Using ‘real world’ data to enhance medication safety during pregnancy: towards a ‘fit-for-purpose’ registration system on maternal medication use and mother-infant outcomes (BELpREG)

A Data Management Plan created using DMPonline.be

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Project abstract:

Evidence on medication safety in pregnancy is lacking for most products, despite their frequent use. As randomized controlled trials cannot be performed in this population, opportunities of ‘real-world’ data collection for pharmacoepidemiologic research should be fully exploited. In 2021, a prototype of a comprehensive registration system on maternal medication use and mother-infant outcomes (BELpREG) was developed at KU Leuven, allowing data entry by women. Although the prototype was tested ‘in-house’, pilot-testing ‘in real-life’ and subsequent modifications are pivotal to result in a robust research instrument, ready for large-scale implementation. This FWO project focuses on the feasibility assessment and validation of the BELpREG prototype. During a pilot period, data completeness, correctness, representativeness of the sample, and women’s / healthcare professionals’ (HCPs) experiences with data entry / recruiting women will be assessed (WP 1). In WP 2, additional features to the BELpREG system will be explored, including data registration by HCPs, long-term data collection on infant development and linkage with external databases. In WP 3-4, ‘use cases’ based on BELpREG data will be performed for hypothesis-generating (‘drug utilization studies’) (WP 3) and hypothesis-testing purposes (‘analytic pharmacoepidemiology’) (WP 4). This will eventually result in a ‘fit-for-purpose’ system, ready to contribute to increasing the knowledge on medication safety in pregnancy.

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Application DMP

Questionnaire

Describe the datatypes (surveys, sequences, manuscripts, objects …) the research will collect and/or generate and /or (re)use. (use up to 700 characters)

Personal and health-related data will be online registered by women in the BELpREG data registration system, using REDCap as data capturing and management system and stored on a separate KU Leuven server. The BELpREG data will be compared with data collected from medical/obstetric records. Quantitative and qualitative data on the feasibility of the BELpREG registration system will be obtained from women and healthcare professionals by using surveys, semi-structured interviews and focus groups.

Specify in which way the following provisions are in place in order to preserve the data during and at least 5 years after the end of the research? Motivate your answer. (use up to 700 characters)

Although BELpREG principal investigator Prof. Veerle Foulon is ultimately responsible for data storage, I will also apply good data management, including data collection, processing, and storage. Therefore, I followed a workshop on Research Data Management (RDM) in 2021. Close collaboration with external legal consultants (Allen&Overy) and the KU Leuven Data Protection Officer is pursued to (continue to) meet legal data preservation requirements. The BELpREG data(base) will be stored on separate KU Leuven servers according to the applicable terms. Multifactor authentication is always required to log in to the REDCap database.

What’s the reason why you wish to deviate from the principle of preservation of data and of the minimum preservation term of 5 years? (max. 700 characters)

There is no reason to deviate from the minimum data preservation term of 5 years.

Are there issues concerning research data indicated in the ethics questionnaire of this application form? Which specific security measures do those data require? (use up to 700 characters)

Not applicable.

Which other issues related to the data management are relevant to mention? (use up to 700 characters)

The privacy statement of the BELpREG registration system is available (in Dutch) on the BELpREG website: https://belpreg.be/privacyverklaring/. Only data without patient identifiers will leave the BELpREG database. Specific (limited) database rights will be defined for the BELpREG steering committee members. The applicable guidelines regarding authorship will be applied throughout the entire FWO project.

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DPIA

DPIA

Have you performed a DPIA for the personal data processing activities for this project?

- Yes

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GDPR

GDPR

Have you registered personal data processing activities for this project?

- Yes

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FWO DMP (Flemish Standard DMP)

1. Research Data Summary

List and describe all datasets or research materials that you plan to generate/collect or reuse during your research project. For each dataset or data type (observational, experimental etc.), provide a short name & description (sufficient for yourself to know what data it is about), indicate whether the data are newly generated/collected or reused, digital or physical, also indicate the type of the data (the kind of content), its technical format (file extension), and an estimate of the upper limit of the volume of the data.

