Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

# Pharmacogenetic testing in Belgium

## KCE – report findings

# KCE, Belgian Health Care Knowledge Centre

www.kce.fgov.be

- Public institution (independent research center)
- Operational since 2003

- +- 60 researchers
  - medicine & paramedical, economics
  - statistics, sociology, law

- Studies
  - Clinical practice guidelines
  - Health services research (HSR)
  - Health technology assessment (HTA)

    + KCE Trials (started in 2016)

- Policy recommendations, no decisions

# Context

- **… request from the Belgian payer (RIZIV-INAMI)**
  - **Personalised medicine era**
  - **Large European study (PREPARE study - results 2023)**
  - **Technological evolution – panel testing**
  - **Belgian PGx interest group**

AS IS ➔ TO BE

# Methods

- **Online survey**
- **Contact experts**
- **Literature review (cost) - effectiveness**
- **International comparison**

# Interpretation of PGx

PharmacoGENETICS

Germline variations in the DNA

DNA coding for enzymes, transport molecules, immune reactions

Somatic variations (tumour)

Targeted medications

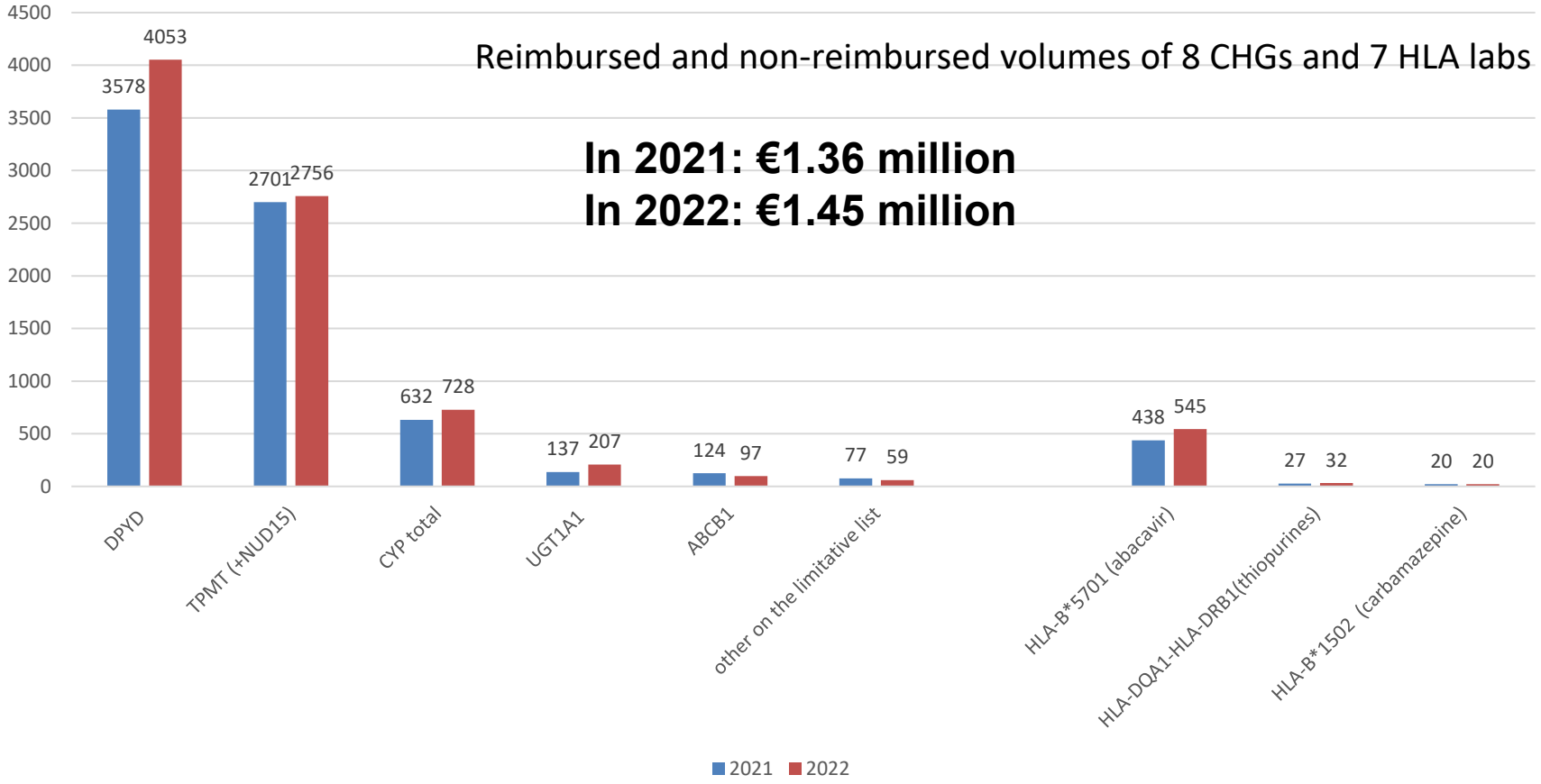
# Current Belgian situation

- **Reimbursement**
  - **+- 20 indications that are fully reimbursed**
    - **indications ≈ gene(s) to test**
    - **not always clear link with medications**
    - **Per indication a fee: 'simple' testing 185 euros - 'Complex' testing (> 1 gene, exons sequencing) 426 euros**
  - **No restriction in prescribers (physicians)**
  - **'Centralisation' of testing in 8 centres of human genetics (CHG) + approval of medical geneticist**
  - **Lab determines which technique/methodology used**

