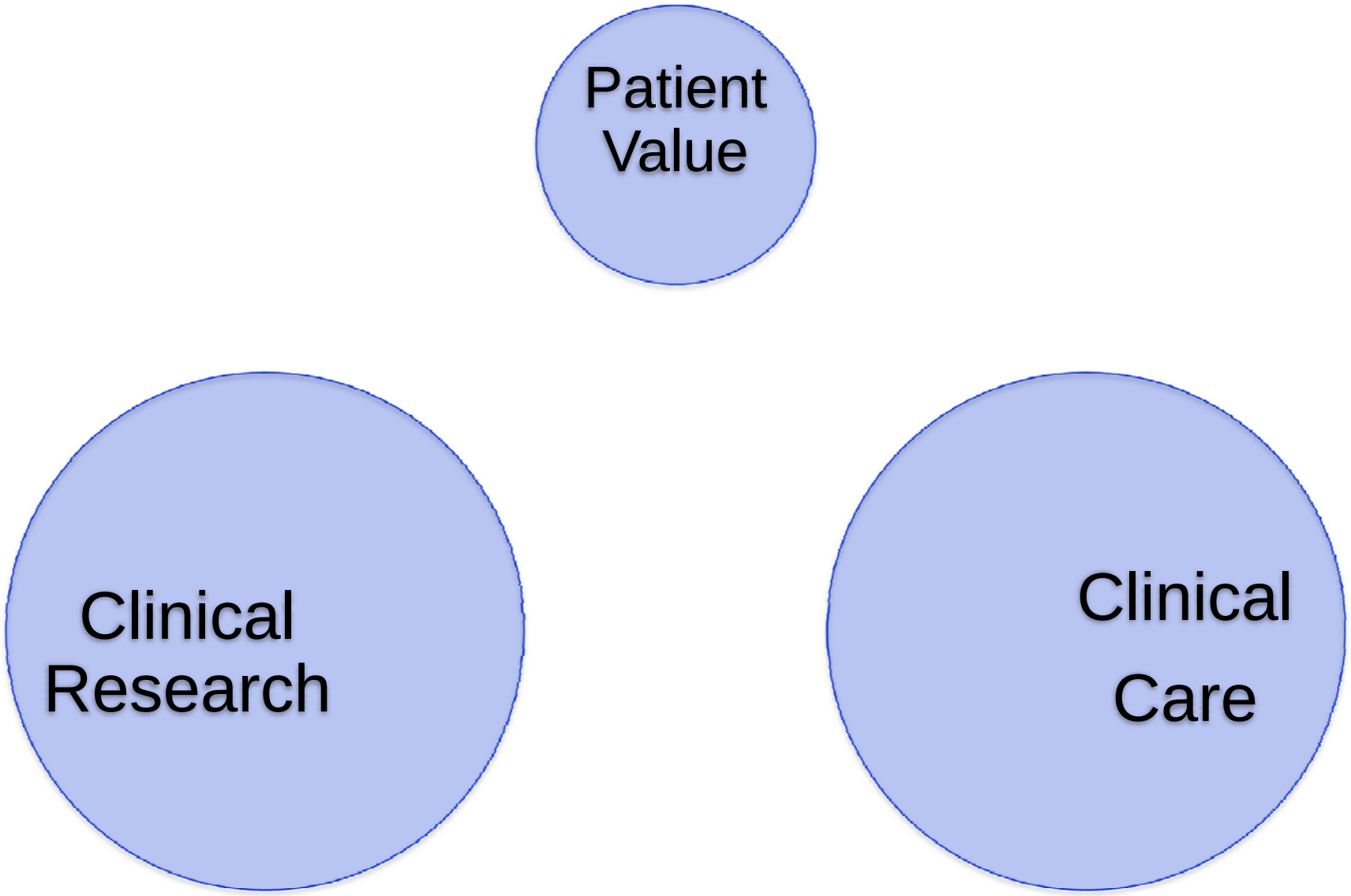


Molecular medicine

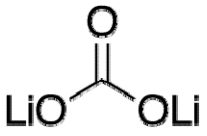
Doctor role

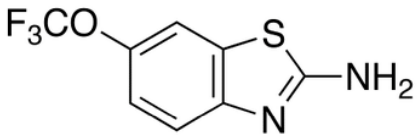
New clinical data sources

Ongoing reform

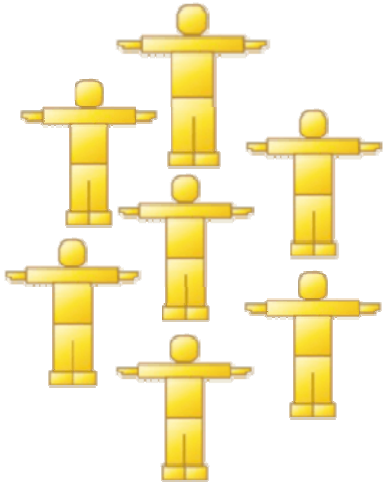

Patient
Value
Clinical
Research
Clinical
Care

Clinical Research

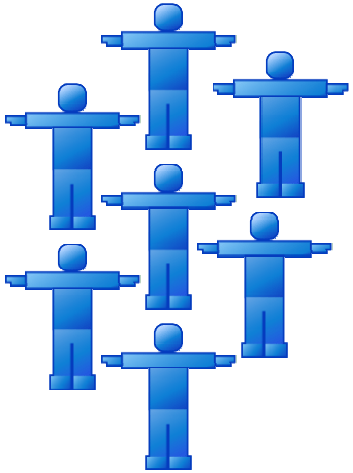




Lithium Carbonate & Riluzole



Treatment



Control

	Start	3m	6m	9m	12m	15m	18m
ALS-FRS							
FVC							
Survival							
Blood Tests							
Etc…							

Lithium delays progression of amyotrophic lateral sclerosis

Francesco Fornai*†‡, Patrizia Longone§, Luisa Cafaro†, Olga Kastsiuchenka*, Michela Ferrucci*, Maria Laura Manca¶, Gloria Lazzeri*, Alida Spalloni§, Natascia Bellio†, Paola Lenzi*, Nicola Modugno†, Gabriele Siciliano¶, Ciro Isidoro†, Luigi Murri¶, Stefano Ruggieri†, and Antonio Paparelli*

*Department of Human Morphology and Applied Biology, and ¶Department of Neuroscience, Clinical Neurology, Universi
†Istituto Neurologico Mediterraneo, Istituto Di Ricovero e Cura a Carattere Scientifico Neuromed, 86077 Pozzilli (IS), Italy;
Santa Lucia Foundation, 00179 Rome, Italy; and †Department of Medical Sciences, University of Novara, 28100 Novara, Ital

Edited by Thomas C. Südhof, University of Texas Southwestern Medical Center, Dallas, TX, and approved December 21, 20
August 24, 2007)

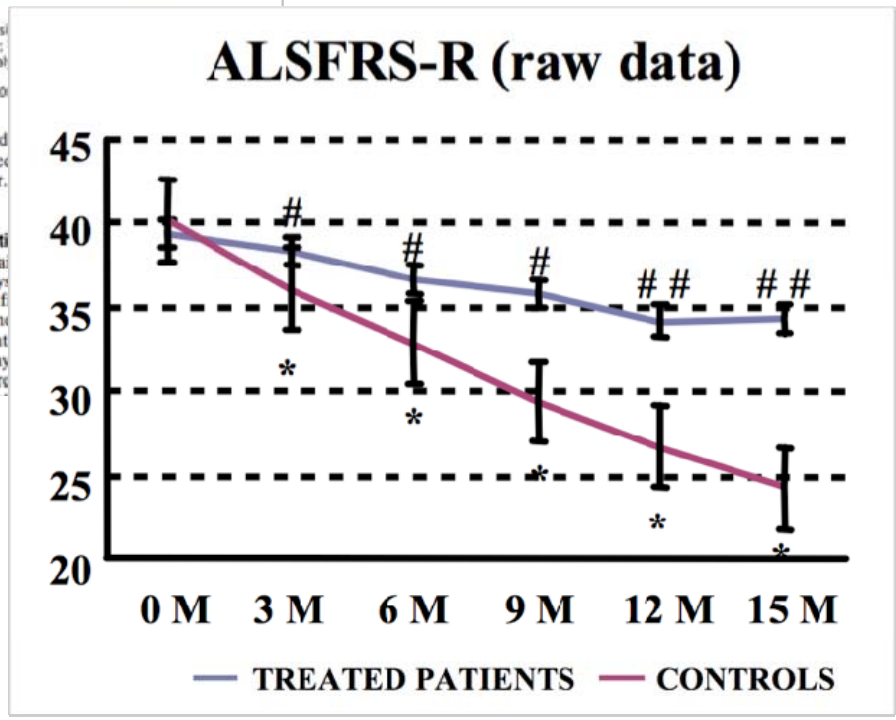
ALS is a devastating neurodegenerative disorder with no effective treatment. In the present study, we found that daily doses of lithium, leading to plasma levels ranging from 0.4 to 0.8 mEq/liter, delay disease progression in human patients affected by ALS. None of the patients treated with lithium died during the 15 months of the follow-up, and disease progression was markedly attenuated when compared with age-, disease duration-, and sex-matched control patients treated with riluzole for the same amount of time. In a parallel study on a genetic ALS animal model, the G93A mouse, we found a marked neuroprotection by lithium, which delayed disease onset and duration and augmented the life span. These effects were concomitant with activation of autophagy and an increase in the number of the mitochondria in motor neurons and

G93A ALS mouse model. Based
obtained in mice we quickly move
now at the end of its second year.

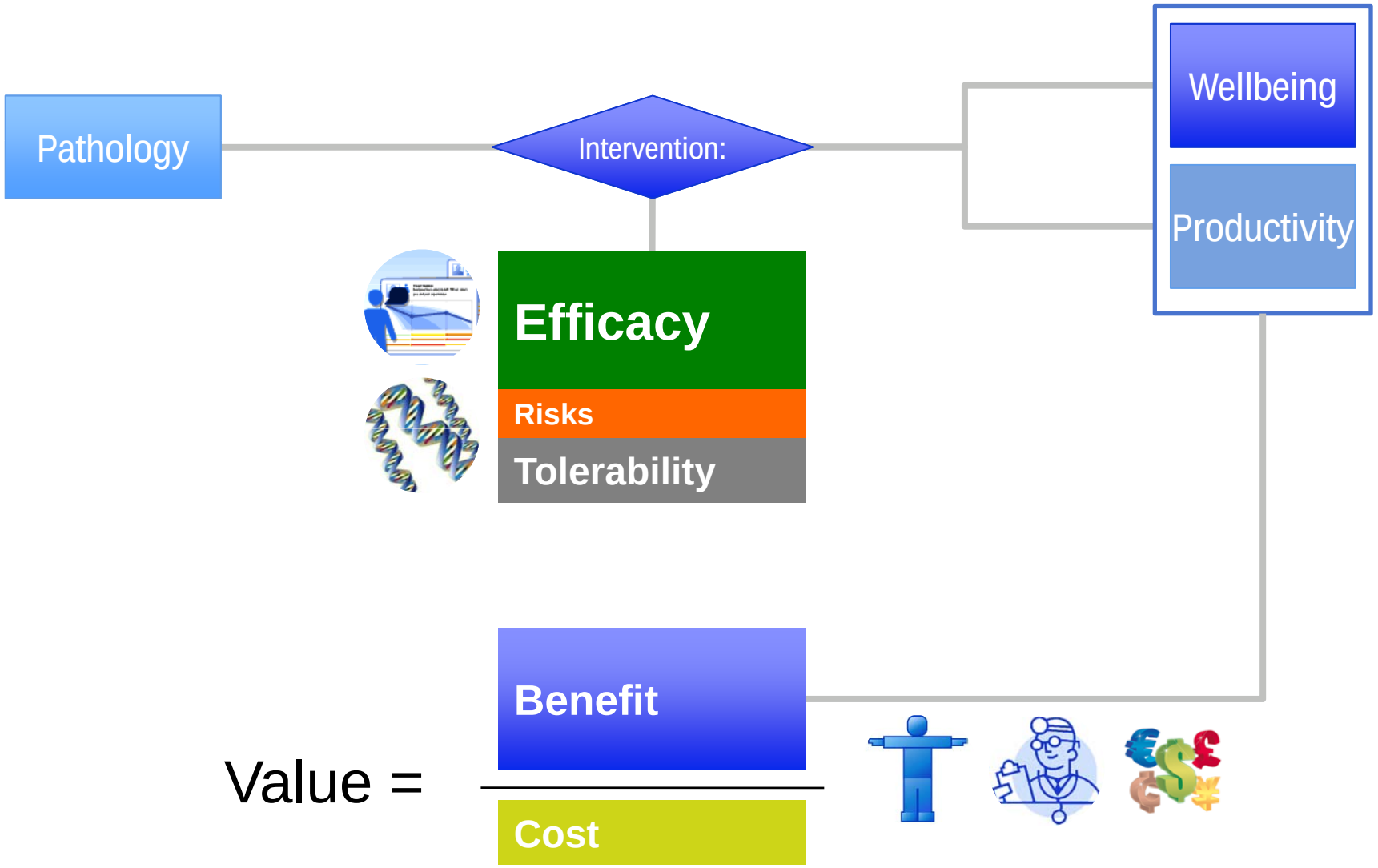
Results

Effects of Lithium on Disease Durati

G93A male mice were treated da
mEq/kg, i.p.), starting at 75 day
prolonged the mean survival time f
to 148 ± 4.3 (n = 20, ~36% of th
1a; $P < 0.001$) and, most important
(from a mean of 9 days to >38 day
compared with the G93A mice tr



