Lessons from Israel:
Finding Cancers with AI and EHR Data

Session 106, February 13, 2019
Prof. Varda Shalev, MD MPA
CEO, Institute for Research and Innovation at Maccabi Health Services
Conflict of Interest

Varda Shalev, Director of Research and Innovation Center, Maccabi Health Services

Salary: No

Royalty: Commercial agreement between Maccabi and Medial EarlySign

Contracted Research: Yes

Other: Mutual patent
Agenda

1. Maccabi and Healthcare in Israel
2. Precision Medicine & Health Care Data
3. Maccabi’s AI-Based CRC intervention
4. Results
5. Takeaways
Learning Objectives

Session learning objectives:

• Demonstrate how the U.S. health system can learn from Israel’s approach to digital health and the use of existing EHR data

• Discuss clinical and ROI results of a real-world, machine-learning case study that used only blood count results and demographics to successfully detect individuals at risk of cancer

• Identify the processes necessary for a streamlined and simple AI implementation, aligned with clinical workflow, to support an effective patient-centric health system
Israel at a glance

Population
9 million

Capital
Jerusalem

Languages
Hebrew, Arabic, English, Russian
Maccabi Healthcare

$4.5B  Annual Budget
Israel’s 2nd largest healthcare provider
Serving 2.3M people - 25.5% of Israeli population
< 1% Dropout yearly

Fully integrated healthcare
13 hospitals  |  Thousands of PCPs and specialists in diverse medical areas

1615 GPs  |  110 gastroenterologists  |  9 GI centers
63,000 colonoscopies annually
Data: a Natural Healthcare Resource

“Data is the world’s next natural resource”

Ginni Rometty, IBM CEO (March 21, 2017)
Maccabi’s Research and Innovation Institute

CEO, Maccabi Research and Innovation Institute

- Maccabitech - Epidemiological Research
- The Clinical Research Unit
- MK&M - Big Data
- BioBank
Maccabi’s EHR Data Sources

- 5,000 Physicians
- 95 Nurse stations
- 24 Imaging centers
- 36 Physiotherapy clinics
- One Central Lab
- 300 Lab collection points
- 140 Primary Care Clinics
- 700 Pharmacies
- 32 Hospitals
- Home care
HCSRN Members: Years with EMR

- HFHS 1988
- Maccabi (25+ years) 1993
- MCRF 1994
- GHS 1995
- KPNW 1997
- KPCO 1997
- KPSC 2004
- KPH 2004
- HPRF 2004
- GHC 2005
- MPCI 2006
- KPG 2006
TIPA Bio Bank

Personalized Medicine
Is the next step in prevention and cure of disease

Digital + Genetic + Biologic
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What is Precision Medicine?

“The tailoring of medical treatment to the individual characteristics of each patient”*

Precision Medicines 4 P’s:

Predictive
Personalized
Participatory
Preventive

*Priorities for Personalized Medicine
President’s Council on Advisors on Science and Technology, September 2008
Can We Utilize Medical Data to Intervene Earlier?

- Early detection of at-risk patients
- Provide **personalized** evidence to enable proactive decisions

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Analytics Categories

Descriptive (85%)
Tells you what happened and often why

Predictive (12%)
Tells you what will happen

Prescriptive (3%)
Tells you what to do about it
Example: one patient during 3 years (2003–2005)

Standard Complete Blood Counts (CBC) results

<table>
<thead>
<tr>
<th>Test</th>
<th>16-Jul-03</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC Leucocytes</td>
<td>8.1</td>
</tr>
<tr>
<td>RBC Red Blood Cells</td>
<td>5.48</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>15.7</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>44.0</td>
</tr>
<tr>
<td>MCV Mean Cell Volume</td>
<td>80.3</td>
</tr>
<tr>
<td>MCH Mean Cell Hemoglobin</td>
<td>28.6</td>
</tr>
<tr>
<td>MCHC Mean Cell Hb Concent.</td>
<td>35.7</td>
</tr>
<tr>
<td>RDW Red Cell Distr. Width</td>
<td>15.0</td>
</tr>
<tr>
<td>Platelets</td>
<td>206.0</td>
</tr>
</tbody>
</table>

Diagnosis date: 28/12/2006

Within the norm
Previous CRC Work was Descriptive

Variations in hemoglobin before colorectal cancer diagnosis
Inbal Goldshtein, Uri Neeman, Gabriel Chodick and Varda Shalev

Controls: Random age, gender matched
Cases: N=1074, age 45-75

Hemoglobin level drops 3-4 years prior to current cancer diagnosis!

The Shift to Predictive Analytics → Machine Learning

Is it possible to proceed from an epidemiological **observation** to a personalized **predictive** risk score for Colorectal Cancer using Machine Learning?

A meaningful arrow…
The Shift to Predictive Analytics ➔ Machine Learning

What is Machine Learning?

• A data analysis method which automates analytical model building

• Uses algorithms that learn from data iteratively

• Computers find patterns within a large amount of data without being explicitly programmed where to look
Machine Learning vs Regression Modeling
Increased Risk Indicator*

Predictive Model
 Implemented by Maccabi, developed by a leading developer of machine learning-based healthcare solutions.

Score
  +
Age
  +
Sex

Flagged Patient
  ➔
Expedited Assessment

No Flag
  ➔
Follow Guidelines

A meaningful arrow…
Model Implemented in Clinical Practice in Israel*

The machine learning-based model finds trends and variations within normal ranges, and was used by Maccabi to identify individuals at increased risk of CRC using only complete blood count (CBC) test results, age and sex.

