ARTIFICIAL INTELLIGENCE (AI) AND PRECISION MEDICINE: DOES THE HEALTH ECONOMIST NEED TO ADAPT TO THE MACHINE?

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CONCLUSION
Artificial intelligence predicts cardiovascular risk factors based on retinal images.
AGENDA

• How AI relates to Precision Medicine
• Introduction to AI
• AI-backed precision medicine
  – An illustration: skin cancer detection
  – A definition
  – Advantages and challenges
  – Market access considerations
• Real-life examples
  – Cardiac arrhythmias detection
  – Lung cancer detection
  – Diabetic retinopathy detection
• Impact on health economics
• Conclusion

HOW AI RELATES TO PRECISION MEDICINE
PRECISION MEDICINE

• **Definition** – an emerging approach for disease prevention and treatment that takes into account people’s individual variations in genes, environment and lifestyle (NIH)

• **Personalized medicine** – an older term that can be misinterpreted to imply treatments and preventions are uniquely developed for each individual (NRC) Still continues to be used interchangeably by some people

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AI-enabled Precision Medicine

• AI is an important enabler of PM
• Primarily for big data analytics
  – Analyze large medical data sets
  – Draw conclusions
  – Find new correlation based on existing precedences
  – SUPPORT the doctor’s job in decision-making
Relationship of AI to Precision Medicine

• Make patients the point of care
• Create vast amounts of data that require advanced analytics
• Establish the foundation of precision medicine
• AI is key technology that can bring these opportunities to everyday practice

Challenges

• Need to create ethical standards
• Incremental development to evaluate all implications
• Medical professionals need to learn how AI works in practice
• Patients need to become accustomed
• Decision-makers need to assess effectiveness
What is required

• Patient-centric approach
• Appropriate regulatory framework
• Appropriate ethical framework to proactively address ethical challenges
• Consumer education

A QUICK INTRODUCTION TO AI
Voice recognition

www.searchcrm.techtarget.com/definition/voice-recognition
MACHINES CARRY OUT TASKS IN A “SMART” WAY

Artificial Intelligence

Machine Learning

Deep Learning

This last category will be covered today!
A smoker has twice the chance of developing a CV event as compared to a non-smoker (the other parameters being the same)

Source: Framingham CVD risk estimate, Lisa Sullivan, Boston University School of Public Health, 2016

LINEAR REGRESSION

\[ Y = w_0 + w_1 \cdot X_1 + w_2 \cdot X_2 + w_3 \cdot X_3 \]

LINEAR RELATIONS between \( X \)

<table>
<thead>
<tr>
<th>Interpretability</th>
<th>Predictive power</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Low</td>
</tr>
<tr>
<td>&quot;We, poor humans, need to see&quot;</td>
<td>Because most real-life optimization problems are non-linear</td>
</tr>
</tbody>
</table>
The curse of high dimensionality

\[ Y = f(X_1) \]
\[ Y = f(X_1, X_2) \]
\[ Y = f(X_1, X_2, X_3) \]
\[ Y = f(X_1, X_2, X_3, \ldots, X_{1,000,000,000}) \]

Is linear regression sufficient here?

DEEP LEARNING

NON LINEAR RELATIONS between \( X \)

\[
Y = \frac{1}{1 + e^{-\left(\sum_{i=1}^{3} w_i x_i + b\right)}}
\]

<table>
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<tbody>
<tr>
<td>Low</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

This extra performance comes at the cost of interpretability!
AI-BACKED PRECISION MEDICINE

SKIN CANCER DETECTION

SKIN CANCER (in US)
• 5.4 million new cases / year

MELANOMAS (in US)
• Fewer than 5% of all skin cancers
• 75% of all skin-cancer-related deaths (10,000 deaths annually)
• 5-year survival rate
  • 99% if detected in its earliest stages
  • 14% if detected in its latest stages
→ Early detection is critical

130,000 labelled clinical images

Let $Y = f(X)$

A simple image processing technique

Each image is transformed into a series of pixel squares.

Each pixel is converted to a number.

Each pixel is a predictor.

$X_1 = 170$
$X_2 = 238$
$X_3 = \ldots$
Pre-defined algorithm is pre-trained on non-health-specific images!