Clinical Research Claim

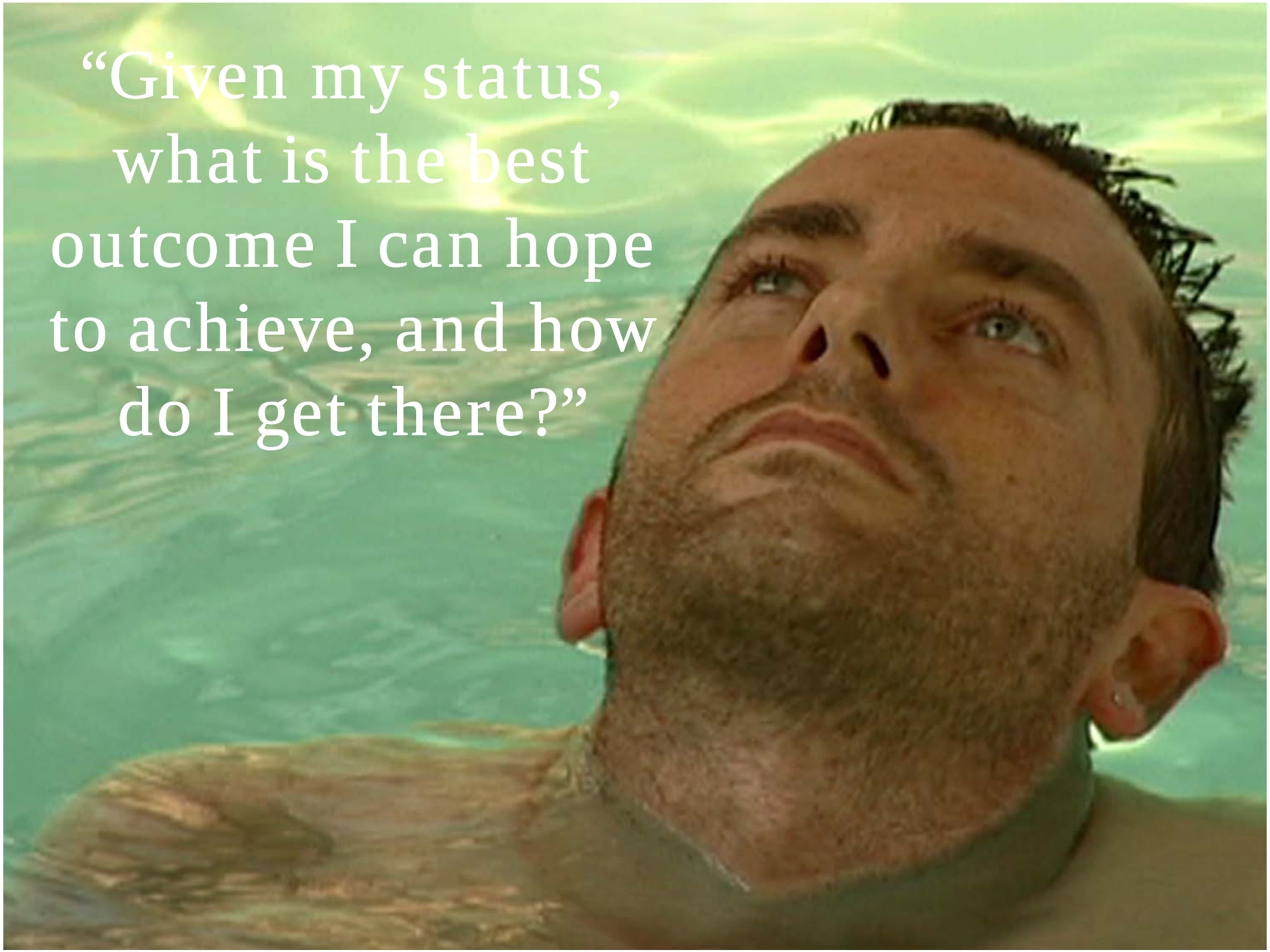


Clinical Care

Date: 2/28/2008
Patient has ALS with loss of function in arms and foot drop, FVC is 80%

Med list: riluzole (100mg), baclofen (as needed)

Chief complaint: insomnia, excess saliva
– prescribed ambien, detrol


“Given my status, what is the best outcome I can hope to achieve, and how do I get there?”

alsking101

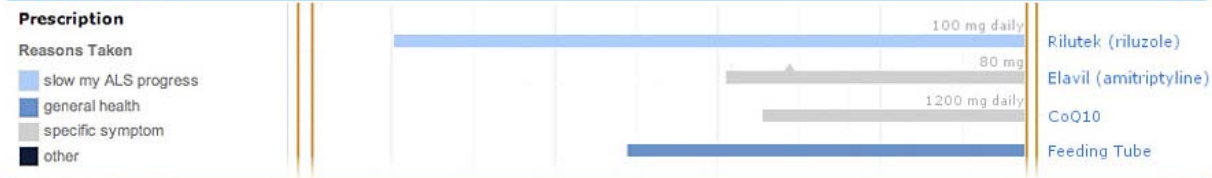
Male, 38 years
Newton, MA

Diagnosis Summary
Onset: Arms
First symptom: Nov 1997
Diagnosis: Jan 1998
Deceased date: Nov 26, 2006

Updates
Last updated: Oct 15, 2006

ALS Condition

Treatments



Symptoms

"The real voyage of discovery consists not in seeking new landscapes, but in having new eyes"

Marcel Proust

patientslikeme®

Username or Email | Password | Login

Remember me | Forgot password? | Secure login

everon
shared a treatment

115,496 patients
500+ conditions

Who's like you?

Share your experience.

The more you share, the easier it will be to find patients like you. Start by adding a condition, symptom or treatment.

I have

Type at least 3 letters of a condition

I take

Type at least 3 letters of a treatment

You have questions about your disease — but you also have answers for others. Change your life while helping others change theirs.

By learning from **other patients like you...**

- In **Forum Discussions**
- Through **Private Messages**
- From **Profile Comments**

and seeing the **community experience...**

- Browse **Symptom Reports**
- Explore **Treatment Reports**
- Check out **Treatment Evaluations**

YOU can take control of your disease.

- **Profile charts** let you see how your treatments affect your health over time
- **Doctor Visit Sheets** help you improve your discussions with your doctors

Search this site | Search

- **Find Patients Like You**
- **Explore our Treatment Reports**
- **Learn about Symptoms**
- **Review our Research**
- **Check for your Conditions**

Patient Testimonials

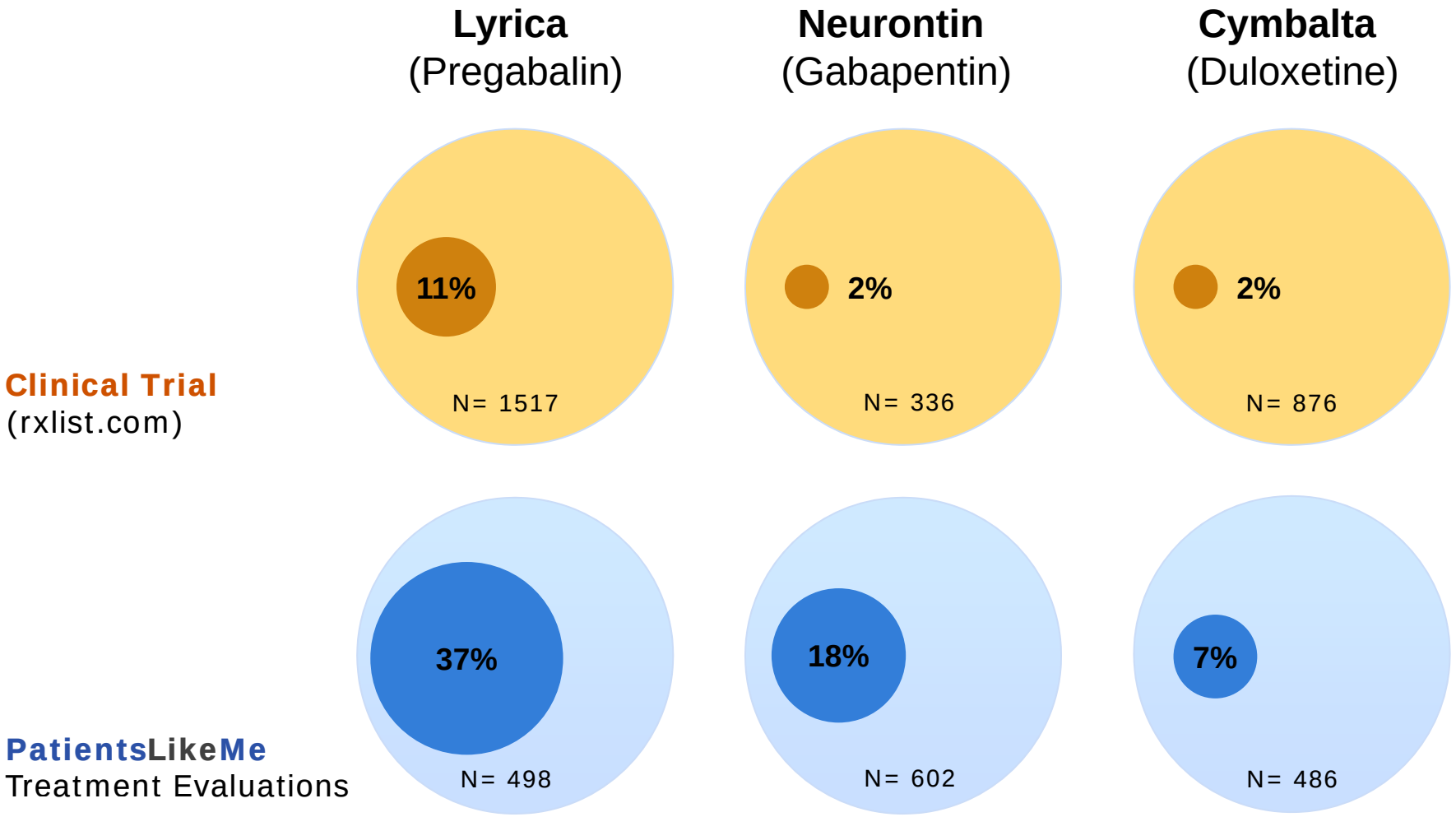
" The patient profiles are my favorite. You can learn what does and does not work for other people. "