	Only for digital data	*Only for digital data*	*Only for digital data*	*Only for physical data*			
Dataset Name	Description	New or Reused	Digital or Physical	Digital Data Type	Digital Data Format	Digital Data Volume (MB, GB, TB)	Physical Volume
BELpREG dataset on perinatal medication use and mother-infant outcomes (Dataset 1)	Pregnant woman prospectively register data on maternal medication use and mother-infant outcomes using online data registration forms in REDCap. They are followed up during pregnancy and in the first 8 weeks postpartum. Optional extension of the database: registration of some variables by HCPs in BELpREG, long-term data collection on infant development (after 8 weeks postpartum) (see WP 2).	☒ Generate new data ☐ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☒ .xml ☐ .tab ☒ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☒ other: REDCap ☐ NA	☐ < 100 MB ☐ < 1 GB ☐ < 100 GB ☒ < 1 TB (100GB) ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA The volume of the ‘infrastructure’ included (i.e. the REDCap data registration system).	
User’s experiences – survey (Dataset 2)	Survey data on user’s experiences collected in Qualtrics	☒ Generate new data ☐ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☐ .xml ☐ .tab ☒ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☐ other: ☐ NA	☒ < 100 MB ☐ < 1 GB ☐ < 100 GB ☐ < 1 TB ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA	
User’s experiences – interviews (Dataset 3)	Transcripts of interviews with BELpREG participants	☒ Generate new data ☐ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☐ .xml ☐ .tab ☐ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☒ other: .docx ☐ NA	☒ < 100 MB ☐ < 1 GB ☐ < 100 GB ☐ < 1 TB ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA	
Experiences of HCPs – interviews (Dataset 4)	Transcripts of interviews with HCPs	☒ Generate new data ☐ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☐ .xml ☐ .tab ☐ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☒ other: .docx ☐ NA	☒ < 100 MB ☐ < 1 GB ☐ < 100 GB ☐ < 1 TB ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA	

Pregnancy and fetal-maternal outcome and other health data (Dataset 5)	For a maximum set of 200 BELpREG participants pregnancy and fetal-maternal outcome and other health data will be registered in Qualtrics by their physicians and/or midwives as part of the validation study (WP 1).	☒ Generate new data ☐ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☐ .xml ☐ .tab ☒ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☐ other: ☐ NA	☒ < 100 MB ☐ < 1 GB ☐ < 100 GB ☐ < 1 TB ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA	
Pooled dataset for a collaborative perinatal pharmacoepidemiologic study (Dataset 6)	BELpREG data anonymously pooled with organizations within ENTIS (i.e., European Network of Teratology Information Services)	☐ Generate new data ☒ Reuse existing data	☒ Digital ☐ Physical	☒ Observational ☐ Experimental ☐ Compiled/ aggregated data ☐ Simulation data ☐ Software ☐ Other ☐ NA	☐ .por ☐ .xml ☐ .tab ☒ .csv ☐ .pdf ☐ .txt ☐ .rtf ☐ .dwg ☐ .tab ☐ .gml ☐ other: ☐ NA	☐ < 100 MB ☐ < 1 GB ☒ < 100 GB ☐ < 1 TB ☐ < 5 TB ☐ < 10 TB ☐ < 50 TB ☐ > 50 TB ☐ NA	

If you reuse existing data, please specify the source, preferably by using a persistent identifier (e.g. DOI, Handle, URL etc.) per dataset or data type:

Pooled BELpREG data for a collaborative perinatal pharmacoepidemiologic study (dataset 6): The possibilities of pooling international data with BELpREG data will be explored in this project. Linkages with databases of organizations within ENTIS (i.e., European Network of Teratology Information Services) will be explored; the specific sources cannot be defined yet since this will only be clear in a later phase of the project.

