Using Personal (Pharmaco) Genomic Data within Primary Care: Two Mixed-Method Studies for Stakeholder Engagement of the Personal Genetic Locker

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OVERVIEW

The first study evaluates stakeholders' perspectives, including healthcare users and professionals, on personalized genomic medicine and the Personal Genetic Locker (PGL), a personal health data space (PHDS). A mixed-methods design (surveys, interviews, focus groups) was used. Several meta-themes were generated (i) Participants were interested in genomic information, (ii) Participants valued data control, robust infrastructure, and sharing data with non-commercial stakeholders. (iii) Autonomy was a central concern for all participants. Identified limits to individual autonomy included obligations towards others and healthcare professionals' duty to prevent medical harm. (iv) Relatedly, institutional and interpersonal trust is highly significant for genomic medicine.

In the second study we piloted a PGL in a hospital setting. This pilot also had a mixed-method design (using surveys and interviews in combination with a demonstration of the pilot) for the use of a PGL for pharmacogenetics perceived as added value by the medical professionals: (i) The PGL application itself makes the translation of pharmacogenetic standards into a format usable by prescribers. (ii) Knowledge from outside the organization (in this case following themes were seen in the field of pharmacogenetics) can be applied within the local clinical process. (iii) The information within the application can also be used within the electronic health record of the patient. The solution thus connects to existing developments and environments. During the study, point 2 was especially seen as an important development, since knowledge from outside of the hospital (such as pharmacogenetics knowledge) can be used in daily medical practice. **To conclude, we formulate recommendations based on the opinions of a diverse set of stakeholders for implementing genomic medicine in the Belgian and Dutch healthcare context as it relates to EU personalized health and health data strategies**. This study should be repeated within the primary care setting to be able to formulate recommendations in this particular setting.

METHODS

Study I: Stakeholders' perspectives on PHDS and genomic medicine.

- Collaboration VITO and University of Antwerp (**IAM Frontier**) and Leiden University Medical Center (LUMC) (**PGL**).
- **IAM Frontier**: Longitudinal precision medicine feasibility study aiming to define and investigate the implementation of personalized health profiles.
- **PGL**: Personal Genetic Locker project that aims to define standards and prototypes for a safe environment where individuals can store, view, and interpret their personal genetic data in a personal health data space.
- **Design: Mixed-Methods**
  - **Interviews** (VITO, UA): in-depth semi-structured interviews with healty volunteers (N=6).
  - **Surveys** (VITO, UA): healty volunteers (N=30).
  - **Focus groups** (LUMC): one focus group with healthcare users (N=6) and one focus group with healthcare professionals (N=4).
- **Data anlysis:** Thematic analysis (coding reliability and reflexive TA).
- **Triangulation** between datasets for broader, richer stakeholder perspectives.

Study II: Pilot on stakeholders' perspectives on applying PGx in hospital setting.

- Collaboration between 4MedBox, Isala hospital and University Medical Center Groningen.
- Implementation of a **PGL** for the use of **pharmacogenetic data** for prescription of colon cancer medication.
- **Design: Mixed-Methods**
  - **Survey** (Isala, UMCG): healthcare professionals (N=25) in Isala filled in a survey to better understand the way they use pharmacogenetics.
  - **User-Experience interviews** (Isala, 4MedBox, UMCG)**:** Studying the way a prescribing medical professional can easily use pharmacogenetic data in their day-to-day care (using 10 virtual patients).

PERSONALIZED MEDICINE - OPPORTUNITIES

PERSONALIZED MEDICINE

- Involves the physician considering family history, genetics and pharmacogenetics in daily clinical practice.
- Access to an individual's genetic and pharmacogenetic makeup source of personalized data, will support to:
  - Define the nature of a disease, predictability of risk of disease.
  - Find most effective treatment for a particular patient, in order to avoid ineffectiveness and unexpected side effects.
  - Administer treatment regimens that are personalized and adapted to each person's genetic makeup.
  - Pre-symptomatically diagnose and discuss individualized treatment plans.

