TIMESPAN

Management of chronic cardiometabolic disease and treatment discontinuity in adult ADHD patients

H2020 – 965381

D7.1. – Report on Ethics Monitoring Strategy

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Abbreviations

WP	Work Package
GDPR	General Data Protection Regulation
EDMB	Ethics and Data Management Board
EDAC	Ethics and Data Advisory Committee
GA	General Assembly
EC	European Commission
AA	Ad hoc advisor
AU	Aarhus University
UiB	University of Bergen
UCL	University College London

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1. Executive Summary

The main important objective of D7.1. Report on Ethics Monitoring Strategy is to ensure compliance with the 'ethics requirements' set out in this work package. This work package sets out the 'ethics requirements' that the project must comply with.

In case of further processing of previously collected personal data, an explicit confirmation that the beneficiary has lawful basis for the data processing and that the appropriate technical and organisational measures are in place to safeguard the rights of the data subjects must be submitted as a deliverable. The beneficiary must evaluate the ethics risks related to the data processing activities of the project. This includes also an opinion if data protection impact assessment should be conducted under Art 35 General Data Protection Regulation (GDPR) 2016/679.

This task follows an interdisciplinary research approach and consists of various methodical components. Therefore, it needs a clear description of available data and the intended personal data processing. For all data used in TIMESPAN we will closely monitor the ethical approvals and approvals for data access. This accounts for all already existing cohorts but also for the newly collected data set located in WP5 (The ART-CARMA study).

This detailed description is required to further assess the legal and ethical risks and consequences for the further impact assessment in the project.

Within D7.2. we will clearly describe the data management within TIMESPAN therefore we would like to refer to D7.2. for all data management related issues.

2. Deliverable report

Ethical questions deal with the preconditions and the evaluation of basic human attitudes and human action, critically reflecting on specific moral action. Ethics is not only concerned with applicable morals in a society, but strives to adopt a superordinate and critical standpoint that aims for general validity.

The ethical frame of reference for TIMESPAN is based on the fundamental question of the extent to which we are dealing with just, reasonable and meaningful attitudes and actions that contribute to a good life or at least do not contradict it.

Within this deliverable report we will present our planned ethics monitoring strategy, ethical risks and how we are planning to monitor them on a regular basis.

In order to ensure a proper handling of the personal data used (WP1, 2, 3, 4 and 6) and generated (WP5) within TIMESPAN we have established an extra Work Package (WP) on Ethics and Data Management in the project (WP7). The overall objective of this WP is to develop an overarching ethical strategy addressing information use from the existing databases, but also for newly generated data as part of WP5. This will be an on-going process, particularly with the GDPR as different Member State follow different interpretations and implementations resulting in different storage and access procedures. We will involve ethics experts in decisions that relate to clinical protocols, assessments and data analysis to ensure the highest ethical standard possible.

At the start of the project we have establish an Ethics and Data Management Board (EDMB) including senior members of each partner of the consortium. The function of the board is to oversee the implementation of the Ethics and Data management plan (D7.2). The EDMB will be supported by the Ethics and Data Advisory Committee (EDAC, which is comprised of external members). The EDAC is an advisory committee to provide expert advice to EDMB. This board will advise on Ethics and Data Management work issues, such as GDPR. It will review the Data Management Plan (D7.2.) and provide feedback in case of concerns. In addition, it will also consider and mention any ethical issue which

might require (stronger) attention and will be informed about possible recommendation provided in the course of an ethics review.

The EDMB will meet at the General Assembly (GA) meetings and discuss any issues ad hoc via telephone conferences if this is needed. The Board will implement an ethical review and monitoring process to ensure proper conduct of all partners over time, which includes the compiling of Ethics Monitoring Reviews every 18 months. The EDAC members will be invited to the GA meetings to join the discussions and will mention any ethical issues which might require (stronger) attention in their feed-back. They will further receive the Periodic Reports of TIMESPAN and be informed about possible recommendations provided in the course of an EC ethics review.

