Challenges in developing, validating and implementing clinical decision support algorithms

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Swiss Tropical and Public Health Institute, UNIBAS (SwissTPH)
Almost all areas of health are becoming **e-health**…

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>1</strong></td>
<td>Client education &amp; behaviour change communication (BCC)</td>
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<tr>
<td><strong>2</strong></td>
<td>Sensors &amp; point-of-care diagnostics</td>
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<tr>
<td><strong>3</strong></td>
<td>Registries / vital events tracking</td>
</tr>
<tr>
<td><strong>4</strong></td>
<td>Data collection and reporting</td>
</tr>
<tr>
<td><strong>5</strong></td>
<td>Electronic health records</td>
</tr>
</tbody>
</table>
| **6** | Electronic decision support
   Information, protocols, algorithms, checklists |
| **7** | Provider-to-provider communication
   User groups, consultation |
| **8** | Provider workplanning & scheduling |
| **9** | Provider training & education |
| **10** | Human resource management |
| **11** | Supply chain management |
| **12** | Financial transactions & incentives |

Are electronic clinical decision support algorithms really new..?

“The times have passed when a single human mind could even pretend to know all that might be useful in aiding patients.”

L.C. Payne, The role of the computer in refining diagnosis, The lancet 1964
What is available on the market?

Babylon

Your summary
People with symptoms similar to yours usually have the following condition:

Migraine
8 out of 10 people with these symptoms are likely to have this condition (disorder causing severe

Flu
2 out of 10 people with these symptoms are likely to have this condition (infection with influenza virus.)

...biggest disruption of general practice in years"

Isabel

Symptom checker - Verificateur de symptômes
4.3*

Symptom Check Sante Assistance
4.2*

Symptom Checker Offline, Tiny Sym.
3.6*

Symptom Checker Plain Assistant Inc
3.3*

Dog Symptom DerpAssist
1.0*

Symptoms Checker Franco Tavani

Dr. Isabel

Isabel

Symptom Checker

Isabel

Search for symptoms

What are you experiencing today?

Symptom

Symptom checker - Verificateur de symptômes
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Search for symptoms

What are you experiencing today?

Symptom

ADA

Your Health Guide
4.7*

WebMD Reimbursement
4.2*

Leptospirosis
Sepsis and Shock
Influenza
Swine Flu
Thrombotic Thrombocytopenic Purpura
Viral Meningoencephalitis
Toxoplasmosis

Add - Your Health Guide
4.7*

WebMD Reimbursement
4.2*

Leptospirosis
Sepsis and Shock
Influenza
Swine Flu
Thrombotic Thrombocytopenic Purpura
Viral Meningoencephalitis
Toxoplasmosis

What are you experiencing today?

Symptom

Fever

Flu
Influenza infection
Can usually be managed at home
5 out of 10 people with these symptoms had this condition.

Trench fever
Seek medical advice
Fever in one out of 10 people with these symptoms had this condition.

Boutonneuse fever
Seek medical advice
Fever in one out of 10 people with these symptoms had this condition.

Sepsis
Seek emergency care
Fever in one out of 10 people with these symptoms had this condition.

Viral meningitis
Seek emergency care
Fever in one out of 10 people with these symptoms had this condition.

What is available on the market?
Babylon signs a contract with NHS.

8 complaints filed by GPs in UK.

The UK Care Quality Commission concludes that in some areas Babylon is not safe. (report censured by High Court).

Letter to the BMJ: “Could Babylon please supply evidence?”

Letter to the Lancet: “serious methodological problems”

“Babylon at the heart of controversies…”

“We are one of the safest primary care provider of UK.”

Some would like to see us fail and use anonymous and wrong allegations. Some even pretend to be physicians…

“Babylon technology is certified as a medical device.” (classe 1)

Internal study with 50 case scenarios: “Babylon do better diagnosis than human beings.”

2.5 millions people in UK, Rwanda and Ireland are presently using Babylon…
Babylon at the heart of controversies...

8 complaints filed by GPs in UK.

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The UK Care Quality Commission concludes that in some areas Babylon is not safe. (Report censured by High Court).

2.5 million people in UK, Rwanda and Ireland are presently using Babylon.