1.28 million images (1,000 object categories) from the 2014 ImageNet Large Scale Visual Recognition Challenge

GoogleNet Inception v3 CNN

Training and test
OBSERVATIONS (from the last layer)
- We see clusters of points of the same clinical classes
- Benign classes are separated from their malignant counterparts

PERFORMANCE

CONCLUSION
The machine is on par with the performance of the dermatologists and outperforms the average.
AI-BACKED PRECISION MEDICINE

Definition

This is NOT ...

Social networks

Omic data

Connected devices

AI-BACKED PRECISION MEDICINE

Definition

**PRECISION MEDICINE**
Medical decisions are tailored to patient characteristics.

**ARTIFICIAL INTELLIGENCE**
Device that mimics human learning and reasoning.

Machine that can advice a patient with health behaviors ... without human supervision!
# AI-BACKED PRECISION MEDICINE

## ADVANTAGES

### Manufacturer
- Shorter time, less expensive and less risky development (From 10 years – pill – to a few days – app – to reach the market)
- High-performance tool (Sensitivity and specificity)

### Payer
- Higher detection of false positive (Those often result in unnecessary invasive biopsies) and false negative (More lives are saved)
- Easier to set up performance-based risk sharing agreement (Cheaper post-launch studies)

### Physician
- Augmented clinical decision-making for specialists
- Limited time dedicated by the specialist

### Patient
- Reaching underserved communities (6.3 billion smartphones will exist by 2021)
- Health-promoting behaviors

## DRAWBACKS

### Manufacturer
- Performance are data-dependent (Asthma understood by AI as a protective factor for pneumonia whereas the original study advised asthma patients to be treated in ICU)
- Lower interpretability (« Black box » model)
- Stronger competition (40,000 health-related apps are today available)

### Payer
- Tests might be expensive
- Tests might be over-/under-prescribed

### Physician
- “Deskillig” = human expertise likely to disappear (14% decrease in diagnostic sensitivity when human readers are facing computer-aided detection)
- “Demise of context” = lack of ability to assess patients holistically (Only visual and dermoscopic inspection of a skin lesion)

### Patient
- Data privacy (Sensitive patient information and data security breaches)
- Responsibility (in case of false positive diagnosis)

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**Regulatory overview**

**TRADITIONAL DRUG DEVELOPMENT**
- Takes years
- Applies on static products
- Aims at being transparent

**AI-bases HEALTH DEVICES**
- Need months
- Always learning “on the fly”
- “Black box” models

**FDA AGENDA**
- 2017: Selection of 9 pilot partners for AI-related assessment (Apple, Google Verily, Fitbit, Johnson & Johnson, Roche, Samsung, Tidepool, Pear Therapeutics, Phosphorus)
- 2018: FDA approves first AI software that can identify disease (no specialists needed).

**MAIN NEW REGULATORY APPROACH**
- Excellence rather than compliance (= companies with proven track-report enjoy fast-track approval)
- Breakthrough Device designation (= intensive interaction between manufacturer and FDA to optimize the device development)

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https://www.wired.com/2017/05/medicine-going-digital-fda-racing-catch/

H2020 program – 7.5b€ to position EU as a top healthcare actor in the world

Clinical guidelines

Definition of a performance metric for AI-based medical diagnostic tool
- Sensitivity
- Specificity
Payer overview

Today, AI generates traction among payer bodies in Europe

New guidelines are being set up

→ Illustration: NIA and Alivecor

REAL-LIFE EXAMPLES
Alivecor and atrial fibrillations

ATRIAL FIBRILLATIONS
- Irregular heart rhythm that is often abnormally fast
- 5-fold increase in the risk of stroke and 50% more at risk of death

AI SOLUTION
- Heart rate/activity discordance identifies times when a user should take an ECG.

There is a complex “non-linear” relation between heart rate and activity.

Heart rate was outside the range which AliveCor predicted for the level of activity at that time.

We looked at the UK system...
NICE Headlights

**ALIVECOR**
- Sensitivity = 98.5%
- Specificity = 91.4%

VS.