—PatientsLikeMe member

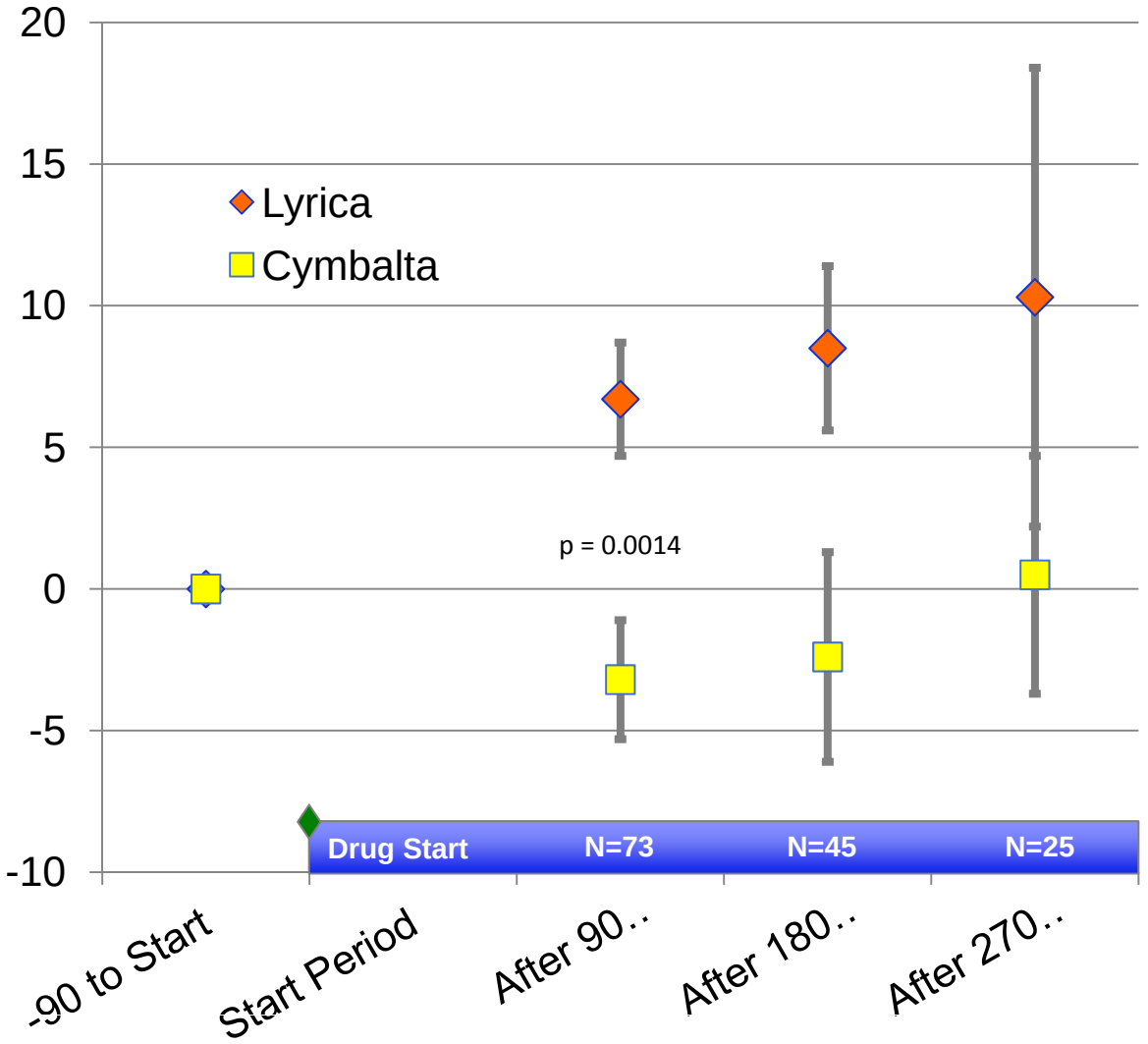
About PatientsLikeMe

- Read about the company
- How we make money
- Be part of our team
- Contact Us

Weight Gain Side Effect (Comparing Across Drugs)



Observed Coincident Weight Change
(lots of caveats)



Step 1:
Create/update and share your health profile

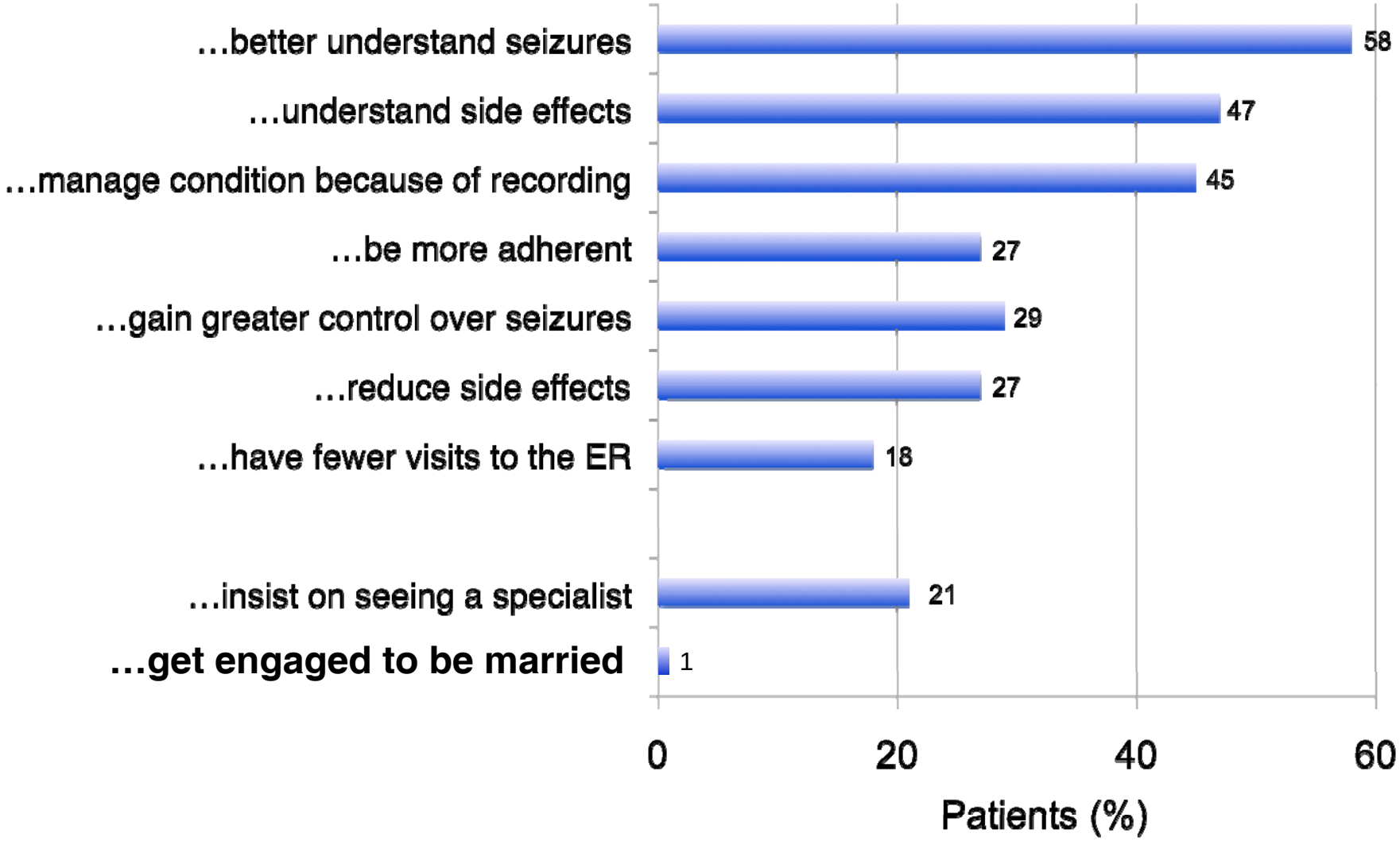
Step 2:
Find support from others like you and compare experiences

Step 3:
Learn from aggregated community Treatment and Symptom Reports

Step 4:
Take profile to your doctor to have an improved treatment conversation

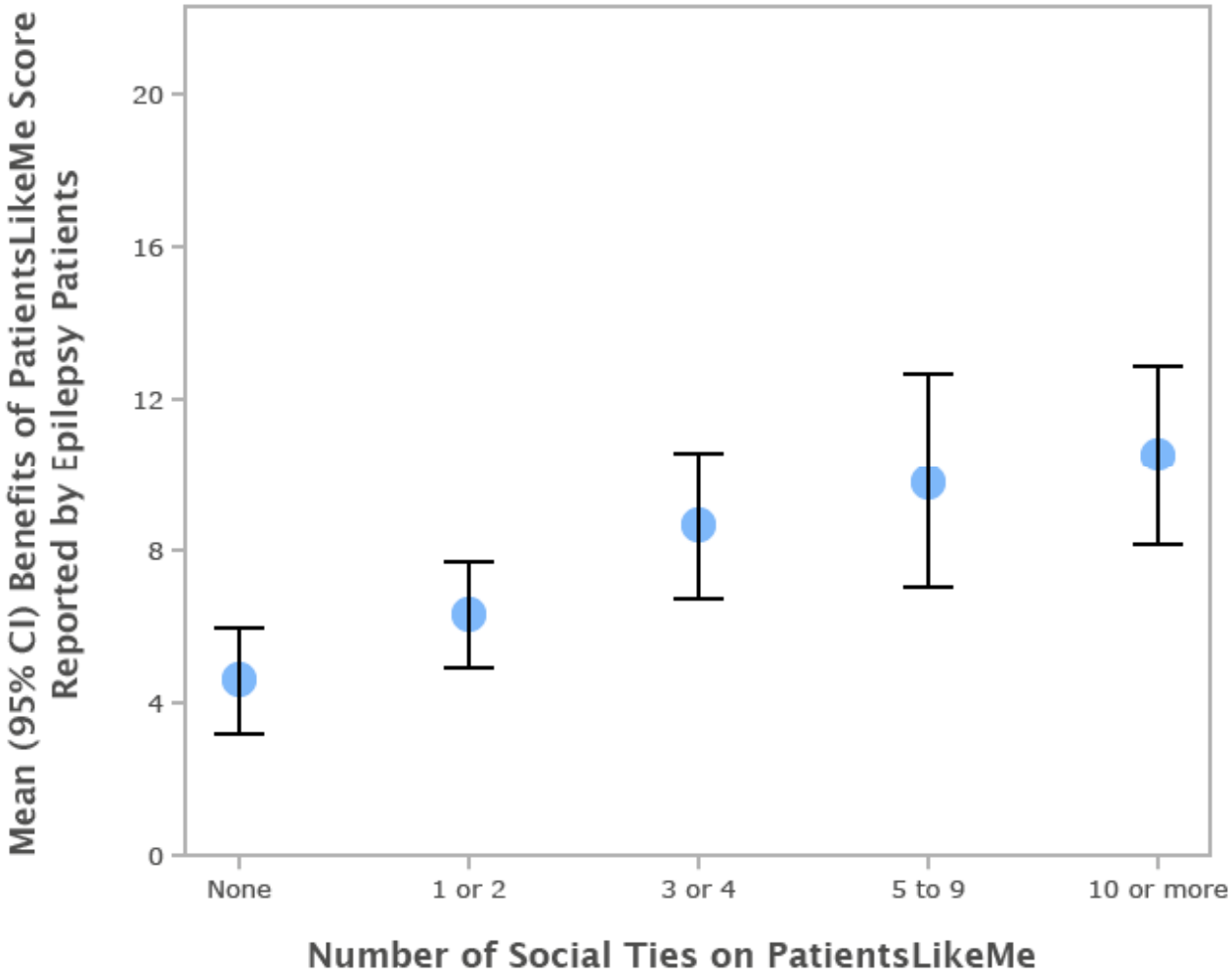
Step 5:
Play an integral part in your own health care

Users reported that PatientsLikeMe helped them…



PLM, data on file

Social ‘Dose response’ curve



($p<0.001$) for differences between “none” and all other categories

Wicks P, et al. Submitted

"The real voyage of discovery consists not in seeking new landscapes, but in having new eyes"

Marcel Proust

Lithium delays progression of amyotrophic lateral sclerosis

Francesco Fornai*†‡, Patrizia Longone§, Luisa Cafaro†, Olga Kastsiuchenka*, Michela Ferrucci*, Maria Laura Manca¶, Gloria Lazzeri*, Alida Spalloni§, Natascia Bellio†, Paola Lenzi*, Nicola Modugno†, Gabriele Siciliano¶, Ciro Isidoro†, Luigi Murri¶, Stefano Ruggieri†, and Antonio Paparelli*