*Implemented by Maccabi, this model was developed by a leading developer of machine learning-based healthcare solutions in collaboration with Maccabi.
# Clinical Rigor of AI-Based Algorithm

<table>
<thead>
<tr>
<th>Step</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Create model</td>
<td>Maccabi (Israel)</td>
</tr>
<tr>
<td>Check model performance on “blind” part of the same population</td>
<td>Blindly validate the model (Validation set) 139,205 people (698 CRC patients)</td>
</tr>
<tr>
<td>Check model performance on different population</td>
<td>Blindly validate on independent data-set 25,613 people (5,061 CRC patients)</td>
</tr>
<tr>
<td>Worldwide Validation</td>
<td>Worlds wide</td>
</tr>
<tr>
<td></td>
<td>Studies in leading institutions around the world (Oxford, KPNW, KPNC, CUHK) totaling 5M individuals</td>
</tr>
</tbody>
</table>

* The Health Improvement Network
Training & Validation Performance

Results show accuracy for independent studies in different populations.
Performance at Curable Stages

33.1% In Situ – Stage II Cancers Detected

3% Flagged Population
Overall Performance on Right-Sided Cancers

3% Flagged Population

60% Right-Sided Cancers Found
The Time Factor in CRC Survival Rate*

Typical 5 year survival rate for CRC decreases with time

- **90%** Stage I CRC
- **80%** Stage II CRC
- **40%** Stage III CRC
- **10%** Stage IV CRC

And yet…

- **Only 40%** Are diagnosed at an early stage
- A screening program is in place

And yet …

- **~70% compliance** To screening

*National Cancer Institute
MHS Implementation Clinical Work Flow

Blood Count Ordered and Processed

Part of the Labs Results

Point of Care Alert Flag GP on EMR

MHS Implementation Clinical Work Flow

Age 50-75? Yes

Screening Up-To Date? Yes

Under GI Examination? No

No

Calculate ColonScore

Follow Guidelines

Yes

Above Cut-Off? Yes

No

Lab Results

ColonScore

Follow Guidelines

Blood Count Ordered and Processed

Part of the Labs Results

Point of Care Alert Flag GP on EMR

Lab Results

ColonScore
Passive screening – different approach
Maccabi’s Monthly Volume Estimates

~25,000 monthly (50-75) outpatient blood counts test results

-17,500
Exclude those who are screening compliant

-1,500
Exclude those who are referred for GI consultation (3 m prior to index date)

-500
Exclude those who have a previous diagnoses of cancer

-5,450
ColonScore flags the top 1% highest risk population for further evaluation

Compliance: ~20 Colonoscopies adding < 1% to colonoscopy capacity

Low Burden / High Yield
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Recent Publications (Retrospective)

**Cancer Medicine**
Accepted Aug. 12, 2017
doi: 10.1002/cam4.1183

*Evaluation of a prediction model for colorectal cancer: retrospective analysis of 2.5 million patient records*

Jacqueline Birks¹, Clare Bankhead², Tim A. Holt², Alice Fuller² & Julietta Patnick³

¹Oxford Biomedical Research Centre, Oxford University, Botnar Research Institute, Windmill Rd, Oxford, OX7 3LD, United Kingdom
²Nuffield Department of Primary Care Health Sciences, Oxford University, Radcliffe Observatory Quarter, Woodstock Road, Oxford, OX2 6GG, United Kingdom
³Cancer Epidemiology Unit, Nuffield Department of Population Health, Oxford University, Richard Doll Building, Old Road Campus, Oxford, OX3 7LF, United Kingdom

**Digestive Diseases and Sciences**
Accepted Aug. 11, 2017
(2017) 62:2719–2727

*Early Colorectal Cancer Detected by Machine Learning Model Using Gender, Age, and Complete Blood Count Data*

Mark C. Hornbrook¹ · Ran Goshen² · Eran Choman² · Maureen O’Keeffe-Rosetti¹ · Yaron Kinar²,³ · Elizabeth G. Liles¹ · Kristal C. Rust¹,⁴

Received: 24 June 2017 / Accepted: 11 August 2017 / Published online: 23 August 2017
© Springer Science+Business Media, LLC 2017
Publication of Results of Implementation

JCO Clinical Cancer Informatics
Published March 29, 2018
doi: 10.1200/CCI.17.00130

Computer-Assisted Flagging of Individuals at High Risk of Colorectal Cancer in a Large Health Maintenance Organization Using the ColonFlag Test

Purpose To evaluate in a sample of adults who had been noncompliant with colorectal cancer (CRC) screening whether screening could be enhanced by an automated patient recall system based on identifying high-risk individuals using the ColonFlag test and an electronic medical record database.
Performance of the Model vs. gFOBT

ColonScore Cut-off = 1%
FOBT Positivity rate = 2.5%
Many lives saved for people whose cancers most likely would have otherwise been found too late.
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Decide and Act - Quickly!

“Decisions should be based on 70% of the information. If you wait to have 90% - you’re too slow.

Making a mistake and correcting it is more efficient than not deciding”

Jeff Bezos, Amazon CEO
Implementation - Key Lessons Learned

- Must embed within existing clinical path
- Strong champion within organization
- Immediate positive results get quick buy-in
- Personally address each and every stakeholder along the clinical path
- Easy IT integration
- Continuous and relentless commitment to organization
- Track and monitor performance
Israel Ministry of Health 1st Place for Initiatives in Personalized Medicine
Thank You!

Contact:

Prof. Varda Shalev, MD MPA
Shalev_v@mac.org.il