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## **Precision Medicine: Separating Hype from Reality**

Session 98, March 7, 2017

John Halamka, MD, CIO, Beth Israel Deaconess Medical Center;  
Paul Cerrato, Contributing Writer, Medscape, Medpage Today

# Conflict of Interest

John Halamka, MD

Has no real or apparent conflicts of interest to report.

Paul Cerrato, MA

Royalty: From Elsevier for *Realizing the Promise of Precision Medicine*

# Agenda

- 4 major obstacles/criticisms for precision medicine
- Defining and contrasting population-based and precision/personalized Medicine
- The value of data analytics in personalizing patient care
- Progress on the road to universal interoperability
- Precision Medicine's benefits in 2018 and beyond
- A patient's story illustrates the value of personalized medicine

# Learning Objectives

- Identify obstacles that impede the implementation of precision medicine in clinical practice
- Contrast population-based medicine to precision medicine
- Summarize the state of the art in interoperability as it pertains to personalized medicine
- Demonstrate the real world benefits of precision medicine in today's healthcare setting

## Precision Medicine: Separating Hype from Reality

# Evidence-Based Optimism

## Precision Medicine: Separating Hype from Reality

An oxymoron? A contradiction in terms?  
Many thought leaders say so!

“We need Mr Spock-like logic, complete objectivity, Total reliance on experimental data”

“No place for optimism or pessimism when studying precision/personalized medicine.”

No such thing as absolute objectivity in real world!

## Precision Medicine: Separating Hype from Reality

- 1 year research project justifies evidence-based optimism
- Results: [Realizing the Promise of Precision Medicine](#) (Elsevier/Academic Press)
- Our conclusion: precision/personalized medicine is the future of healthcare
- Quest for impartiality required hard look at precision medicine's obstacles and its skeptics

## Precision Medicine: Separating Hype from Reality

“The stories of extraordinary outcomes from a very few therapeutics have achieved almost mythical proportions. Their stories are told and retold at personalised medicine conferences, with limited presentation on the many failed attempts to reproduce the benefits in more complex diseases..... Is this hype constructive, in engendering appropriate expectations of further success, or destructive?”

Timothy Maughan, The Promise and the Hype of Personalized Medicine. (The New Bioethics, 2017, 1-8)

## Precision Medicine: Separating Hype from Reality

“Precision medicine” is a marketing term; .... the overarching belief that precision medicine is the future of medicine has led to what has been called an “arms race” or “gold rush” among academic medical centers to develop precision medicine initiatives.”

David H. Gorski, MD, PhD, FACS, oncologist at the Barbara Ann Karmanos Cancer Institute

## Precision Medicine: Separating Hype from Reality



## Precision Medicine: Separating Hype from Reality

### The High Cost of Precision Medicine

- *J Econ Perspectives* reviewed 58 cancer drugs, many precision med drugs
  - 1995: additional year of life cost \$54,000
  - 2005: \$139,000
  - 2013: \$207,000
  - ROI: Survival improved by only a few months
- Novartis CAR-T Gene Therapy, called Kymriah
  - The most precise form of cancer therapy yet
  - Price tag: \$475,000 for one time treatment

## Precision Medicine: Separating Hype from Reality

- More positive statistics; Cost effective therapy
- Gleevec (imatinib) for chronic myeloid leukemia
  - Precision approach: addresses key chromosomal translocation—close to a root cause
  - 1980 Life expectancy for CML patient: 3.5 yr
  - 2010: 27.3 years
- Similar success story for Herceptin (trastuzumab) for HER2 positive breast cancer

## Precision Medicine: Separating Hype from Reality

“Physicians already practice personalized/precision medicine”

- Hypercholesterolemia: Choosing lipid lowering drug >> Do you have liver disease? Skip statin
- Infection: Are you allergic to penicillin?
- Type 2 diabetes choices