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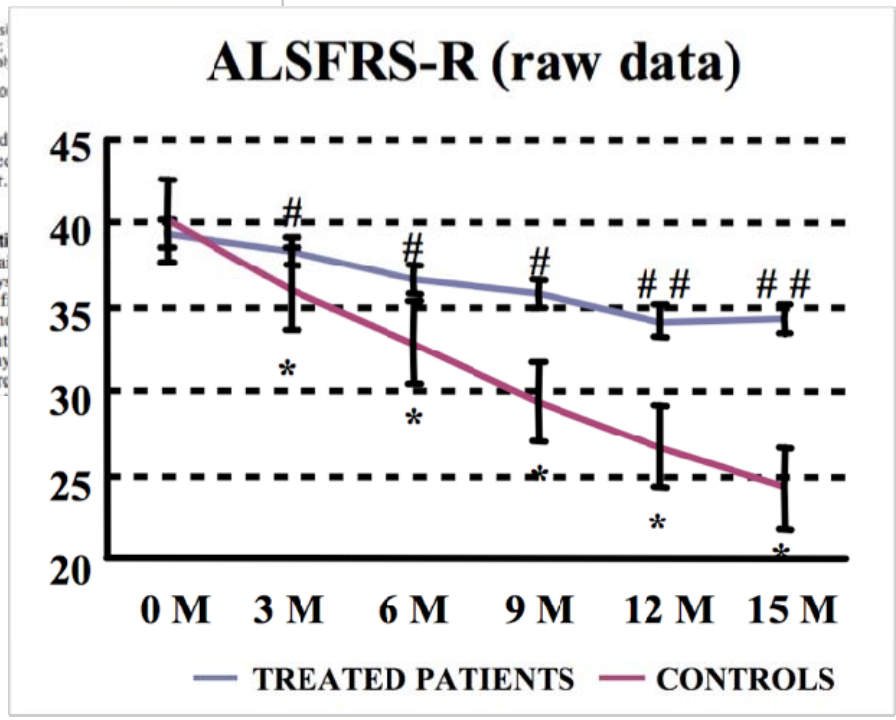
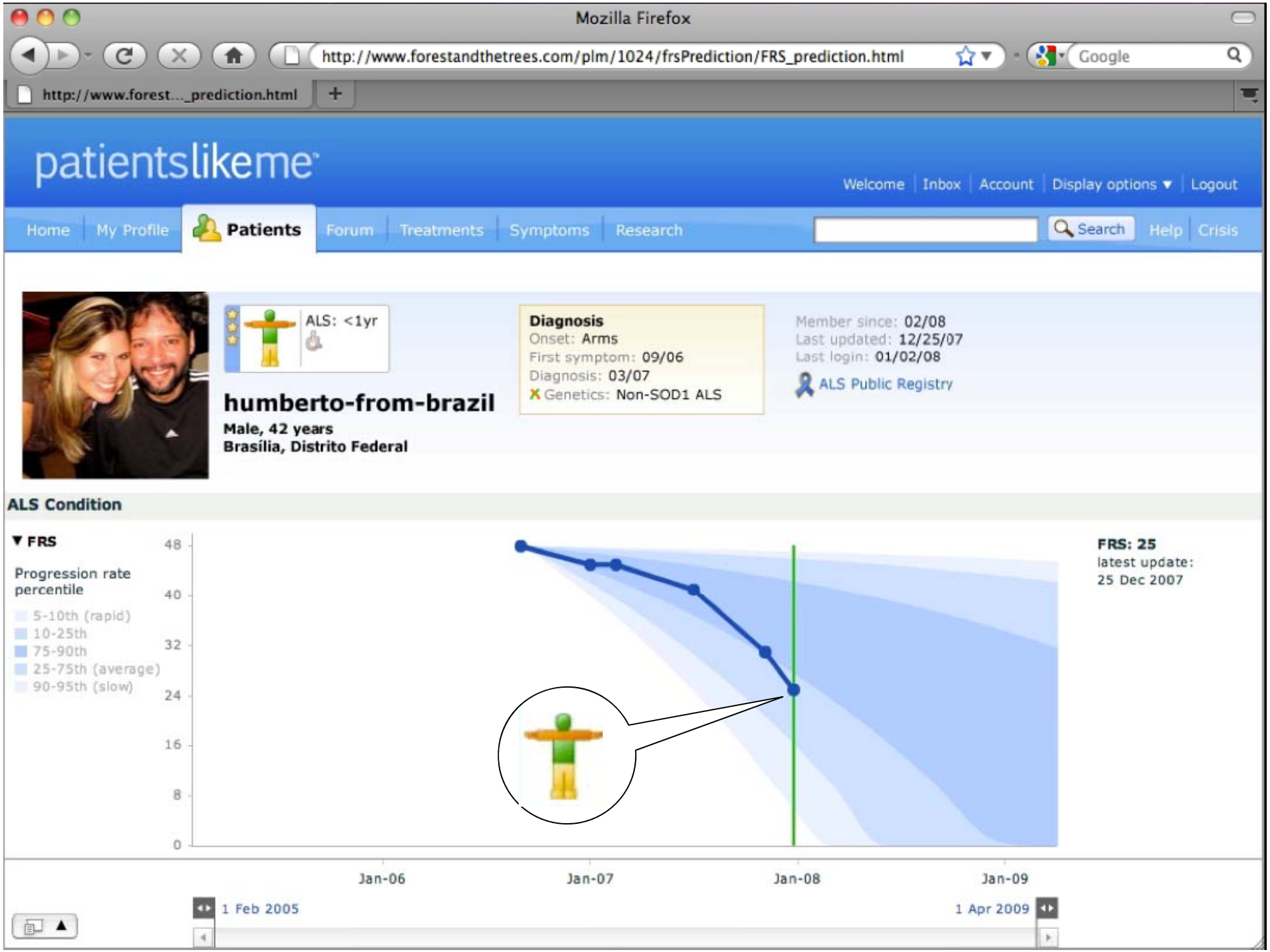


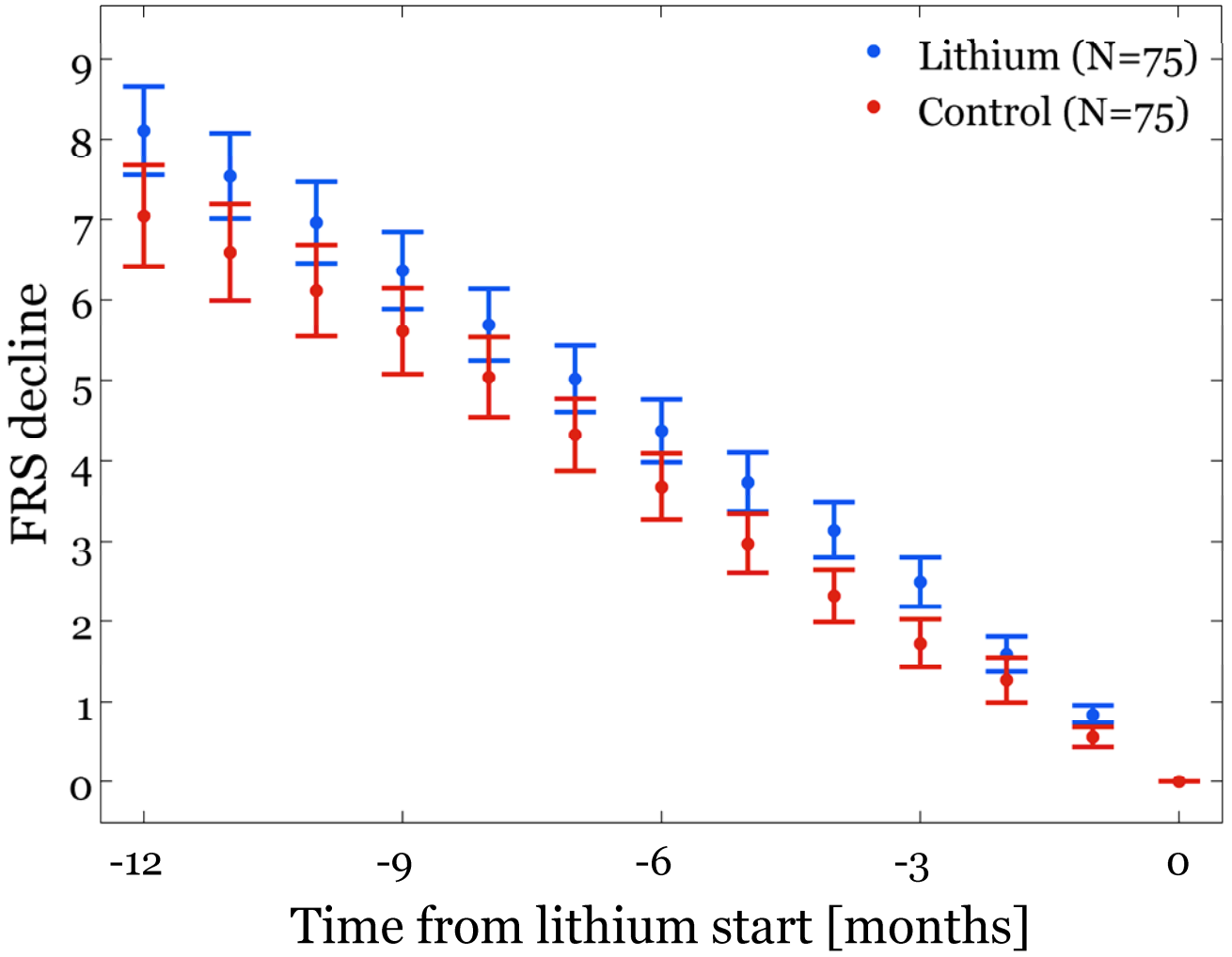

Mozilla Firefox
http://www.forestandthetrees.com/plm/1024/frsPrediction/FRS_prediction.html
Google
http://www.forest..._prediction.html
patientslikeme
Welcome | Inbox | Account | Display options ▼ | Logout
Home | My Profile | Patients | Forum | Treatments | Symptoms | Research
Search | Help | Crisis
ALS: <1yr
humberto-from-brazil
Male, 42 years
Brasília, Distrito Federal
Diagnosis
Onset: Arms
First symptom: 09/06
Diagnosis: 03/07
Genetics: Non-SOD1 ALS
Member since: 02/08
Last updated: 12/25/07
Last login: 01/02/08
ALS Public Registry
ALS Condition
▼ FRS
Progression rate percentile
5-10th (rapid)
10-25th
75-90th
25-75th (average)
90-95th (slow)
48
40
32
24
16
8
0
FRS: 25
latest update:
25 Dec 2007
Jan-06
Jan-07
Jan-08
Jan-09
1 Feb 2005
1 Apr 2009

"All models are wrong,
but some are useful."