PHARMACOGENOMICS

- Pharmacogenomics: clinical application of personalized medicine.
- Aims to optimize drug treatment by personalizing the dose and drug selection based on genetic variation that is causal for the variability in drug response.
- To help primary care physicians (PCPs) and pharmacists with the interpretation of a pharmacogenomic test result, the Dutch Pharmacogenetics Working Group (DPWG) and the Clinical Pharmacogenetics Implementation Consortium (CPIC) have developed pharmacogenomics (PGx) guidelines.
  - Evaluated over 100 gene–drug interactions and provided therapeutic recommendations for ~50 drug–gene pairs.
  - However, applicability is limited by relatively low numbers of patients that have their pharmacogenetic test results.
  - First attempts to implement pharmacogenomics into a decision support system have been made by the industry and will be taken into account.

COMBINING FAMILY HISTORY AND GENETICS

- 2-5 times higher risk for patients with a family history of diseases such as asthma, Chronic Obstructive Pulmonary Disease (COPD), diabetes, cardiovascular diseases or various types of cancers (including prostate cancer, ovarian cancer, melanoma, breast cancer and colon cancer.
- Clinical phenotyping by taking the family history is a useful, low-cost and easy tool for pre-symptomatic risk assessment for multiple common chronic diseases in daily primary care practice.
  - Potential to early prevention of these diseases and their monogenetic disease equivalents Family history and genetic test results will provide even better risk prediction.
  - Find, inform and treat unaffected family members pre-symptomatically.
- Clinicians recognize an urgent need for competence in recording family history data and in the registration of a family history questionnaire in the Electronic Health Record (EHR).

PERSONAL GENETIC LOCKER

The Personal Genetic Locker (PGL) project proposed a digital infrastructure that allows individuals to control their own health data, understand the health implication, add their own health-related information and consent to, or prevent, sharing with treating physicians and/or use for research projects.

The Isala hospital provided the following use-case to validate the architecture of the infrastructure against.

"*A patient visits a peripheral hospital (ISALA hospital) for treatment of colorectal cancer with one of the drugs with pharmacogenetic indication (e.g. 5-Fluorouracil). The specialist orders genetic test (at LUMC, standard pharmacogenetic profiling): a personal locker containing the pharmacogenetic data is prepared and the patient is given access to the locker. The patient authorizes the specialist to access the genetic data contained in their locker and the specialist adjusts the drug dosage according to the pharmacogenetic guidelines. Genetic counselling for pharmacogenetics will be available in ISALA for the local participating patients and their relatives through partner University Medical Centre (UMC) Groningen.*"

UMC Groningen was also interested in the literacy of prescribing doctors in the Isala hospital regarding pharmacogenetics and thus used a questionnaire that was previously created for research in the UMC (doi: 10.3390/jpm10040293), to better understand the situation in the Isala hospital.

PERSONALIZED MEDICINE - CHALLENGES

DIRECT IMPACT BETWEEN MEDICAL CARE AND ACADEMIC RESEARCH

- Findable, Accessible, Interoperable, and Reusable (FAIR) data: immediately available, prepared for reuse.
- If genetic data for a patient have already been generated we could than readily link personal data to the study of possible genetic associations.
- To increase the adoption rate of such an intricate and complex system, one must actively search for feedback from primary care professionals, researchers, and also the general public.

PROVIDING DATA TO THE PRIMARY CARE PROFESSIONAL

- No mechanisms to store the data collected by patients (e.g., commercial tests), and there is no system for viewing, interpreting, and sharing these data.
- New data sources requires primary care professionals to spend time and effort on understanding and interpreting the data, which reduces time available to provide care to those that need it.
- Many obstacles are encountered upon implementation of such a system.

CONTEXTUAL KNOWLEDGE

- **Contextual information is essential. Holistic approach is needed in research and clinical setting**.

PRIVACY AND ETHICS

- The increasing need for **sharing genomic data for research and clinical purposes escalates the tension between genomic privacy and openness**.
- On the one hand, the information is needed to provide medical care or perform genomic research; on the other hand, **the information is directly correlated to an individual and therefore is private information.** These concerns are also reflected in the European Union's proposal for the **European Health Data Space** (EHDS) as a key pillar of its health (data) strategy.
- To mitigate concerns on persisting data asymmetries within the current EHDS proposal, several **Personal Health Data Space** projects (including PGL in the Netherlands and We Are in Belgium) are being developed to **enhance individual agency over data management**.