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? Describe these issues in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes, human subject data

The BELpREG project was approved by the ethics committee UZ / KU Leuven (S66464).

Will you process personal data? If so, briefly describe the kind of personal data you will use in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes

The BELpREG register (dataset 1) will collect the following data from pregnant women: Contact information (e-mail address), Sociodemographic characteristics, Maternal-obstetric history data, Data on medication use and use of other substances, Data on the current pregnancy, Pregnancy and Neonatal outcomes.
The user's experiences survey will collect data on age, place of residence (province), level of education, previous pregnancy(s), pregnancy trimester and how often a BELpREG questionnaire has already been completed. (dataset 2)
Personal data such as relevant sociodemographic characteristics of women and caregivers participating in an interview/focus group discussion will be collected (dataset 3, 4).
The validation study will ask doctors/midwives the following data on specific women from dataset 1 (dataset 5): Data on the course of the pregnancy, Data on delivery, Data on maternal and child health.
A privacy check was performed as part of the ethical approval and registered with number G-2022-4692 in the PRET registry. Further, the BELpREG privacy statement can be found on the study website: https://belpreg.be/privacyverklaring/. The informed consent for participation in the BELpREG register can be downloaded from the study website: https://belpreg.be/informatie-voor-deelnemers/.

Does your work have potential for commercial valorization (e.g. tech transfer, for example spin-offs, commercial exploitation, …)? If so, please comment per dataset or data type where appropriate.

- Yes

The BELpREG data (dataset 1) has the potential to be shared, on an aggregated level, with for-profit organizations (contract research, fee-for-service): data collection by BELpREG can offer pharmaceutical companies a less expensive/time-consuming alternative to setting up (regulator-mandated) drug-specific pregnancy registries to collect pharmacovigilance data, thereby reducing companies' burden. When data are shared, this will always be done in line with an agreement framework in which the recipient agrees never to try to find out which individual may be behind the data.
See our privacy statement on the study website: https://belpreg.be/privacyverklaring/

Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material/Data transfer agreements/ research collaboration agreements)? If so, please explain in the comment section to what data they relate and what restrictions are in place.

- No

Research collaboration agreements may apply for data pooling with other (international) databases (dataset 6).
In case of linkage of BELpREG data with other existing databases in Belgium (i.e., creating a new dataset), agreements will be signed and the DMP will be completed accordingly.

Are there any other legal issues, such as intellectual property rights and ownership, to be managed related to the data you (re)use? If so, please explain in the comment section to what data they relate and which restrictions will be asserted.

- Yes

In case the collected (BELpREG) data (dataset 1) will be shared with pharmaceutical companies or other parties, an agreement shall be signed.

2. Documentation and Metadata

Clearly describe what approach will be followed to capture the accompanying information necessary to keep data understandable and usable, for yourself and others, now and in the future (e.g., in terms of documentation levels and types required, procedures used, Electronic Lab Notebooks, README.txt files, Codebook.tsv etc. where this information is recorded).

The BELpREG data (dataset 1) are collected using REDCap software. In REDCap, the data dictionary can be found: this is a spreadsheet in CSV format representing the structure of the database, allowing the reproduction of the data collection instruments. Further, when extracting data (without identifiers) from REDCap, the codebook will also be extracted to link the variable names with the 'field labels' and 'choice labels'. When the data in REDCap need to be edited, this is only done in accordance with the data manipulation standards as defined by and shared within the research team. The manipulation standards are stored on the KU Leuven One Drive for Business service. Recently, we also published a (preprint) paper describing the design and development of the BELpREG system, including a list of all BELpREG variables as supplementary material (https://doi.org/10.1101/2023.03.01.23286625)

Will a metadata standard be used to make it easier to find and reuse the data? If so, please specify (where appropriate per dataset or data type) which metadata standard will be used. If not, please specify (where appropriate per dataset or data type) which metadata will be created to make the data easier to find and reuse.