George Edward Pelham Box

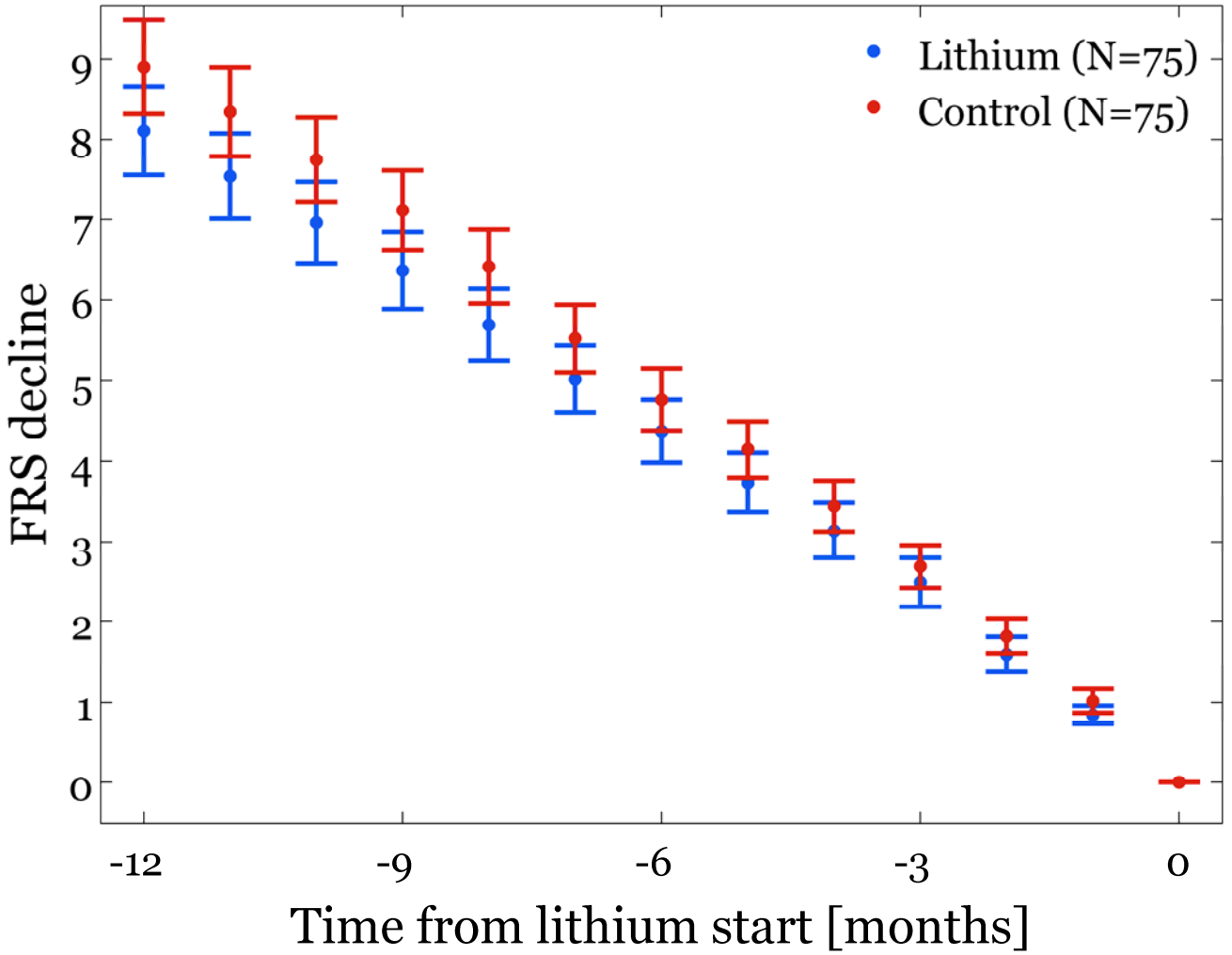
Random Control Matching

Mean decline in FRS over time

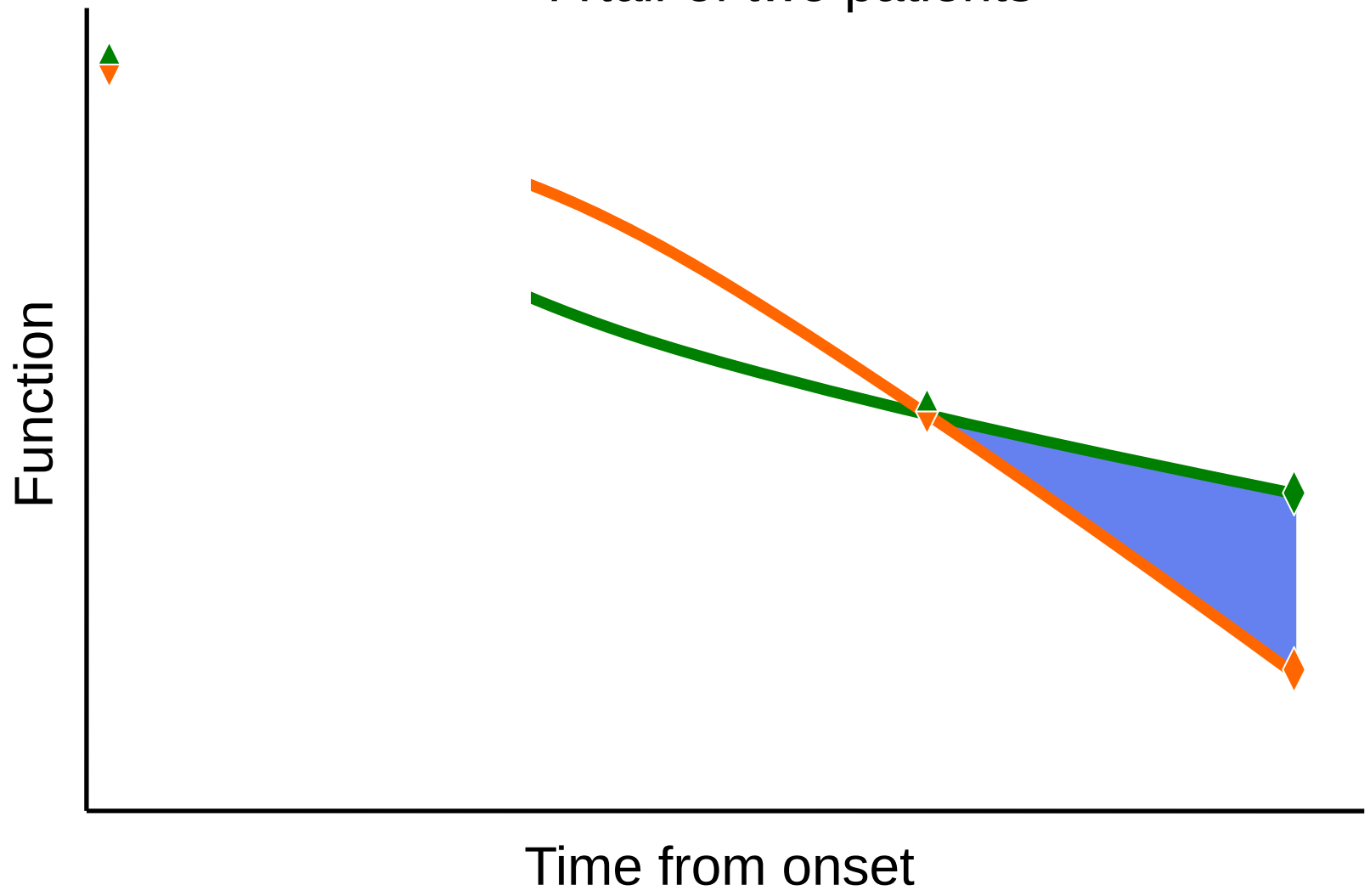


Disease Duration & Disability Matching

Mean decline in FRS over time



A *tail* of two patients



Mozilla Firefox

http://www.forestandthetrees.com/plm/1024/frsPrediction/FRS_prediction.html

http://www.forest..._prediction.html

patientslikeme

Welcome | Inbox | Account | Display options ▼ | Logout

Home | My Profile | Patients | Forum | Treatments | Symptoms | Research | Search | Help | Crisis

ALS: <1yr

humberto-from-brazil

Male, 42 years
Brasília, Distrito Federal

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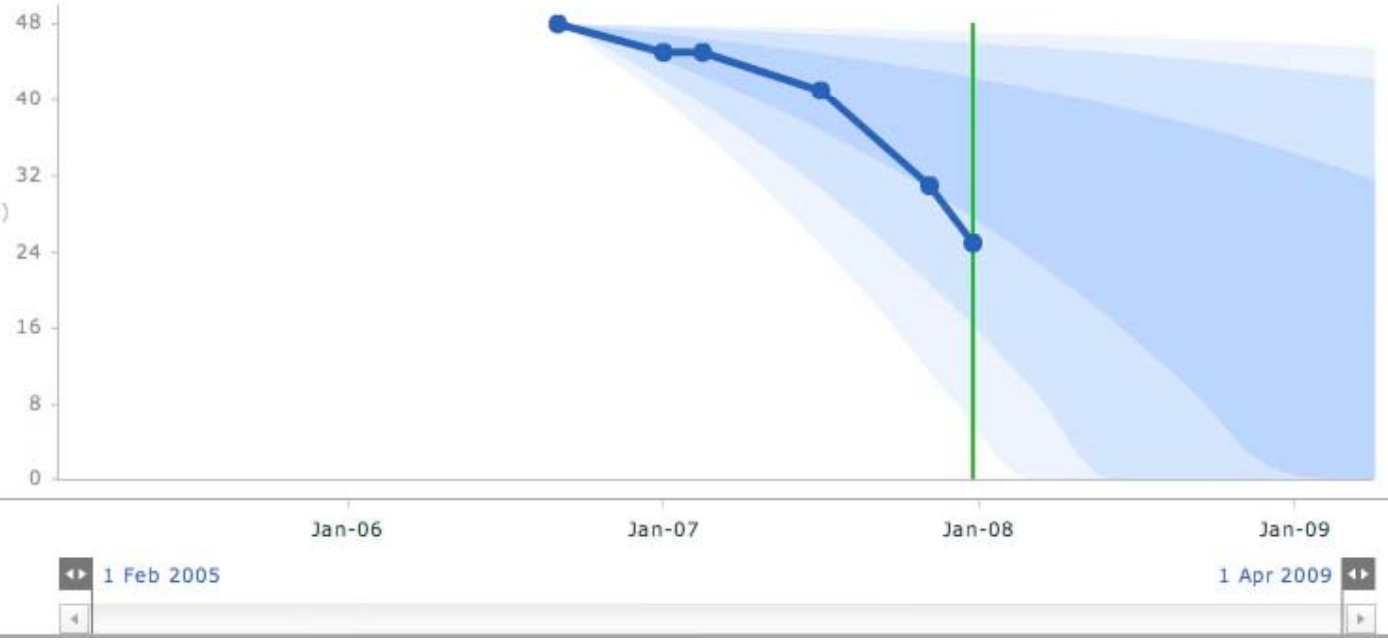
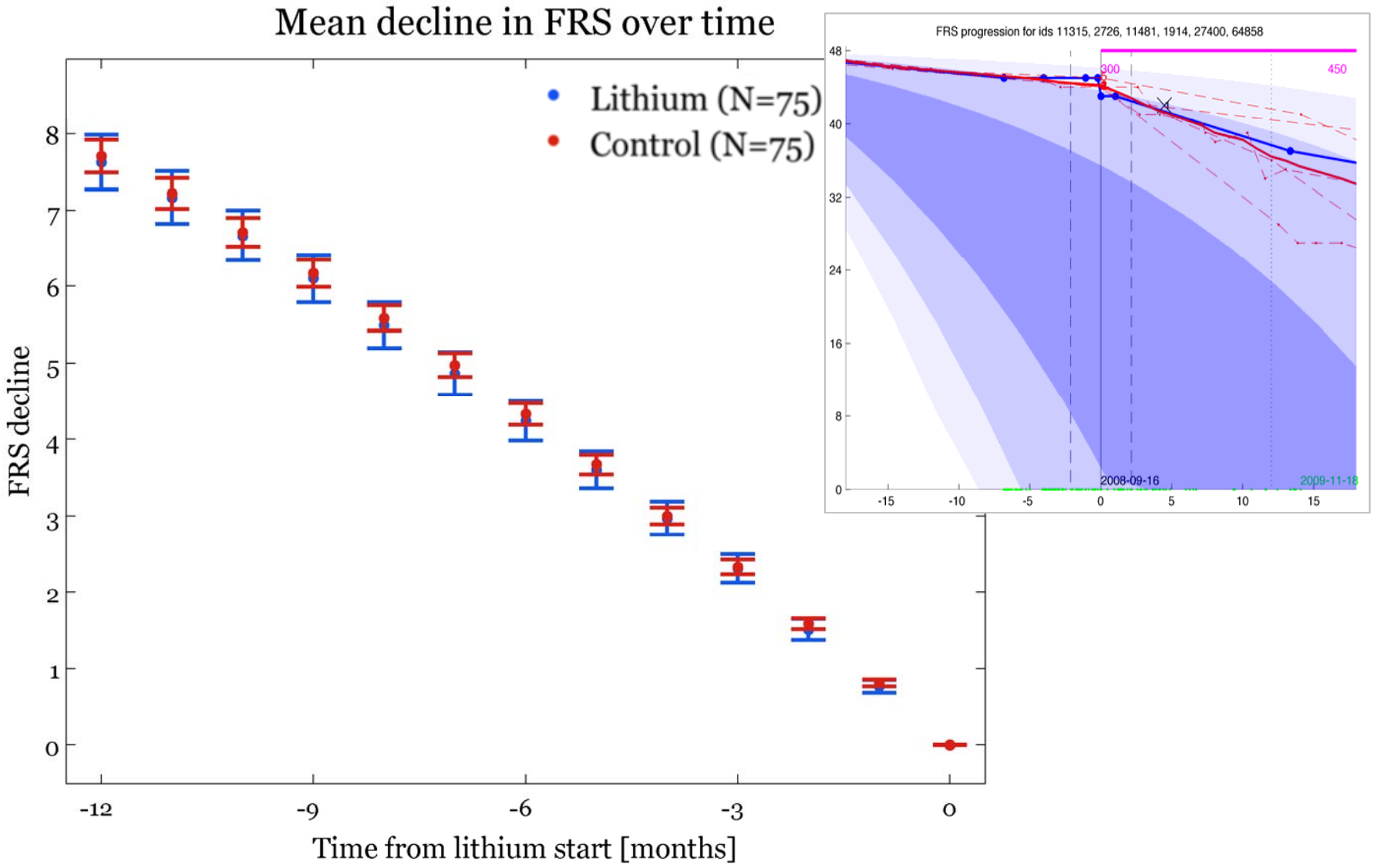
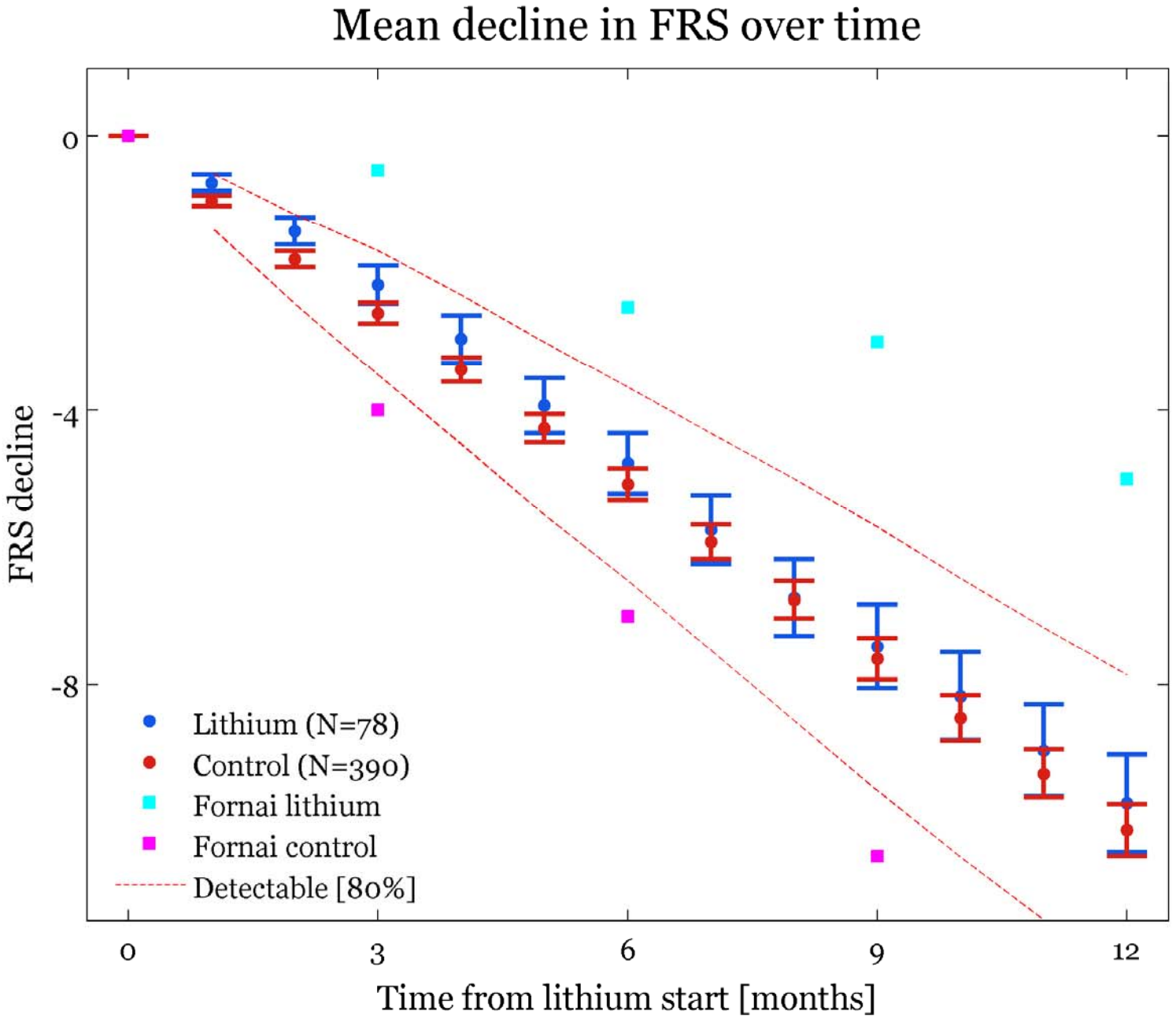