**HUMAN PHARMACIST**
- Sensitivity = 77%
- Specificity = 87%

**COST CONSEQUENCES**
- Fewer GP appointments
- More 12-lead ECGs checks
- More stroke prevention medications (e.g. warfarin)
- Less stroke-related event (e.g. hospitalizations)


Scottish Highlights

Simulation of the cumulative costs and life years of a cohort over a 30 year horizon

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost, £</th>
<th>Incremental cost, £</th>
<th>QALYs</th>
<th>Incremental QALYs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>AliveCor</td>
<td>1,922.93</td>
<td>83.05</td>
<td>9.5496</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Usual Care</td>
<td>2,005.98</td>
<td></td>
<td>9.5336</td>
<td>-0.0160</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

Main assumptions
- High-risk population
- Patients in the comparator arm did not receive screening
- Screening with AliveCor costs £22.02 per patient screened.
Pricing in the US

- Mostly NOT currently reimbursed by private insurers or Medicare
  - Eligible for payment with a Flexible Spending Account, Health Savings Account or Health Reimbursement Arrangement
  - Physicians who purchase device for use in office or bedside can submit for reimbursement with CPT code for 1-3 lead rhythm ECG with interpretation and reports

- Mostly sold directly to consumers (DTC)
  - One-time charge of $99 for basic service
  - Premium service for $10 a month (or $100 a year)
    - Includes features such as medication tracking, unlimited storage, history of heart health data, and the ability for customers to email EKGs to themselves and their doctors.

Enlitic and lung cancers

LUNG CANCERS
- 80% of patients in late-stages die
- If caught early, survival is nearly 10 times more likely
- Hardest cancer to detect in medical images

AI SOLUTION
- AI detects lung cancer nodules in chest CT images 50% more accurately than an expert panel of thoracic radiologists
- AI speed is 50,000 times faster than a human radiologist

ENLITIC
- Founded in 2014, $15 millions in funding
- Current positioning: AI technology "enables" radiologists (and do not replace them)
- Business model: take a cut of the profits realized by the clients that adopt the solution

Avoided biopsies and cancer-related events
- $9 billions being spent in on radiologists
  - Average radiologist’s salary is $286,000 a year
  - 1 radiologist per 10,000 people → 31,800 radiologists in the US
IDx-DR and diabetic retinopathy

**DIABETIC RETINOPATHY**
- If uncaught early, diabetic retinopathy can lead to vision loss.
- 50 percent of diabetic patients do not see their eye doctor on a yearly basis

**AI SOLUTION**
- FDA wanted sensitivity > 85% and specificity > 82.5%.
- IDx-DR passed the bar, with rates of 87.4% and 89.5% percent, respectively.

"[...] IDx-DR makes a clinical decision, without someone like me being involved — it’s fully autonomous."

Michael Abràmoff, ophthalmologist and CEO

Unlike other AI-based tools, IDx-DR is designed to make a directive, not a recommendation.


**IMPACT ON HEALTH ECONOMICS**
Redefining the standard of care

AI-BASED PM TOOL
- Performance
- Sensitivity
- Specificity
- Price

VS.

STANDARD OF CARE

NO DIAGNOSIS
- Performance
  - Sensitivity = 0
  - Specificity = 0
- Cost = 0

Traditional PM tool
- Performance
  - Sensitivity > 0
  - Specificity > 0
- Cost > 0

HUMAN clinician
- Performance
  - Sensitivity > 0
  - Specificity > 0
  - **SALARY** > 0

New claims of interest

AI-BASED PM TOOL
- Performance
- Sensitivity
- Specificity
- Price

VS.

STANDARD OF CARE

Shorter time dedicated by the specialist
Less disease-related event (due to higher sensitivity)
Reduced waste of resources (due to higher specificity)
Increasing relative performance of AI-based PM tools over time

![Graph showing the performance gap between AI-based PM tools and the standard of care over time. The AI engine constantly learns and improves with new data. “Deskilling” = human expertise will likely disappear over time.]

**CONCLUSION**
CONCLUSION

NEW TECHNOLOGY
- Lower interpretability
- Higher performance
  - Sensitivity
  - Specificity

IMPACT ON MARKET ACCESS
- Regulatory
  - New skills needed
  - New way of thinking
- Payers
  - [On the short run] Cost burden will decrease
    - Less specialists
    - Shorter time dedicated by the specialist
    - Less disease-related event
    - Reduced waste of resources
  - [On the long run] Cost burden might increase
    - Lock-in effect
    - Pricing power

Q&A
Responsability

In case the machine goes wrong, who is responsible?

What about the case where the standard-of-care algorithm would have saved the patient?

Data security

When you undergo diagnostic tests to determine the best way to treat your skin cancer, are you concerned your sensitive information will be collected by a machine?
Being a health economist

In your opinion, if IA-based precision medicine tools enter the playground tomorrow, how would health economics be impacted?