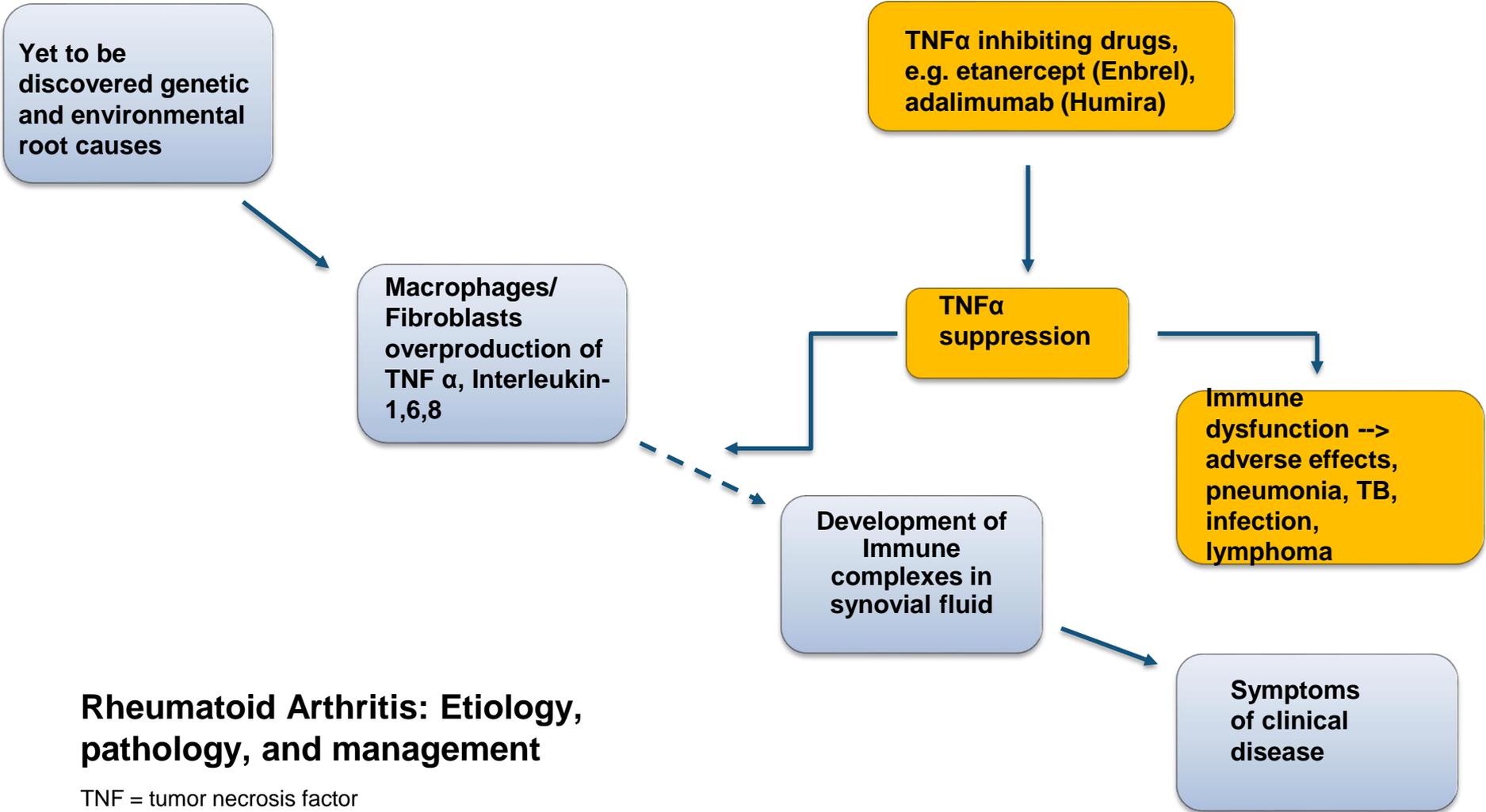
## Old-school Personalized Medicine for Type 2 Diabetes



Inzucchi et al/ Diabetes care 2015;38:140-149.