FRS: 25
latest update:
25 Dec 2007

Algorithmic matching




Mean decline in FRS over time
FRS decline
0
-4
-8
0
3
6
9
12
Time from lithium start [months]
Lithium (N=78)
Control (N=390)
Fornai lithium
Fornai control
Detectable [80%]

Articles

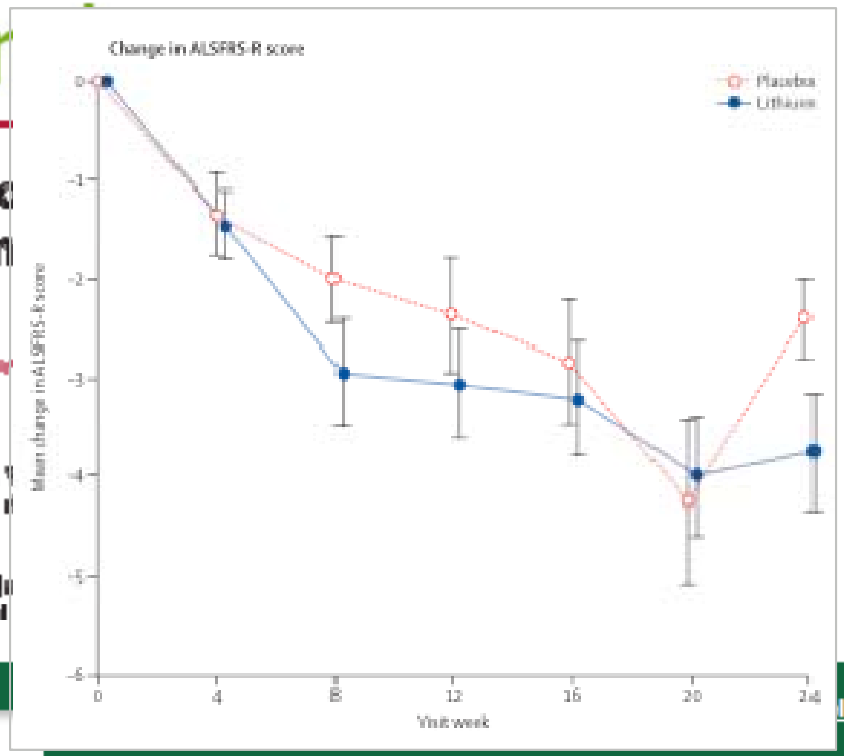
THE LANCET Neur

Safety and efficacy of lithium in combination with riluzo for treatment of amyotrophic lateral sclerosis: a random double-blind, placebo-controlled trial

Summary

Background In a pilot study, lithium treatment slowed progression of amyotrophic lateral sclerosis (ALS). [illegible] to reassess or disprove these findings by assessing the safety and efficacy of lithium in combination with [illegible] patients with ALS.

Methods We did a double-blind, placebo-controlled trial with a time-to-event design. Between January and [illegible] patients with ALS who were taking a stable dose of riluzole for at least 30 days were randomly assigned



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Published online before print August 11, 2010, doi:10.1212/WNL.0b013e3181ed9e7c)

NEUROLOGY 2010;75:619-625

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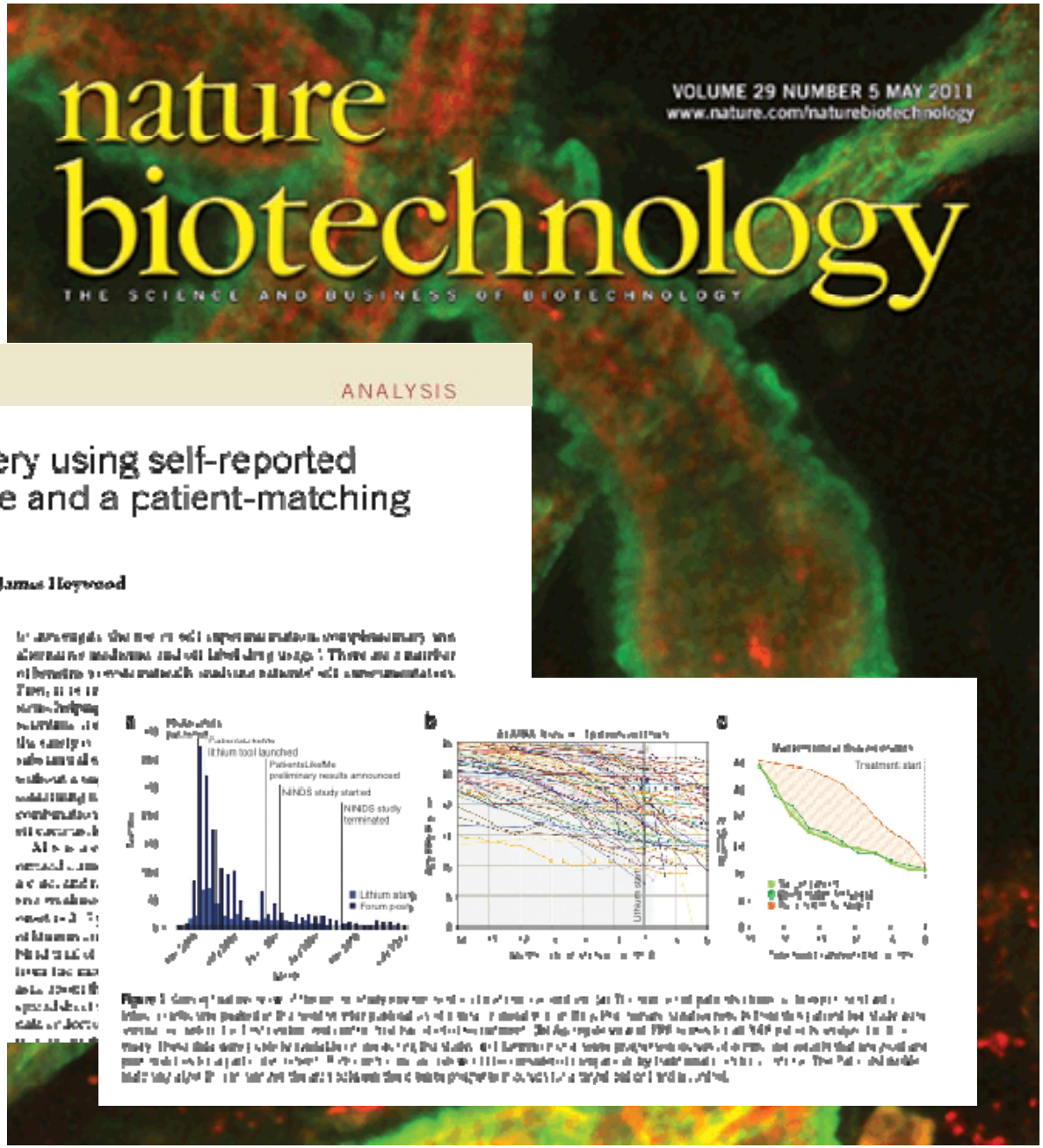
Lithium carbonate in amyotrophic lateral sclerosis

Lack of efficacy in a dose-finding trial

This Article

- Figures Only
- Full Text
- Full Text (PDF)
- Data Supplement
- All Versions of this Article: WNL.0b013e3181ed9e7cv1



computational BIOLOGY

ANALYSIS

Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm

Paul Wicks, Timothy E Vaughan, Michael P Massagli & James Heywood

Patients with serious diseases may experiment with drugs that have not received regulatory approval. Online patient communities structured around quantitative outcome data have the potential to provide an observational environment to monitor such drug usage and its consequences. Here we describe an analysis of data reported on the website PatientsLikeMe by patients with amyotrophic lateral sclerosis (ALS) who experimented with lithium carbonate treatment. To reduce potential bias owing to lack of randomization, we developed an algorithm to match 149 treated patients to multiple controls (149 trials) based on the progression of their disease course. At 12 months after treatment, we found no effect of lithium on disease progression. Although observational studies using undirected data are not a substitute for double-blind randomized control trials, this study reached the same conclusion as subsequent randomized trials, suggesting that data reported by patients over the internet may be useful for accelerating clinical discovery and evaluating the effectiveness of drugs already in use.