Below you can find a list of the members of those two ethics monitoring boards:

Ethics and Data Management Board (EDMB)

- Ditte Demontis (P3 AU)
- Kari Klungsøyr (P4 UiB)
- Ian Wong (P9 UCL)
- Stephanie Witt (Ad hoc Advisor (AA))
- Ulrich Muller-Sedgwick (AA)

Ethics and Data Advisory Committee (EDAC)

- Stephanie Witt (AA)
- Ulrich Muller-Sedgwick (AA)
- Jonas Ludwigsson (AA)
- George Davey Smith (AA)
- Susannah Whitwell (AA)

Below you can find a list of all critical implementation risks and their mitigation actions. We have marked all ethical risks in grey. We will constantly monitor those risks throughout the project and act if this is needed.

Risk Number	Description of risk	WP Number	Proposed risk mitigation measures
1	Data access will not be granted	1,2,3,4,6,	Highly unlikely given that for each dataset we have experienced staff who have received data access for different research questions in the past. If this happens we still have widespread access to data from many countries with different health systems.
2	Data access will be later than planned	1,2,3,4,6,	The period between data access granted and analysis ready has purposely been planned with a buffer. In addition, researchers can work on the analysis plan without the data being accessible yet and thus

			start preparations while waiting for the approval.
3	Estonian biobank, Icelandic SAGA and UK biobank data already outside of collection are not financed by TIMESPAN so we don't control their timeline.	1	We have planned 6 extra months after the planned release date of these data to get access to the data. If the data release would for some reason be even more delayed we will start with the analyses of the register data. Moreover, the period between data access granted (month 15) and first delivery date (month 38) allows flexibility on which task is done first.
4	Harmonising data across sites may lead to loss of information	1	If absolutely necessary, we can use a country specific approach for our tasks if the information we would get out of a such analyses would be more valid or more important for the patients.
5	Delays in obtaining data	2,3	If delays are short, we will be able to catch up since algorithms and syntaxes for data analysis will be ready, and can be applied immediately. If delays are long, we will use data from the countries where data is available. This would only have a minor impact and the overall objective could still be reached.
6	Unexpected quality issues with the data	1,2,3,4,6,	If data lack the level of detail expected, analyses may be done on a less detailed level. If there are severe quality issues from one data source, these data will be eliminated. This would only have a minor impact and the overall objective could still be reached.
7	Problems defining a common data structure and analysis plan for joint publications	1,2,3,7	We will do joint analyses using crude definitions, and conduct local analyses using detailed information. This would only have a minor impact and the overall objective would still be reached.
8	Different levels of detail in information from the Prescription databases will make harmonization challenging	3	We will apply two definitions of treatment discontinuation; one crude where all databases can provide data and where the definition of clear treatment gaps or discontinued treatment will be possible. For countries with more detailed information on dosage, a more

			accurate definition will be applied, where treatment non-adherence and titration periods may also be defined.
9	Risk of access by unauthorized persons to genetic iPSYCH data. We will characterize this risk as almost non-existent	4,6	Access to of data is only possible with special permission by Statistics Denmark. Currently, the SUNY members of TIMESPAN have access via secure VPN so it is feasible.
10	Ethics approval is delayed	5	Ethics approval is currently being processed so any delays should be negligible.
11	Patients do not complete smartphone app questions	5	Involving parents and patients early in the study will minimize these issues as will use of smartphone reminders.
12	Technological redundancy	5	We are choosing technology which is backward and upward compatible.
13	Integration of Embrace-Plus with RADAR-base	5	We would use the E4 wearable device (earlier version of the EmbracePlus device) instead. The E4 device has already been integrated into the RADAR-base.
14	Invalid sensor signals	5	Maintain a generic platform not reliant on a single sensor.
15	Model cannot be programmed.	6	We would use alternative machine learning packages (e.g., R).
16	Models not sufficiently accurate.	6	Check learning curve diagnostics, add more features, reduce parameter space via feature pruning and/or aggregation, sparsify models

Next to our various ethics boards we have various ethics deliverables which will ensure a correct handling of data and ethical issues within TIMESPAN. Please see all ethic deliverables listed below.