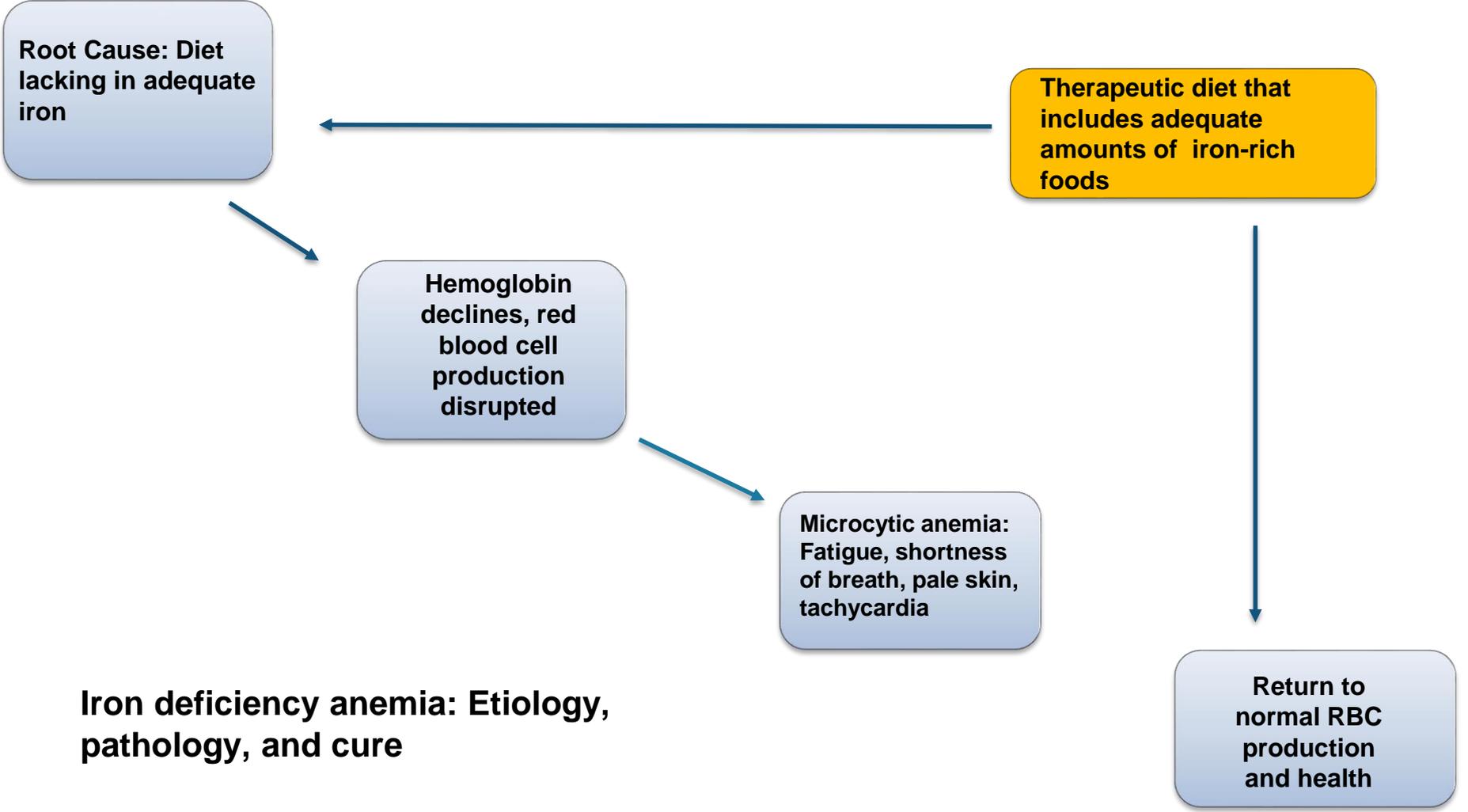
## Precision Medicine: Separating Hype from Reality

- Sequential precision medicine
- Trial and Error medicine
- Let's aim for Precision Medicine with upper case P
  - Addressing numerous contributing risk factors
  - Addressing **root** causes—when possible
  - Population-based, imprecise medicine
  - Relies too heavily on randomized clinical trials (RCTs)
  - Often addresses **intermediate** steps in pathogenesis



## Rheumatoid Arthritis: Etiology, pathology, and management

TNF = tumor necrosis factor



**Root Cause: Diet lacking in adequate iron**

**Therapeutic diet that includes adequate amounts of iron-rich foods**

**Hemoglobin declines, red blood cell production disrupted**

**Microcytic anemia: Fatigue, shortness of breath, pale skin, tachycardia**

**Return to normal RBC production and health**

**Iron deficiency anemia: Etiology, pathology, and cure**

## Precision Medicine: Separating Hype from Reality

The charts beg the Q: How do we find root causes and contributing risk factors for individual patients or subgroups? **Precision Medicine Initiative** and **Data Analytics**

### ***Diabetes Prevention Program (DPP) (NEJM 2002)***

- RCT 3,000+ patients at risk of Type 2 diabetes
- 3 Risk factors: Overweight, elevated fasting blood glucose, and abnormal glucose tolerance test
- Three test groups in DPP:
  - Intensive Lifestyle modification: A 16-lesson curriculum covering diet, exercise, and behavior modification, one on one counseling for 24 weeks
  - Metformin: Popular diabetes drug
  - Controls: advised to eat healthy diet, and given placebo pills

Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin N Engl J Med 2002; 346:393-403

## Precision Medicine: Separating Hype from Reality

### Diabetes Prevention Program (DPP) Results:

- Intensive Lifestyle mod: Reduced diabetes incidence by 58%, when compared to placebo. Not 100%. Metformin reduced DM incidence by 31%
  - Intensive modification: 1079 patients, 20% develop diabetes, **215 pts**
  - Metformin group: 1073 pts; 28% develop diabetes, **300 pts**
  - Control group: 1082 pts; 37% develop diabetes, **400 pts**
- Metformin: Among 1073 adults, 773 avoid diabetes but 300 STILL develop disease despite treatment.
- DPP researchers suggested applying results to millions of at-risk patients would be a good thing.... REALLY ?

***TAKE HOME MESSAGE: No way to predict which ones would and would not respond to Metformin. Could not Personalize Tx.***

## Precision Medicine: Separating Hype from Reality

- Jeremy Sussman et al reanalyzed raw data from Diabetes Prevention Program to personalize Tx
- Identified 7 key risk factors (out of 17 considered)
  - fasting blood glucose
  - hemoglobin A1c
  - family history of elevated blood glucose
  - blood triglyceride level
  - waist measurement in centimeters
  - waist-to-hip ratio.
  - Height

## Precision Medicine: Separating Hype from Reality

- Sussman divided each of 3 groups into quarters: from lowest to highest risk
- Results: “Average reported benefit for metformin was distributed very unevenly across the study population, with the quarter of patients at the highest risk for developing diabetes receiving a dramatic benefit (21.5% absolute reduction in diabetes over three years of treatment) but the remainder of the study population receiving modest or no benefit.”

***Take home message: More detailed set of risk factors enabled Sussman to ID individuals more likely to benefit from Tx and those who would not.***

***“Extra Credit” on data analytics: Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: machine learning... - Baum A, et al. Lancet Diabetes Endocrinol. 2017 July 12, Published online.***

# Realizing the Promise of Precision Medicine

## Diabetes risk prediction tool

**IMPORTANT NOTE: This is not a diagnostic tool. Talk to your doctor about your results.**

### INSTRUCTIONS

Measure or look up your value for each item below.  
Put your cursor or finger over your value on the number line for the first item.  
Then move your cursor or finger straight up to the Points line.  
Write down the number of points you earned for that item.  
Repeat for each of the seven items. Then, total up your score.

Points	0	10	20	30	40	50	60	70	80	90	100	My Points
What's your fasting blood sugar (in mg/dL)?	90	100	110	120	130	140						
What's your long-term blood sugar, or A1C (in %)?	3	4	5	6	7	8	9					
Family history of high blood sugar? (0 for no, 1 for yes)	0	1										
What's your blood triglyceride level (in mg/dL)?	0	200	400	600	800	1000						
What's your waist measurement, in centimeters? (multiply inches by 2.54)	60	90	120	150	180	210						
How tall are you, in centimeters? (multiply inches by 2.54)	200	180	160	140	120							
What's your waist to hip ratio? (take your waist measurement at smallest point, and hip measurement at widest point. Divide the first number by the second.)	0.5	0.75	1	1.25	1.5	1.75	2					
												My Total

**Total score of 146 or above:** Talk to your doctor soon about your risk of diabetes, and what preventive steps you should take.

**Lower scores:** At your next checkup, discuss with your doctor how you can keep your risk of diabetes from increasing.

If you haven't had a blood sugar test and you're over age 45 or you have a high body mass index (over 25), talk to your doctor about being tested. Also talk to your doctor if you haven't had your triglyceride levels measured in the last five years.

**Model based on data from adults over age 25 who took part in the Diabetes Prevention Program.**  
**More information about the research behind this model: <http://umhealth.me/diabpre>**

Used with permission, Univ of Michigan, Tufts University. Prediction tool is still undergoing clinical confirmation.