51% of actual diagnoses were among the top 3 diagnoses provided by the algorithm.

Letter to the Lancet: “serious methodological problems”

Letter to the BMJ: “Could Babylon please supply evidence?”

51% of actual diagnoses were among the top 3 diagnoses provided by the algorithm.

Semigran et al, *BMJ* 2015
We Need an FDA For Algorithms

UK mathematician Hannah Fry on the promise and danger of an AI world.

BY MICHAEL SEGAL
NOVEMBER 1, 2018

In the introduction to her new book, Hannah Fry points out something interesting about the phrase “Hello World.” It’s never been quite clear, she says, whether the phrase—which is frequently the entire output of a student’s first computer program—is supposed to be attributed to the program, awakening for the first time, or to the programmer, announcing their triumphant first creation.
What type of algorithm for whom?

Patient

Front-line physician/clinician

Specialized physician

1. Refer or admit?
2. Which lab test?
3. Meaning of the result in the clinical context (specific treatment)?

You don't have to go to a physician.
You don't need to stay in bed but avoid physical efforts.
Don't stay in the sun and drink a lot. Take paracetamol.

Dose of paracetamol

SHOULD I GOTO A PHYSICIAN?

You don't have to go to a physician.

Don't stay in the sun and drink a lot. Take paracetamol.

Dose of paracetamol

Infectious Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Probabil</th>
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<tbody>
<tr>
<td>Gastroenteritis - viral</td>
<td>35%</td>
</tr>
<tr>
<td>Influenza</td>
<td>19%</td>
</tr>
<tr>
<td>Enterovirus infection</td>
<td>18%</td>
</tr>
<tr>
<td>Infectious mononucleosis or EBV infection</td>
<td>9%</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae infection</td>
<td>8%</td>
</tr>
<tr>
<td>Parvovirus B19 infection</td>
<td>2%</td>
</tr>
<tr>
<td>Campylobacteriosis</td>
<td>2%</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>2%</td>
</tr>
<tr>
<td>Salmonellosis 😞</td>
<td>2%</td>
</tr>
<tr>
<td>Meningitis - aseptic (viral)</td>
<td>1%</td>
</tr>
<tr>
<td>Parainfluenza virus infection</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Shigellosis 😞</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
First step: Define target user and patient

- Traveler or migrant upon return from the tropics with fever
- Primary care clinician
- Physician at hospital
- Pharmacist
- Community health worker
- Child 2 months – 5 years with history of fever or high temperature
2nd step: Structured review of the literature

12'124 articles
3rd step: studies to measure disease prevalence

**Febrile adult travellers**

- Tropical infections: 45%
- Acute febrile diarrhoea: 15%
- Respiratory infections: 13%
- Viral diseases: 5%
- Other: 3%
- Skin & soft tissue: 3%
- Genitourinary: 4%
- Neurological infections: 0.6%
- Mononucleosis: 2%
- Noninfectious: 2%
- Unknown: 14%

Based on 25'743 biological tests

*Buss et al., in preparation*

**Febrile Tanzanian children**

- Upper respiratory tract infection: 36%
- Acute respiratory infection: 51%
- Systemic infection: 11%
- Nasopharyngeal viral infection: 10%
- Gastroenteritis: 8%
- Malaria: 9%
- Typhoid fever: 3%
- Meningitis: 0.2%
- Skin or mucosal infection: 1%
- Urinary tract infection: 5%
- Non-radiologically confirmed pneumonia: 10%
- Bronchiolitis: 3%
- Radiologically confirmed pneumonia: 3%
- Unknown: 3%

Based on 25'743 biological tests

*D’Acremont et al., NEJM 2014*
4th step: CART analyses to best combine clinical predictors

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>46%</td>
<td>93%</td>
</tr>
<tr>
<td>LR+</td>
<td>LR-</td>
</tr>
<tr>
<td>6.57</td>
<td>0.58</td>
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</tbody>
</table>
5th step: novel host biomarkers that predict disease