KEY FINDINGS

Study 1: Stakeholders' perspectives on PHDS and genomic medicine

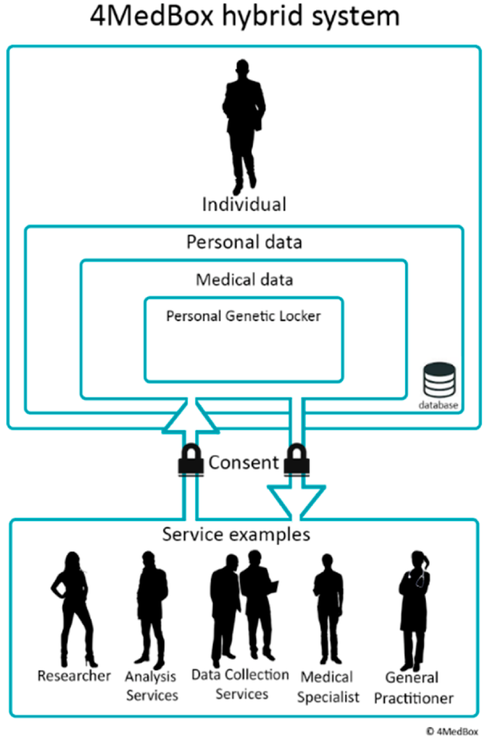
- Participants were generally interested in receiving genomic information.
- Participants value **data control** and robust, safe infrastructure.
- Participants are generally willing to **share data with family, researchers and HCPs.**
- **Autonomy** is highly valued across domains, but participants recognize its **limits**.
- Institutional **trust**, trust in science and interpersonal trust, are crucial considerations for genomic medicine.
- Navigating between the duty of care (i.e., healthcare professionals' responsibility to prevent harm) and patient autonomy is a central challenge for pharmacogenomic medicine, PGL makes it usable.
- Participants encourage the implementation of the Personal Genetic Locker (PGL), a safe, user-friendly, interoperable digital environment in which individuals can store, view, and interpret their genomic information.
- The PGL is thought to facilitate the use of genomic data and empowers patients to be in control over their data.

Study 2:The following themes were described as important reasons for attractiveness for the PGL for pharmacogenetics in the hospital setting

- The PGL application itself translates **pharmacogenetic** standards into a format that is usable by prescribers
- **Knowledge** from outside the organization (in this case in the field of pharmacogenetics) can be **applied within the local clinical process**
- Information within the application can also be used within the electronic health record (EHR). Thus, the solution connects to existing developments and environments

FIGURE 1

The interaction in the 4MedBox system between an individual and examples of possible medical services an individual can use. The image visualizes control over the data by the individual by giving consent.



FINDINGS: ADOPTION

- Publics recognize benefits genetic research.
- Major concerns regarding the **Ethical, Legal, and Social Implications (ELSI)** involve topics such as consent, disclosure, data sharing, privacy, and confidentiality.
- Since the individual's needs and choices are the core of the PGL, we involved future individual users in the developmental process as early as possible to match the PGL to the stakeholders' needs and wishes and to take their concerns into consideration.
- Prescribing doctors have to be taken into account on an early stage during the development of the user-experience of a PGL that is used in a daily medical practice.
- Not all prescribing doctors have the needed knowledge about pharmacogenetics to be able to use it in day-to-day care. The Decision Support System used in clinical decision making needs to provide insights that the prescriber understands in the limited time they have, while being transparent in how they got to that decision.

FINDINGS: ETHICS

Our study highlights several stakeholder-informed ethically significant contentions informative for ongoing debates on data management in genomic medicine.

- Despite the ubiquity of ownership rhetoric in genomic medicine, participants' concerns about genomic data management were better captured in terms of ***data control***.
- With regards to **autonomy**, participants often stressed the **individuals' choice** in genome sequencing and data control.
- Despite this emphasis on autonomy, participants often admitted to **limits to individual autonomous choice**, including (i) the **asymmetry** in (clinical) care relations, (ii) negotiating between the **sensitivity and usefulness** of medical data, (iii) the lack of **genetic literacy** in the general population, and (iv) (moral) **obligations towards others.**
- Our findings suggest that in a healthcare climate dominated by technological (and biological) complexities, a **trusting**, **transparent** and **enabling** infrastructure (through regulatory, competency, and accountability structures) are necessary to garner a form of ***reflexive, active trust*** as a precondition for decision-making.

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