# Realizing the Promise of Precision Medicine

The role of patient data, mobile technology,  
and consumer engagement



Paul Cerrato and John Halamka



## Dispatch From a Broken Healthcare System

- On September 1, 2017, Kathy Halamka receives the following letter from Harvard Pilgrim Healthcare (the #1 HMO in the US)
- “We are denying coverage for your ongoing cancer care because we found a paper published 27 years ago that suggests a different treatment is better”
- The responsible physician for making this decision is Larry, a retired psychiatrist who is licensed in New Hampshire
- “We have not reviewed any of your records, your protocols, or your preferences”
- You can appeal this process by managing an appeal process over months, managing a project across numerous providers, a board of payer experts, and the medical literature.

## The Outcome

- Hours later, I write an article documenting the complete failure of care management
- All payer decisions are immediately reversed
- The HPHC medical director comes to my home to outline a collaborative path forward
- We agree to write a series of articles
- The psychiatrist is removed for medical management of oncology cases

## How it Should Have Worked

- A cloud hosted precision medicine service provider curates the literature and not only provides a library of evidence but grades the evidence for accuracy/impact/relevance
- EHRs use the FHIR Clinical Decision Support Hooks to send salient patient data to the cloud. Clinicians receive guidance showing possible treatment choices and objective rankings of safety, quality, efficiency, cost, and availability
- Clinicians and patients have a discussion and via shared decision making develop a care plan
- Open source apps are used to display care plans, patient generated healthcare data, and patient report of outcomes
- The payer “gold cards” this process

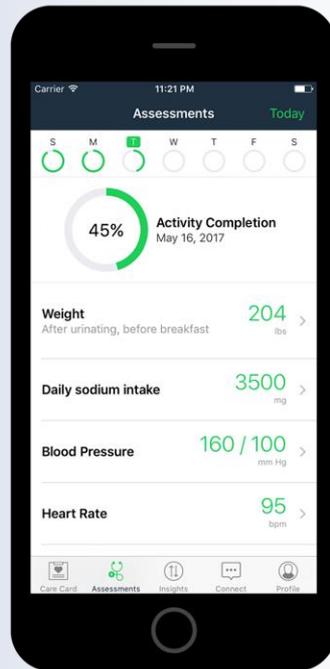
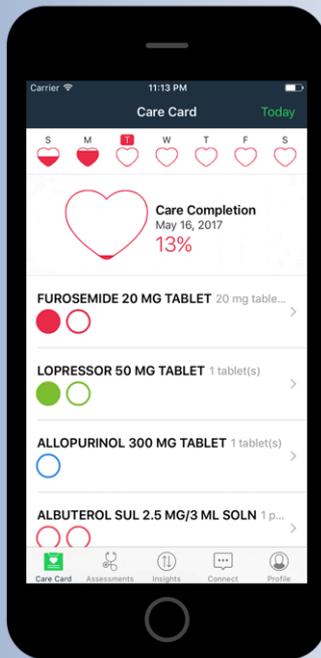
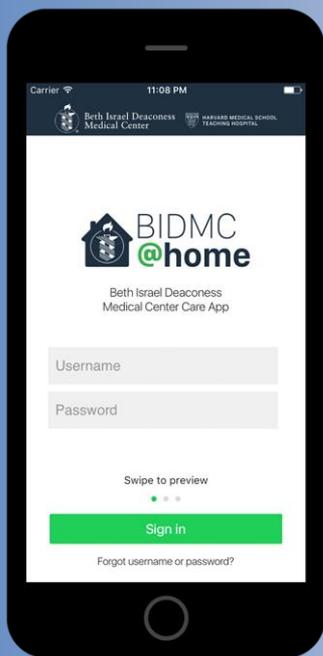
## Emerging Trends

- The rise of app stores/third party tools that layer on top of electronic health records.
- Work on the infrastructure that will accelerate data sharing - nationwide patient matching strategy, electronic provider directories, data governance/policy frameworks
- The urgency to reduce costs as part of the move from fee for service to value-based purchasing
- Reduced pace of government regulatory efforts
- The leadership of the private sector