# Current Belgian situation

- **Peculiarity**
  - **Somatic panels performed on tumour tissue do have PGx targets included (DPYD, TPMT…)**
  - **HLA labs don’t have direct access to reimbursement**

# Number of tests per gene target




Source: KCE survey in 2023

# Which drug-gene to test?

- **Adoption of CPIC, RNPGx, DPWG?**



FARMACOGENETICA UPDATE


- **Recommendations produced by PGx expert consortia are often not reflected in clinical practice guidelines**
  - **Medical professionals unaware?**
  - **Or not convinced?**
  - **Alternatives available (phenotyping?)**

# Example of discrepancy

- **Clopidogrel for acute/chronic myocardial infarction**
  - **PGx guidelines: a MUST**

| Genotyping recommen-dation | Meaning | Gene-drug interactions with this recommendation |
|---|---|---|
| essential | Genotyping must be performed before drug therapy has been initiated. | Abacavir/HLA-B*5701<br>Azathioprine/NUDT15<br>Azathioprine/TPMT<br>Capecitabine/DPYD<br>Clopidogrel/CYP2C19, patients with a percutaneous coronary intervention, stroke or TIA<br>Fluorouracil,systemic/DPYD<br>Irinotecan/UGT1A1<br>Mercaptopurine/NUDT15<br>Mercaptopurine/TPMT<br>Simvastatin 80 mg/day/SLCO1B1<br>Tegafur + DPD-inhibitor/DPYD<br>Thioguanine/NUDT15<br>Thioguanine/TPMT |

  - **European Society of Cardiology**

- Whether platelet function testing or genetic testing to guide de-escalation of oral $P2Y_{12}$ receptor inhibitors after the first month of therapy following PCI improves clinical management and outcomes remains unclear.

    - **2023 ESC guidelines on AMI (Byrne et al 2023)**

# Which drug-gene to test?

- **Drug label (SmPC) = source of information**
  - **Several ‘locations’ in the SmPC**
  - **Formulation not standardized**

- **For some drugs, the testing requirement is explicitly stated in the drug label ~ companion diagnostic?**
  - **abacavir, siponimod, mavacantem and eliglustat**

# Evidence – RCTs?

➔ **RCT comparing PGx guided therapy and standard of care?**

| yes |
| --- |
| Abacavir – HLA : Predict- study |
| Clopidogrel – CYP2C9: TailorPCI and POPular Genetics |
| Antidepressants – CYP2C19 and CYP2C9: Guided-study |
| … |

| no |
| --- |
| Fluoropyrimidines – DPYD |
| Siponimod – CYP2C9 in drug label |
| Mavacantem – CYP2C9 in drug label |
| … |

**Bulk of evidence is based on association studies between a certain gene variant and a (surrogate) outcome**

➔ **Evidence base differs**

# PANEL- testing

- **While the technology is used in the labs, the clinical benefit is uncertain (the pre-emptive part of the panel)**
  - **Most studies do not run long enough to inform on effectiveness of pre-emptive part**
  - **Is the 'extra' cost justified?**
  - **Is the information stored and shared correctly so other prescribers can 'easily' access it?**
  - **Did the patient consent to have multiple targets tested?**
  - **The TAT issue can be resolved**

# PANEL- testing - International context

- **The (semi)-preemptive PGx strategy is not reimbursed by national health insurance in examined countries**
- **semi-preemptive = run a panel when there is an indication to test at least one gene (of the panel)**
  - **HAS is evaluating whether NGS gene panels should be included in the official nomenclature → 1 year process – specific data-collection**
  - **In the Netherlands only in selected supplemental health insurance plans**
- **Research context in EU**
  - **PROGRESS study in UK (primary care) – a lot of preparing IT**
  - **Personalised therapeutics study in Leiden (hospital)**
  - **…**

# Recommendations

- **Guidelines**
  - **Define the need for PGx with the clinical field**
  - **Transparancy on evidence**
- **PGx as part of the clinical pharmacology (e.g. phenotyping)**
- **Standardised SmPC**

# Recommendations

- **Access to results is important**
  - **Turnaround time**
  - **Electronic patient record - Avoid repetition**

# THANK YOU

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Full report:
https://kce.fgov.be/en/pharmacogenetic-tests-in-belgium