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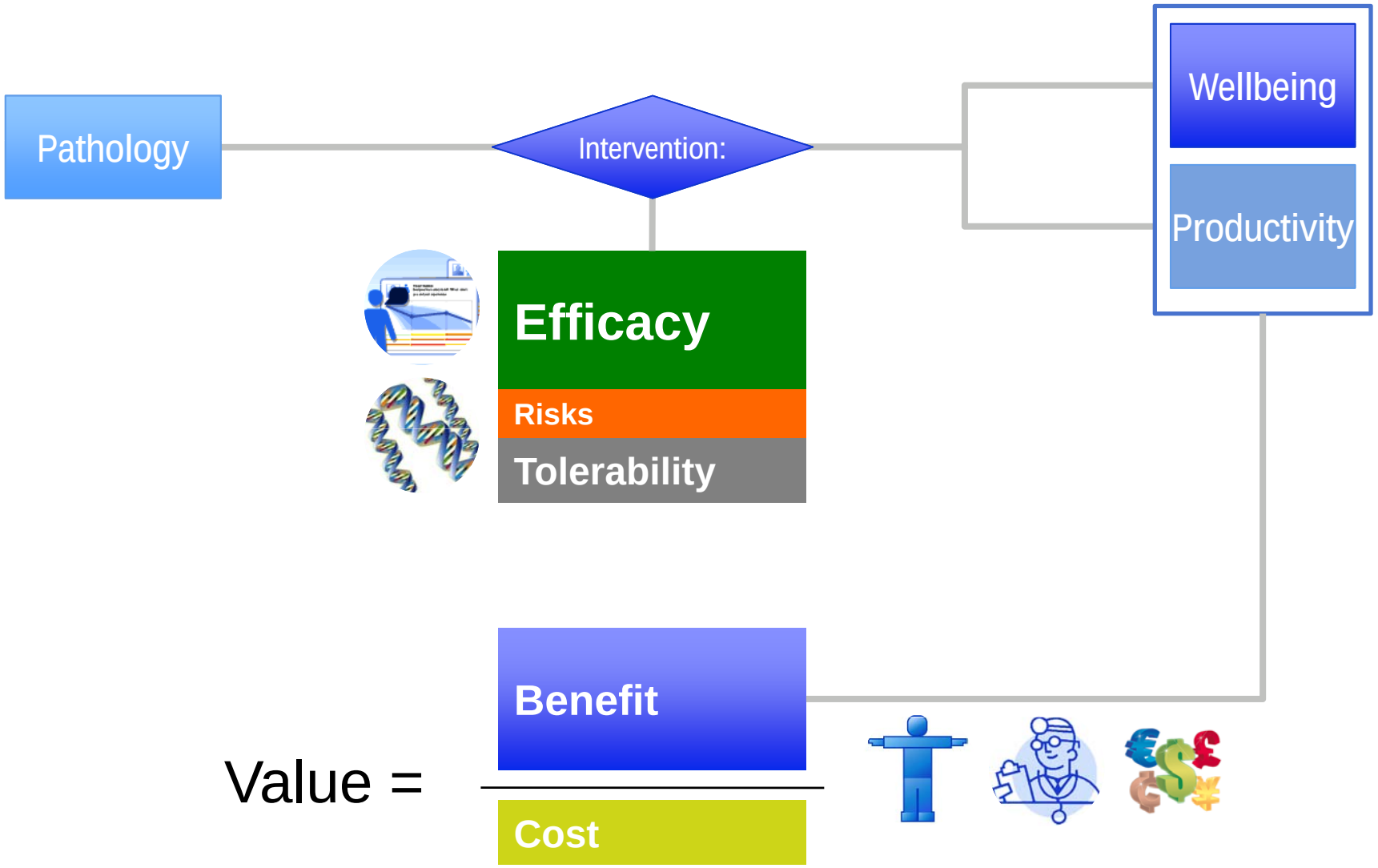
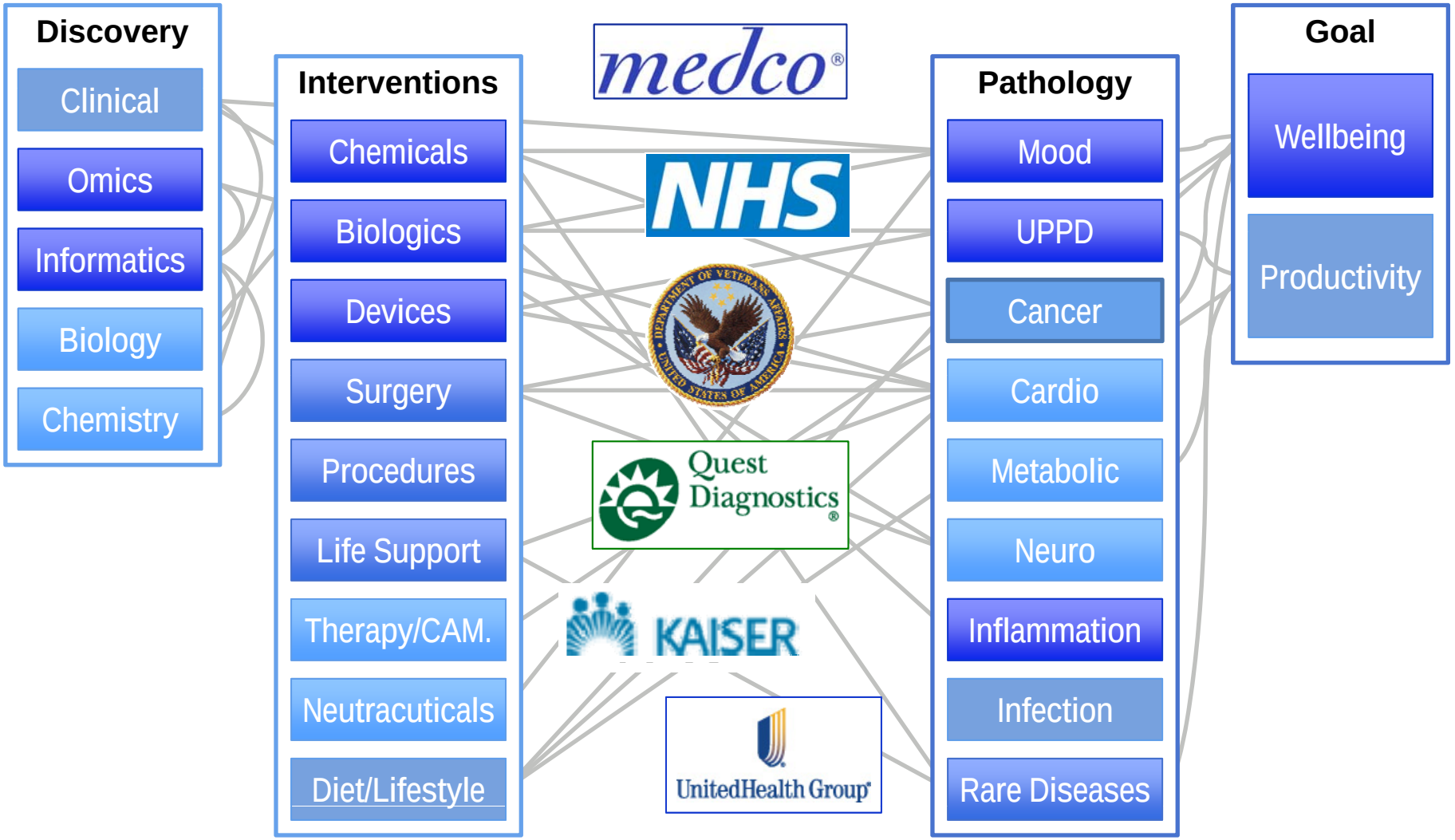
Clinical Research Claim



Personalized Medicine Network



Improvements are needed:

Truth Standards: Meaningful, computable, measurable, symtomplogy, pathology, molecular, and functional impact of disease

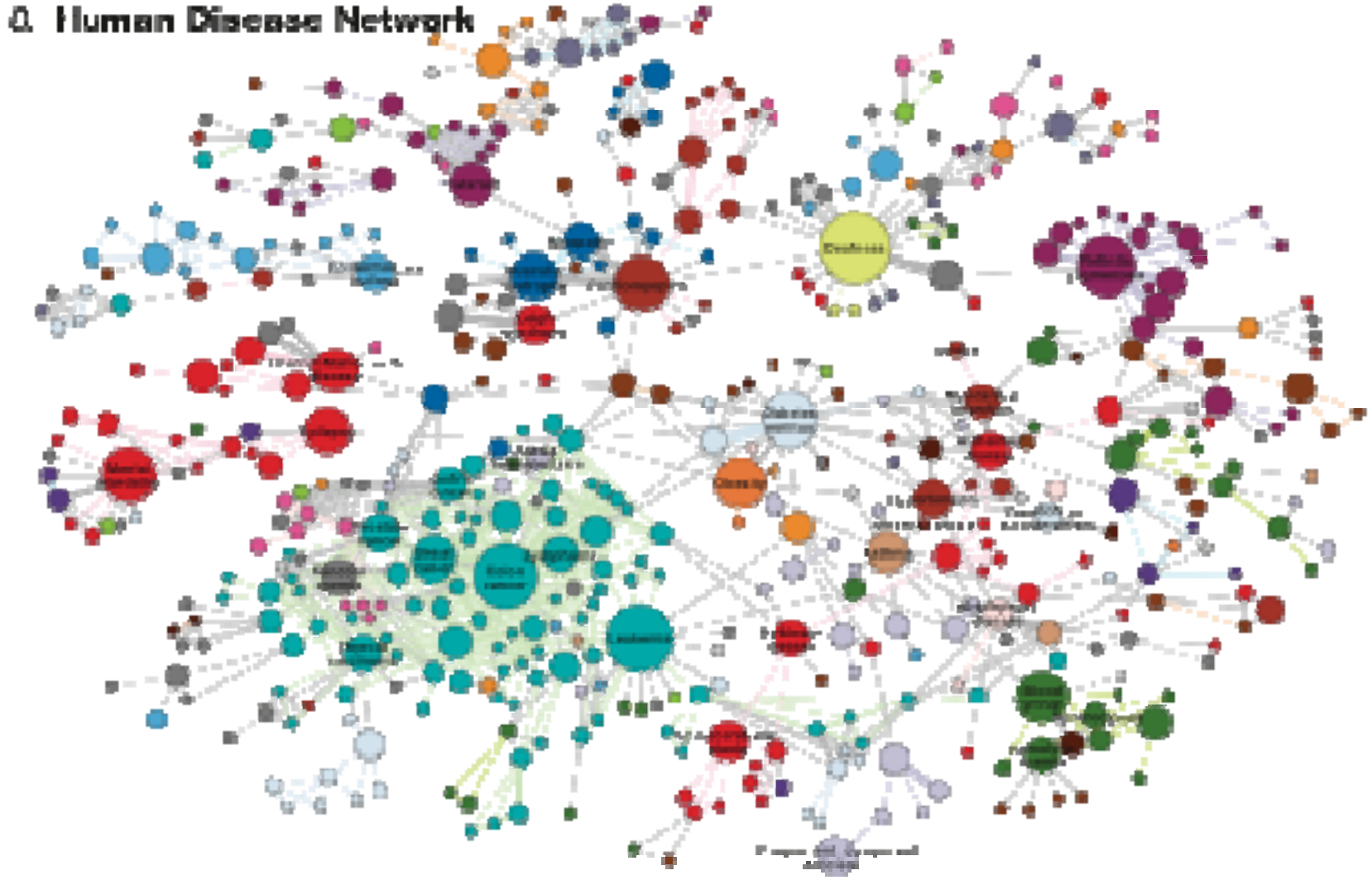
Host Health: Improved understanding of the dynamics and range of normal human health

Incidentalome: Respect for and understanding the variations of normal that confound with disease

Vector Measurement: A shift from static/diagnostic health concepts to longitudinal vectors with origins and magnitudes