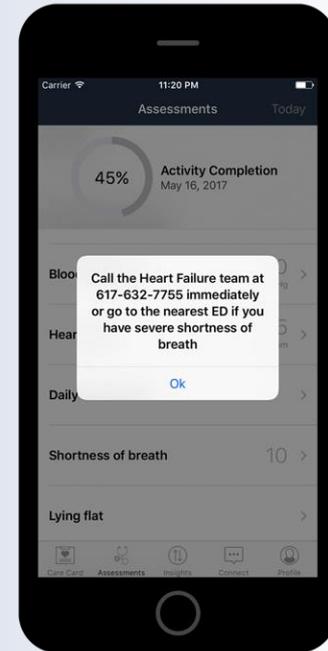
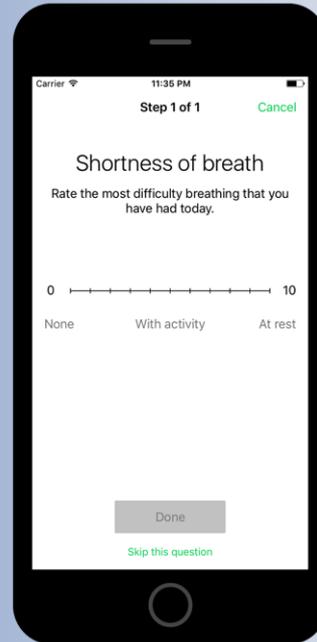
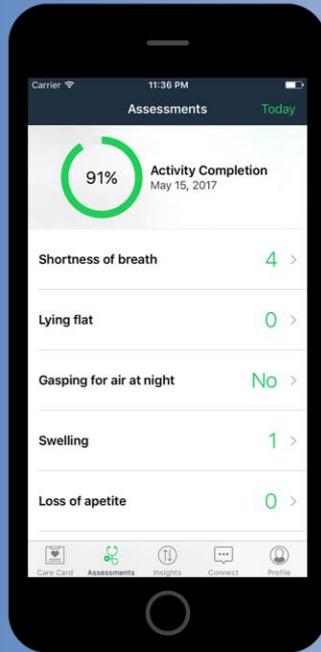
## Further examples

- EHR - my wife's thyroid issues and the need for “social” precision medicine
- Patient/Family engagement - my recent hypertension diagnosis and “internet of things” precision medicine
- Big Data Analytics - my wife's cancer experience and “clinical trial of one” precision medicine

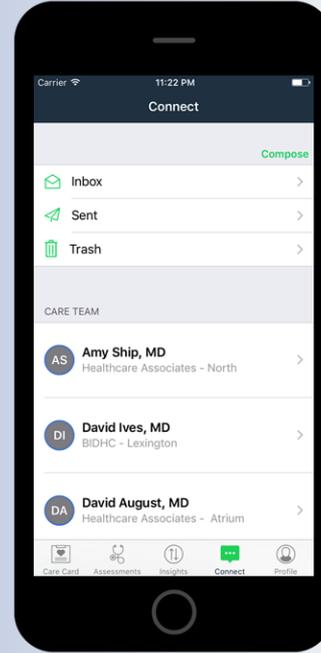
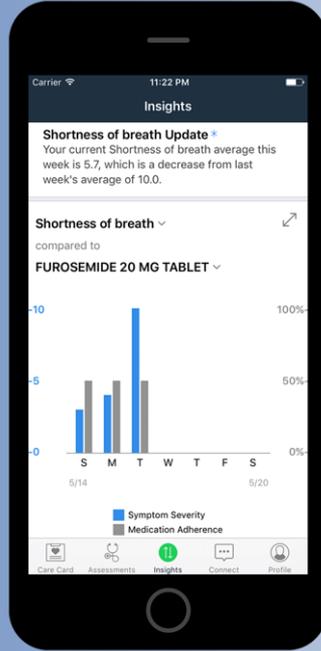
# BIDMC@Home