- Yes

In the BELpREG register (dataset 1), some variables are collected using metadata standards. This is the case for names of medicinal products (ATC classification, through the SAM database), underlying medical conditions and indications of medication use (ICD-11 and MedDRA) and some sociodemographic variables (postal and NATO codes). For the other variables, the codebook will be used as metadata.

3. Data storage & back-up during the research project

Where will the data be stored?

To ensure the security of the BELpREG data collected in REDCap (dataset 1), the BELpREG database (and backup) are being hosted on a separate KU Leuven server (separate from other REDCap projects). Only pseudonymised data (no identifiers) will be extracted from REDCap and stored on KU Leuven Business One Drive cloud services.
Responses to the user's experiences survey (dataset 2) are collected on the Qualtrics platform, which meets the highest standards of data security and protection (https://www.qualtrics.com/platform/security/ and https://www.qualtrics.com /security statement/). During the data collection period, these data are stored on a European server (Frankfurt). At the end of the data collection, data are extracted and removed from Qualtrics and will be stored on KU Leuven Business One Drive cloud services.
Anonymised / pseudonymised datasets (dataset 2-6) will be stored on secured KU Leuven Business One Drive cloud services. Regarding datasets 3-5, the document with the key for the study codes will be password protected and saved on the personal One Drive storage of the principal investigator.

How will the data be backed up?

The BELpREG data (dataset 1) that are collected in REDCap follow the standard back-up procedures of KU Leuven gbiomed ICTS (with Gert Goos as REDCap administrator). For all other data, which are stored on KU Leuven Business One Drive cloud services, automated backups are made by KU Leuven ICTS following their standard procedures.

Is there currently sufficient storage & backup capacity during the project? If yes, specify concisely.
If no or insufficient storage or backup capacities are available, then explain how this will be taken care of.

- Yes

The KU Leuven Business One Drive cloud storages allow storage of data up till 2TB, the BELpREG server currently allows up till 100GB (which can be enlarged when needed).

How will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

BELpREG data (dataset 1) are stored using REDCap, which is compliant with KU Leuven data security standards, and requires a multi-factor authentication procedure to gain access. Only authorized users with fixed roles (user rights) have access to the database; only Veerle Foulon, Michael Ceulemans and Laure Sillis have full access to all data collected in the database. The BELpREG user rights are managed by the Clinical Trial Center (CTC). Access to REDCap (records) is automatically logged and changes to the data are stored in independent audit trails. The BELpREG server and REDCap software are frequently upgraded according to the procedures of ICTS gbiomed.
The user experiences survey data (pseudonymized - dataset 2) are collected using Qualtrics, which also requires a multi-factor authentication procedure to gain access. In the validation study (dataset 5), physicians and/or midwives will receive patient identifiers and study code via the Belnet Filesender (encrypted) and will register data in Qualtrics by using the BELpREG study code of patients.
Datasets 2-6 will be stored on the password protected cloud service of KU Leuven Business One Drive; computers will be used which can only be accessed by using a login and password. A clean desk policy will be followed: no papers potentially containing personal data will be left unattended and visible. Screens of laptops will be locked when left unattended.

What are the expected costs for data storage and backup during the research project? How will these costs be covered?

The cost for the virtual REDCap server, including the server storage (100GB), is €287 + €50,37 / year. This cost is currently covered by the available project funding of the BELpREG project (C3/20/095).
KU Leuven Business One Drive cloud services are free for KU Leuven employees (the given free storage capacity is sufficient for this project).

4. Data preservation after the end of the research project

Which data will be retained for at least five years (or longer, in agreement with other retention policies that are applicable) after the end of the project? In case some data cannot be preserved, clearly state the reasons for this (e.g. legal or contractual restrictions, storage/budget issues, institutional policies...).

The collected data (dataset 1-6) are stored for 25 years, as recommended by EC UZ / KU Leuven for studies that fall under under the Belgian Law of 7 May 2004 on Experiments on the Human Person. After this period, the data will be destroyed if it is no longer needed for research purposes.

