Cost-effectiveness analysis of rapid diagnostic tests for G6PD deficiency in patients with *Plasmodium vivax* malaria in the Brazilian Amazon

**Conclusion:** The CS-G6PD strategy is cost-effective for adequately diagnosing cases and avoiding hospitalization. This information can help in decision-making, both in incorporating prior diagnosis in the use of PQ and to promote greater safety among G6PD deficient individuals in the Brazilian Amazon *P. vivax* endemic areas.
Personalized Medicine
(or precision medicine)
Better targeted treatment
thanks to new technologies
... expecting being more effective and safe!
Personalized Medicine (or precision medicine) is not handicraft medical practice, but rather «mass customization» delivery of HC.
• Pharmacogenetics (PGx) has the potential to personalize pharmaceutical treatments
• Many relevant gene-drug associations have been discovered
• 137 PGx associations found in the FDA table
• 44 economic evaluations, relating to 10 drugs
  – 57% in favour of PGx testing: 30% cost-effective and 27% cost-saving
• If genetic information is freely available
  – 75% in favour of PGx testing: 25% cost-effective, 50% cost-saving
Table 2. Drugs for which a PGx-guided strategy was studied in economic evaluation(s)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Therapeutic area</th>
<th>Gene</th>
<th>Notes (based on PharmGKB.org)</th>
<th>Number of reviewed publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td></td>
<td></td>
<td>Contraindicated for HLA-B*5701 carriers as they are at high risk of hypersensitivity reaction.</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Cardiology</td>
<td>CYP2C19</td>
<td>CYP2C19 poor metabolizers have reduced response to carbamazepine and alternative treatment should be considered (refs 25, 26, 60–63)</td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>Cardiology</td>
<td></td>
<td>HTR2A are associated with citalopram response.</td>
<td>6</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Cardiology</td>
<td>CYP2D6</td>
<td>Poor metabolizers may require reduced clozapine dose. Six polymorphisms in H2, 5-HTT, 5-HT2A and 5-HT2C are associated with clozapine response.</td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>Oncology</td>
<td>TPMT</td>
<td>Reduced starting dose of irinotecan.</td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Oncology</td>
<td></td>
<td>Reduced starting dose of irinotecan.</td>
<td></td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>Oncology</td>
<td></td>
<td>Carriers of one nonfunctional TPMT allele may require reduced mercaptopurine dose. Carriers of two nonfunctional TPMT alleles are at high risk of myelotoxicity and alternative treatment should be considered (ref. 69)</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>Cardiology</td>
<td>CYP2C9, VKORC1</td>
<td>Genetic variation in VKORC1 and CYP2C9 explain 40% variance in warfarin dose. Genetic and clinical information can be used to determine starting dose.</td>
<td>12 (refs 22–24, 30, 70–77)</td>
</tr>
</tbody>
</table>

Abbreviation: PGx, pharmacogenetics. *Gene not mentioned on FDA drug label but appears in economic evaluations.
Scenario of no extra cost for genetic information
Scoping Review
Economics and Precision Medicine
*(preliminary results)*

• **Definition for this Scoping Review**
  – **Precision Medicine** MeSH “Clinical, therapeutic and diagnostic approaches to optimal disease management based on individual variations in a patient's genetic profile” (U.S. National Library of Medicine, 2017).

• **Search Strategy: Jan. 2014 – Nov. 2017**
  – English, German, French
Scoping Review
Economics and Precision Medicine
(preliminary results)

• PubMed search: 713 articles
• Relevant for the review: 84 selected papers
  – exclusion: not precision medicine, opinion articles, no economical analysis, discussions on models only, R&D only, doublons
• 23% from the USA – 27% Europe (10% UK) – 18% Asia
• 15% are Systematic Reviews (e.g. Verbelen et al, 2017)
• Heterogeneity: Cost-effectiveness thresholds: from 20’000USD/QALY to 100’000 USD/QALY

<table>
<thead>
<tr>
<th>Main areas of PM</th>
<th>30</th>
<th>36%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>30</td>
<td>36%</td>
</tr>
<tr>
<td>Cardiovascular Diseases</td>
<td>7</td>
<td>8%</td>
</tr>
<tr>
<td>Safety and efficacy</td>
<td>38</td>
<td>45%</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>7%</td>
</tr>
<tr>
<td>Systematic Reviews</td>
<td>3</td>
<td>4%</td>
</tr>
</tbody>
</table>
In most papers:

- Economical analyses using Markov modelling (simulation of disease progression);
- Data based on clinical trials, meta-analyses, expert opinion
- Time frames are heterogeneous;
- Perspective from payer/third party payer/societal

Number of studies published per year

<table>
<thead>
<tr>
<th>Year</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>30</td>
</tr>
<tr>
<td>2016</td>
<td>20</td>
</tr>
<tr>
<td>2015</td>
<td>25</td>
</tr>
<tr>
<td>2014</td>
<td>15</td>
</tr>
</tbody>
</table>
Results

• 63 cost-effectiveness analyses; 4 cost-utility; 17 others (incl. Syst. Rev).
• Majority of analyses find Precision Medicine at least cost-effective (53), some cost-saving (2); Not cost-effective (13);
• 6 papers remain «inconclusive» with regards to economical balance
• 18 (24%) studies were industry funded (and declared). All of them but 2 (inconclusive) find PM as cost-effective.
Results (cont’d)

- Cost-effectiveness is sensitive to:
  - Cost of treatment (if companion treatment)
  - Cost of testing and counselling
  - Positive predictive value of genetic test (and therefore prevalence of mutation in population studied), therefore population based screening programs mostly not cost-effective when cascade screening programs are cost-effective (increased risks expected to be identified by pre-screening)
  - Stage of disease
  - Willingness to pay = threshold of cost/QALY
  - Screening uptake of relatives and compliance to treatment
Genomic to help foodborne outbreak investigations?
Tomorrow
Augmented Public Health?

Equipped HC professionals

Enriched data

Analyses

Real Time Feedback
Stanford algorithm can diagnose pneumonia better than radiologists

Stanford researchers have developed a deep learning algorithm that evaluates chest X-rays for signs of disease. In just over a month of development, their algorithm outperformed expert radiologists at diagnosing pneumonia.

Within a week the researchers had an algorithm that diagnosed 10 of the pathologies labeled in the X-rays more accurately than previous state-of-the-art results. In just over a month, their algorithm could beat these standards in all 14 identification tasks. In that short time span, CheXNet also outperformed the four Stanford radiologists in diagnosing pneumonia accurately.
This is why PM may be useful for global health purposes
Precision Public Health

“providing the right intervention to the right population at the right time”

Khoury, 2016
Miriam Kasztura (PMU-UNIL and BFH)
Dejan Loncar (UNIGE)
Nefti-Eboni Bempong (UNIGE)
April 10-12 2018
Geneva Health Forum