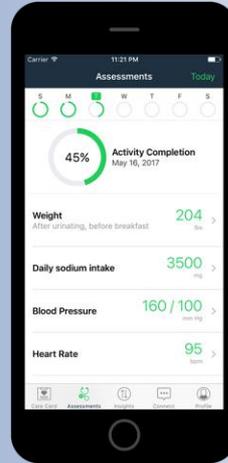
# Monitoring to Management



# Insights and Messaging



# Hub for Wearables and Internet of Things



## What's so great about FHIR?

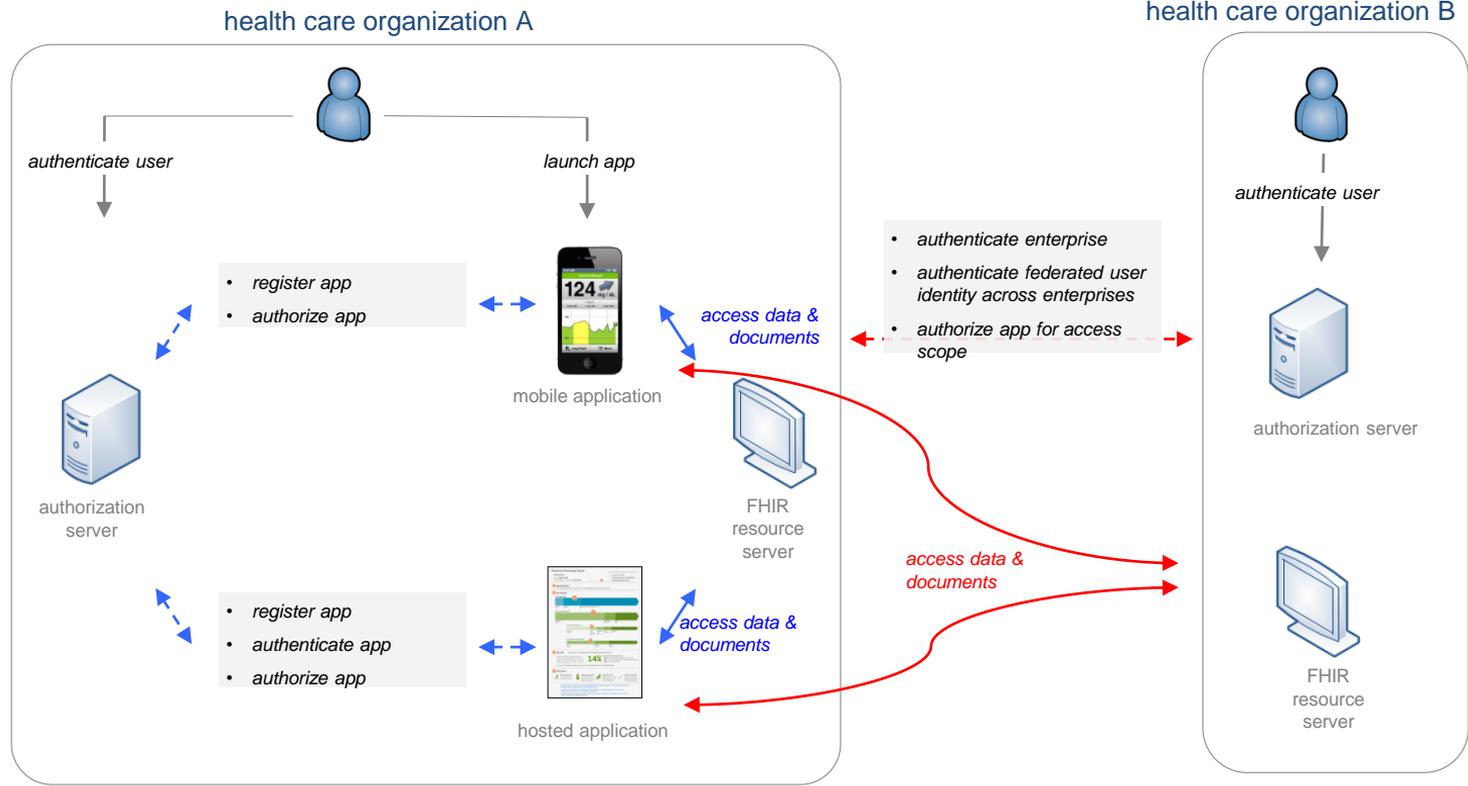
### FHIR (Fast Healthcare Interoperability Resources)

- Flexible to document-level and data-level exchange
  - Sometimes individual data elements are important, sometimes entire documents are appropriate
- Based on modern internet conventions
  - RESTful API – same browser-based approach as used by Facebook, google, twitter, etc
  - Infinitely extensible to detailed resources/profiles to meet any use case
  - Supports push and pull use cases
- Attractive to developers from outside of healthcare