Where will these data be archived (stored and curated for the long-term)?

The generated research data, metadata and documentation necessary to reuse the data will be transferred to the K-drive for long-term data archiving, managed by KU Leuven gbiomed ICTS. The BELpREG data (dataset 1) stay as long as the BELpREG project continues on the secured REDCap server, before being transferred to the K-drive.

What are the expected costs for data preservation during the expected retention period? How will these costs be covered?

The price of the K-drive (100Gb) is €11,38 per year, but the Group Biomedical Sciences sponsors 50% of this cost price.
The cost for the storage of the BELpREG data (dataset 1) is €287 + €50,37 / year (cost for the virtual server including the server storage (100GB)).
Costs will be covered by the research group.

5. Data sharing and reuse

Will the data (or part of the data) be made available for reuse after/during the project? In the comment section please explain per dataset or data type which data will be made available.

- No (closed access)

If access is restricted, please specify who will be able to access the data and under what conditions.

Not applicable.

Are there any factors that restrict or prevent the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)? Please explain in the comment section per dataset or data type where appropriate.

- Yes, Privacy aspects
- Yes, Intellectual Property Rights

Sharing of the data can only be done in accordance to the privacy statement and informed consent, these can be found on the study website: https://belpreg.be/privacyverklaring/ and https://belpreg.be/informatie-voor-deelnemers/.
According to the privacy statement and informed consent, the coded BELpREG data (dataset 1) may be shared with 3rd parties such as Belgian or other regulatory authorities, and with the ethics committees and/or institutions and organizations collaborating with the researchers. The BELpREG data can also be shared in aggregated form with for-profit organizations. When data are shared, this will always be done in line with an agreement framework, which is still under development in collaboration with KU Leuven LRD, and which will be tailored to the type of data sharing (i.e., non-profit or for-profit organization). For collaborative research projects (dataset 6), data sharing will only be done in line with the applicable agreements.

Where will the data be made available? If already known, please provide a repository per dataset or data type.

The researchers will publish the findings resulting from the BELPREG research in national and/or international (specialist) journals, which will be highlighted on www.belpreg.be, including the reference of the publication (see Publications: https://belpreg.be/publicaties/). Data as part of published results will be shared (when applicable) using the supplementary material.
In case of collaborative research studies (dataset 6), further agreements on the sharing of the joint research data will be made.

When will the data be made available?

Upon publication of the research results.

Which data usage licenses are you going to provide? If none, please explain why.

The BELpREG data as such (dataset 1) will not be shared in a repository. In case of a publication, the licence for access of the data (as part of the supplementary material or appendices) will correspond to the licence of the related publication. Open access publications will be pursued as much as possible.

Do you intend to add a PID/DOI/accession number to your dataset(s)? If already available, you have the option to provide it in the comment section.

- No

All publications will have a DOI. The DOI will also refer to the shared data as part of the supplementary material or appendices of the publication.

What are the expected costs for data sharing? How will these costs be covered?

No (large) costs are expected for data sharing.

6. Responsibilities

Who will manage data documentation and metadata during the research project?

The PhD researcher (Laure Sillis) will be responsible for day-to-day data management, under supervision of Michael Ceulemans. The main supervisor (Veerle Foulon) will be responsible for data documentation and metadata in the long term.

Who will manage data storage and backup during the research project?

The PhD researcher (Laure Sillis) will be responsible for day-to-day data management, under supervision of Michael Ceulemans. The main supervisor (Veerle Foulon) will be responsible for data documentation and metadata in the long term.

Who will manage data preservation and sharing?

Veerle Foulon and Michael Ceulemans will be responsible for data preservation and sharing, in collaboration with Laure Sillis.

Who will update and implement this DMP?

The PhD researcher (Laure Sillis) will be responsible for updating and implement this DMP in day-to-day data management. The supervisors (Veerle Foulon and Michael Ceulemans) bear the end responsibility for updating and implementing this DMP.