28-day mortality in febrile Tanzanian adults

Radiological pneumonia in febrile Tanzanian children

Richard-Greenblatt et al, CID 2019

Erdman et al Plos One 2015
6th step: clinical decision support algorithm (CDSA)
7th step: transform medical thinking into software coding
MedAI-C: a software to transform your algorithm into an App
The validation cycle of electronic clinical decision support algorithms

I. Validity and user-friendliness in the IT lab
II. Clinical safety and efficacy
III. Clinical effectiveness
IV. Impact, including on costs

Adaptation time & place, using generated data
Clinical and epidemiological context

Keitel & D’Acremont, Clin Microb & Infect 2018
The new Regulations on medical devices

On 5 April 2017, 2 new Regulations on medical devices were adopted, and they entered into force on 25 May 2017. These replace the existing Directives.


The new rules will only apply after a transitional period. Namely, 3 years after entry into force for the Regulation on medical devices (spring 2020) and 5 years after entry into force (spring 2022) for the Regulation on in vitro diagnostic medical devices.
Impact of e-POCT implementation on cure rate

Potential impact of ePOCT in children in Tanzania:
1 million clinical failures averted per year

Kristina Keitel et al, Plos Medicine 2017
Potential impact of ePOCT in children in Tanzania:

28 million unnecessary antibiotics saved per year

Kristina Keitel et al, Plos Medicine 2017
The validation cycle of electronic clinical decision algorithms

I. Validity and user-friendliness in the IT lab
II. Clinical safety and efficacy
III. Clinical effectiveness
IV. Impact, including on costs
adaptation in time and place, using generated data

Clinical and epidemiological context

DYNAMIC project

ePOCT clinical trial

Kristina Keitel et al, Clin Microb & Infect 2018
The DYNAMIC project

ePOCT: - extended medical content and age range (1 day - 14 years)
- new software with user-friendly interface

Validation:
- 150 health facilities
- low and high endemic areas in Tanzania and Rwanda

Benefits:
1 Mio consultations with sick children

Dynamic algorithm:
Through machine-learning and optimization

Health system:
Enhanced M&E, disease surveillance, epidemic detection

Data sciences:
High number and variability of data
Ecology and durability of smartphones/tablets implementation

We need a FAIRTABLET!

We should not store useless data on long term!
Digital technologies are a limited resource…

### Raw Materials and Recycling

<table>
<thead>
<tr>
<th>Raw Material</th>
<th>% of World Production</th>
<th>Stocks (Years)</th>
<th>Recycling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silver</td>
<td>21%</td>
<td>15-30</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Copper</td>
<td>42%</td>
<td>40</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Indium</td>
<td>&gt;50%</td>
<td>10-15</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Galium</td>
<td>40%</td>
<td>10-15</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Germanium</td>
<td>15%</td>
<td>10-15</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Lithium</td>
<td>20%</td>
<td>Large</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Tantale</td>
<td>66%</td>
<td>150</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Rare Earths</td>
<td>20%</td>
<td>Large</td>
<td>&lt;1%</td>
</tr>
</tbody>
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Eric Vidalenc, “For a digital ecology” 2019

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A. Andrae & T Edler Challenges 2015
Who should benefit from digital health in priority?
Impact of algorithms beyond health

« If you record in the REC, you learn at the same time. If one day there is no tablet, you will still be able to correctly manage the child. »
Accoucheuse, Centre de Santé de Boulma

Yes, it teaches us, as you cannot retain everything in your head. But with the REC, it reminds you at any time. At any time, you have it in front of you and it allows you to master. »
Infirmier, Centre de Santé de Samba

« Now the clinicians ask us more questions on the child and touch him more. »
Président comité de gestion, village de Yako

« On était dans les ténèbres. Maintenant, on est dans la lumière. »
Chef du village de Yako

IeDA project from Terre des hommes in Burkina Faso

Bessat et al, BMC Public Health 2019
Impact of algorithms beyond health

It changes the power balance

Each technical innovation is doubled sided, not due to the good or bad way of using it, but due to the change in the distribution of power. It removes power from some to give it to others, changing the reality for all.


It brings back pride and autonomy

IeDA project from Terre des hommes in Burkina Faso

Bessat et al, *BMC Public Health* 2019
GOVERNMENT INACTION WILL COST COUNTLESS LIVES