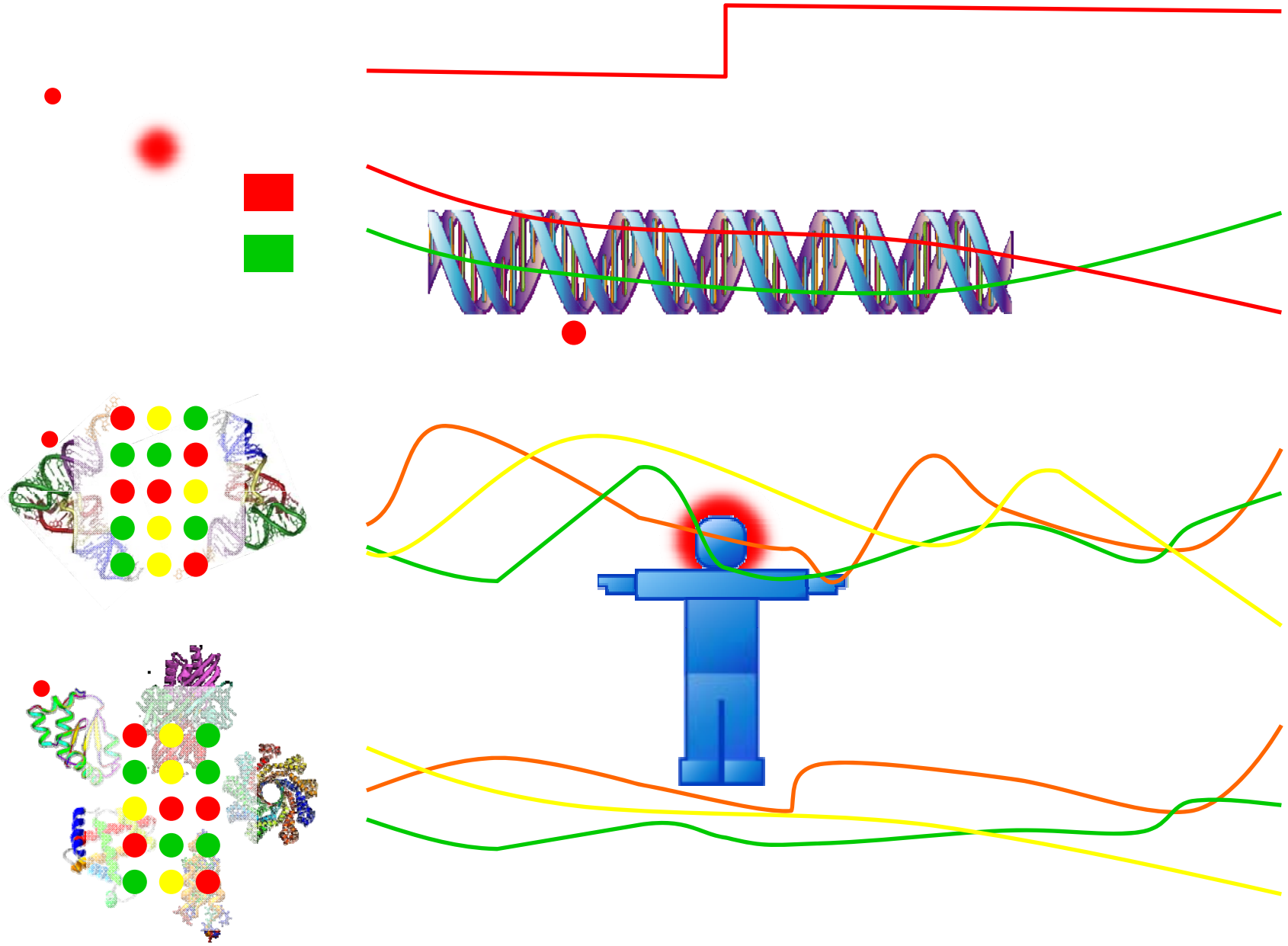
The human disease network

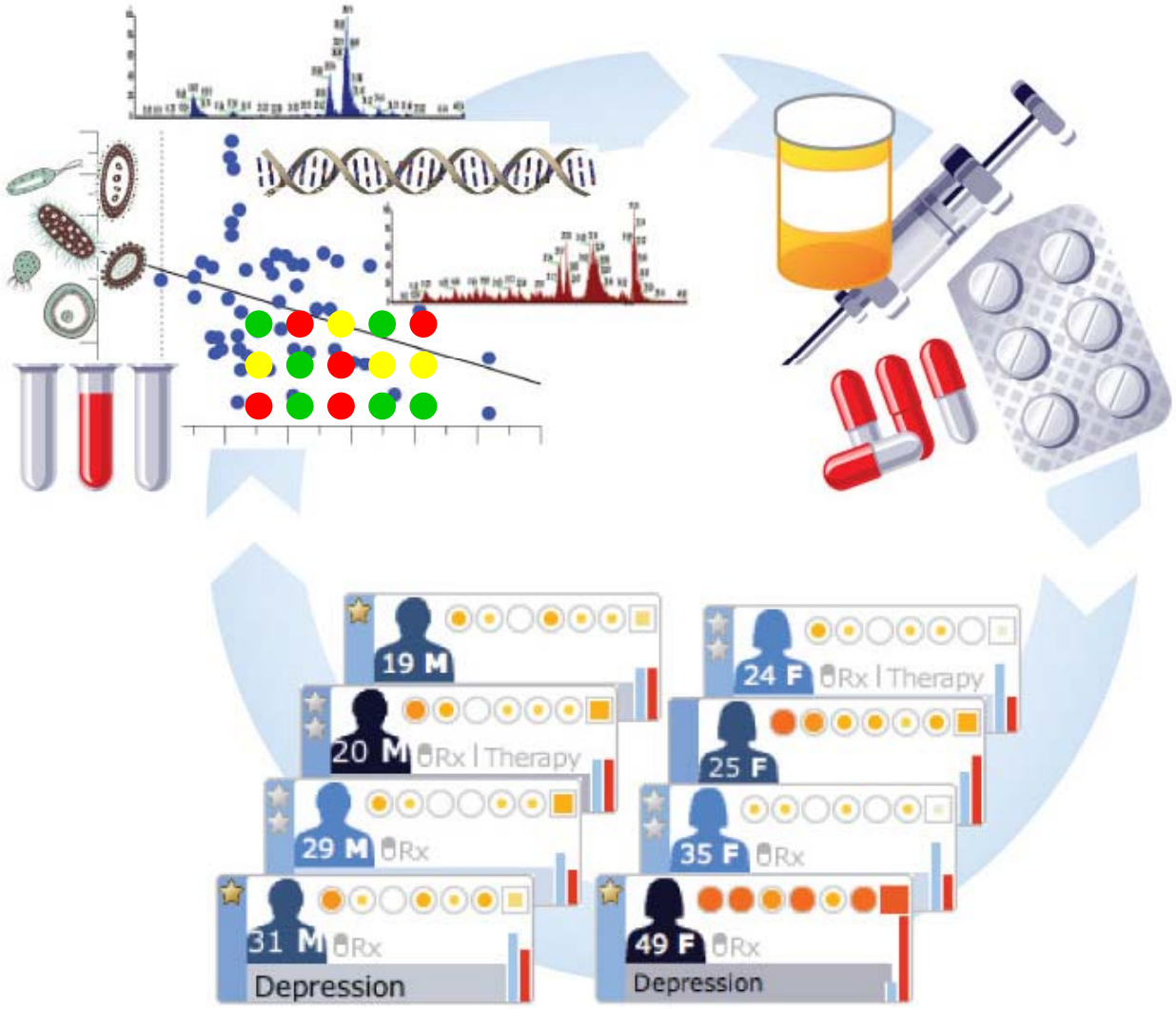
Kwang-Il Goh[†‡§], Michael E. Cusick[†‡§], David Valle, Barton Childs, Marc Vidal[¶‖], and Albert-László Barabási[†‡**]

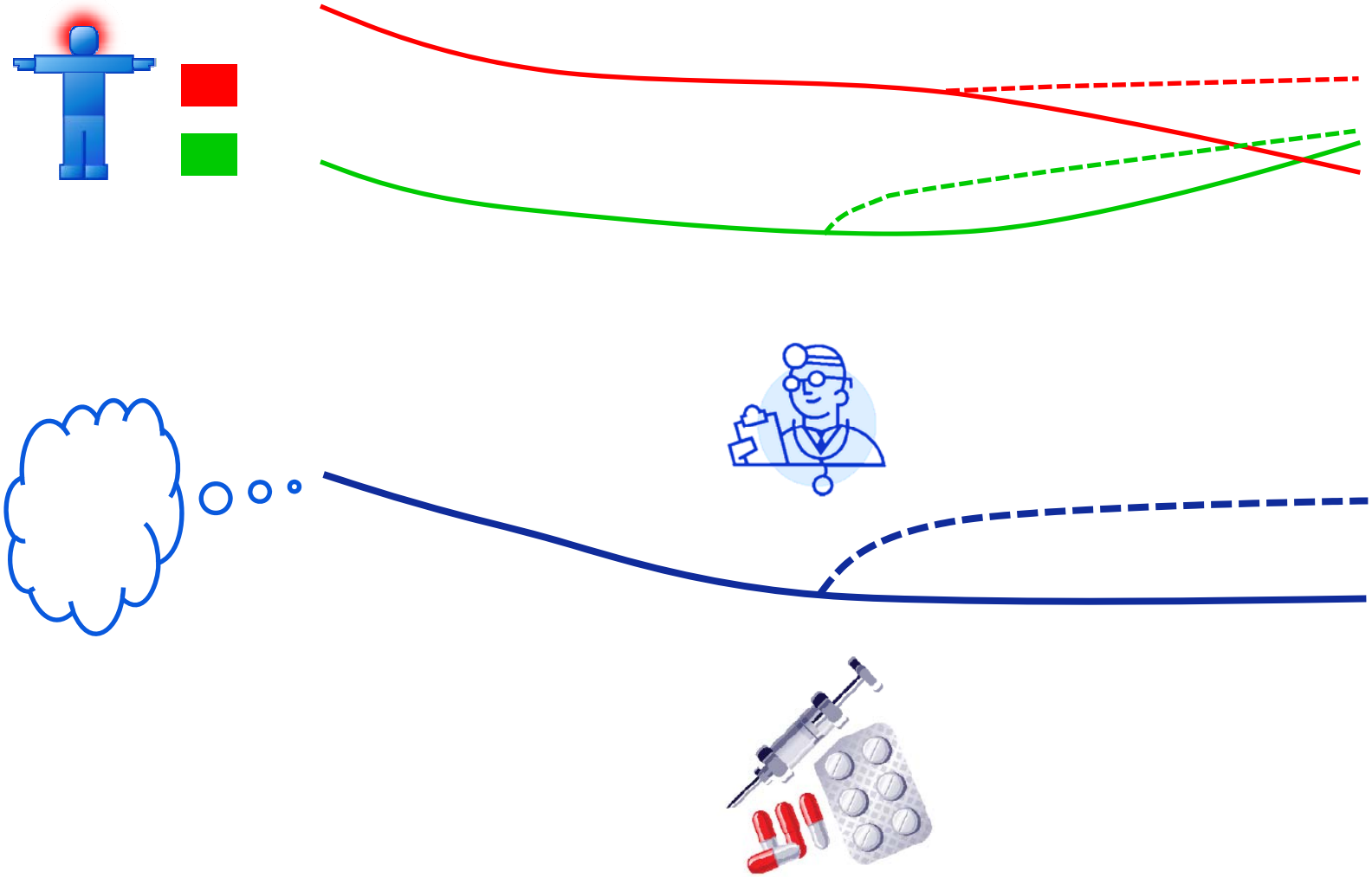


"All models are wrong, and increasingly you can succeed without them"

Peter Norvig

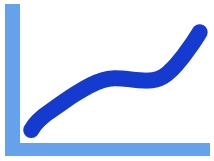



19 M
20 M Rx | Therapy
29 M Rx
31 M Rx
Depression
24 F Rx | Therapy
25 F
35 F Rx
49 F Rx
Depression



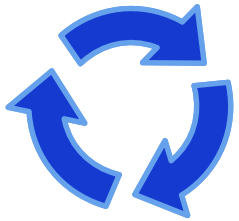
Conclusions:

Each clinical encounter is a unique experiment that currently is not recorded and does not meaningfully advance our understanding of disease



Improvements are needed in the truth standard of disease, its measurement, and the understanding of the dynamics of human heath over time

Understanding the multiplicity and complexity of pathology, symptomatology, and molecular state in the context of the individual will require immense longitudinal datasets



An effective learning health systems requires the integration of clinical discovery information platforms with clinical care

The best way to predict
the future is to create it.

Peter Drucker