- D7.1. Report on Ethics Monitoring Strategy – due month 3
- D7.2. Data Management Plan – due month 6
    - During the grant negotiation it has been addressed that ethical considerations in relation to AI applications are not thoroughly considered in the proposal and should be further developed in terms of fairness, discrimination, inequality, avoidance of harm, conflicts of autonomy, beneficence, non-maleficence, justice, the “black box” problem in AI, and accountability. We will focus on this issue in D7.2 but also in D7.4.
- D7.3. Repository of all ethics and access documents (human studies, incl. existing datasets) in the TIMESPAN intranet – due month 14
- D7.4. EBDM report (incl. EDAC feedback) on TIMESPAN ethics and data management implementation (incl. evaluation of independent ethics advisor) - due month 18

- D7.5. EBDM report (incl. EDAC feedback) on TIMESPAN ethics and data management implementation - due month 36
- D7.6. EBDM report (incl. EDAC feedback) on TIMESPAN ethics and data management implementation (incl. evaluation of independent ethics advisor) - due month 54
- D10.1. H - Requirement No. 1 – due month 12
    - The informed consent procedures that will be implemented for patients recruited to the prospective project study (templates of the informed consent/assent forms and information sheets language and terms intelligible to the participants)
    - Copies of approvals by ethics committees and/or competent authorities for the studies involving patients and healthy controls
- D10.2. POPD - Requirement No. 2 - due moth 14
    - The beneficiary must check if special derogations pertaining to the rights of data subjects or the processing of genetic, biometric and/or health data have been established under the national legislation of the participating EU countries where the research takes place and submit a declaration of compliance with respective national legal framework(s).
    - The host institution must confirm that it has appointed a Data Protection Officer (DPO) and the contact details of the DPO are made available to all data subjects involved in the research. For host institutions not required to appoint a DPO under the GDPR a detailed data protection policy for the project must be submitted as a deliverable.
    - Detailed information on the informed consent procedures in regard to data processing must be submitted as a deliverable.
    - Templates of the informed consent forms and information sheets (in language and terms intelligible to the participants) in regard to data processing must be submitted as a deliverable.
    - As the research involves profiling, the beneficiary must provide explanation how the data subjects will be informed of the existence of the profiling, its possible consequences and how their fundamental rights will be safeguarded.
    - The beneficiary must evaluate the ethics risks related to the data processing activities of the project. This includes also an opinion if data protection impact assessment should be conducted under art.35 General Data Protection Regulation 2016/679.
- D10.3. NEC - Requirement No. 4 – due month 15
    - copies of transfer authorisations, as required by national/EU legislation must be submitted.
- D10.4. Requirement No. 6 – due month 12
    - Details on measures to prevent misuse of research findings related to collection of data on antisocial behaviour through remote technology must be submitted.
- D10.5 POPD- Requirement No.8 – due month 6
    - A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants must be submitted as a deliverable.
    - A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing must be submitted as a deliverable.

In addition, we will also closely monitor the various aspects that have been raised during the grant negotiation.

- Within TIMESPAN we will ensure that the research conducted outside the EU is legal in at least one EU member state.

- Within our Data Management Plan, we will also specifically address the processing of sensitive personal data which is pseudonymized and falls under GDPR. More details can be found in D7.2. Data Management Plan (due in month6).
- Any AI related aspects will be further discussed in D7.2. and D7.4. (for details please see above).

3. Conclusion

We can conclude that due to the deliverables presented above but also the establishment of the EDAC and EDMB we are able to present a good ethics monitoring strategy through TIMESPAN. Given this constant monitoring throughout the project's lifespan we are able to monitor ethical aspects properly and will be able to detect problems at a very early stage and will apply mitigation measures in good time.