# What will Argonaut Implementation Guides allow people to do?

## Within enterprise

## Cross-enterprise



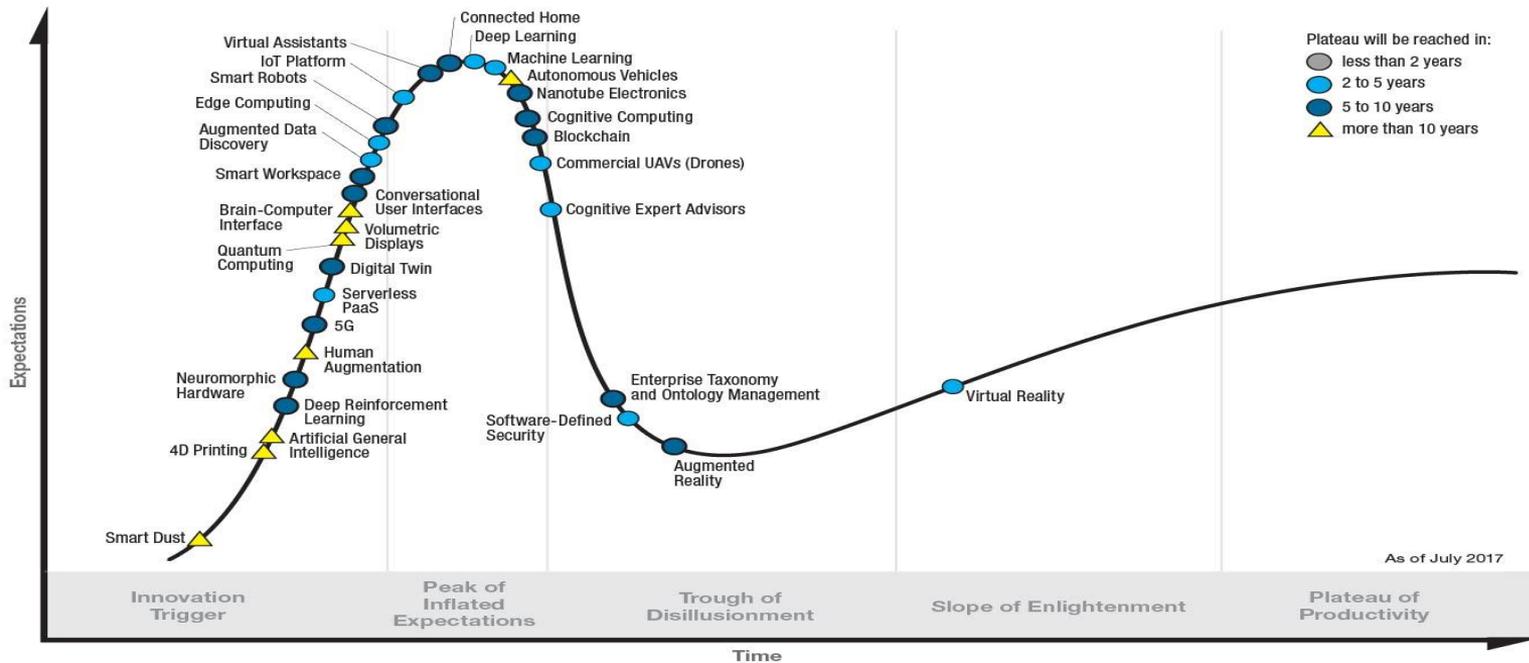
## Who's using the Argonaut Project Implementation Guides

- The following Argonaut founders are basing their FHIR APIs on the Argonaut Implementation Guides:
  - Accenture
  - athenahealth
  - Cerner
  - Epic
  - MEDITECH
  - Surescripts
  - The Advisory Board Company
- The following nationwide health information networks are implementing Argonaut specifications:
  - Carequality – have already implemented a preliminary version of the upcoming Argonaut Project Provider Directory Implementation Guide
  - CommonWell Health Alliance – are building FHIR into their core services using the Argonaut Implementation Guides for Data & Document Access and Provider Directory

## Argonaut Project: 2017 Accomplishments

1. Publication of Provider Directory Implementation Guide based on FHIR STU3
  
2. Scheduling
  - Appointments request – request for appointment
  - Appointment response – reply to an appointment request
  - Slots – blocks of time available for booking appointments
  
3. Enhancing integration of EHRs and Apps (in collaboration with CDS Hooks Project)
  - Integration of an external app into an EHR workflow
  - Validation of security model for integration of external apps with EHRs

# Gartner **Hype Cycle** for Emerging Technologies, 2017



[gartner.com/SmarterWithGartner](http://gartner.com/SmarterWithGartner)

Source: Gartner (July 2017)  
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**Gartner**

# Questions

- John Halamka, [jhalamka@bidmc.harvard.edu](mailto:jhalamka@bidmc.harvard.edu); @jhalamka  
<https://www.facebook.com/geekdoctorhalamka/>
- Paul Cerrato, [plcerrato@gmail.com](mailto:plcerrato@gmail.com); [cerrato@aol.com](mailto:cerrato@aol.com), @plcerrato;  
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