DMP title

Project Name Macronutrient restriction after major surgery and intermittent fasting in prolonged critical illness; impact on acute & long-term-functional outcomes, phosphate, carnitine and choline-homeostasis, muscular integrity and autophagy. - DMP title

Project Identifier 1832822N

Grant Title 1832822N

Principal Investigator / Researcher Michael Casaer

Project Data Contact michel.casaer@uzleuven.be 016348786

Description This DMP applies to my Senior Clinical Investigator Renewal, The main and first research project in this FWO-investigatorship is now initiated and is a post hoc determination of phopshate, carnitine metabolites and choline levels on serum samples from the ICU-FM (Van Dyck Crit. Care 2020) and EPaNIC (Casaer NEJM 2011) RCT's. It includes the ongoing EFECTS RCT (N 300) PI Hans Van Veer, detailed DMP has been submitted by the PI in the context of the TBM funding. The last part of the project , the prospective ICU-FM-PLUS-RCT (N 6930) will be informed by the results of the first work package. These 3 projects will all contribute to a better understanding and clinical application of (intermittent) nutrient restriction aimed at preserving & restoring homeostasis and promoting recovery of physical function in acute illness

Institution KU Leuven

1. General Information

Name applicant

Michael P Casaer

FWO Project Number & Title

FWO Project 1832822N

Macronutrient restriction after major surgery and intermittent fasting in prolonged critical illness; impact on acute & long-term-functional outcomes, phosphate, carnitine and choline-homeostasis, muscular integrity and autophagy.

Affiliation

- KU Leuven

2. Data description

Will you generate/collect new data and/or make use of existing data?

- Generate new data
- Reuse existing data

Describe in detail the origin, type and format of the data (per dataset) and its (estimated) volume. This may be easiest in a table (see example) or as a data flow and per WP or objective of the project. If you reuse existing data, specify the source of these data. Distinguish data types (the kind of content) from data formats (the technical format).

Vital parameters, drugs, nutrition and organ support administered, clinical outcome and premorbid data are analysed for translational, efficacy and safety. All clinical data is collected manually or automatically into CRF’s constructed in Filemaker. Data is exported as EXCEL files analyzed most often in JMP. Lab results (mostly in EXCEL) are transferred to the same filemaker system after accuracy checks and linked to the applicable experiment and time point. 10 - 20 GB in total

Microscopy images (light microscopy), raw and processed are stored as TIFF files and a registry of the TIFF file names is linked to the adequate time point in the experiment. 500 - 600 Muscle biopsies (~ informed consent rate and coagulation) are collected in EFECTS and ICU-FM-PLUS and are stored in the KULeuven Laboratory of Intensive Care Medicine, as in EPaNIC (Lancet RM 2013), the meta-data are stored in the main eCRF. 50 - 150 GB (depending on final design of ICU-FM-PLUS)

Repeated CT-Images are processed and split into muscle, fat and other tissue voxels, eported as excel files and transferred into the filemaker eCRF. (20 - 70 GB)

Metabolomic determinations by Liquid Chromatography with tandem Mass Spectrometry (LC-MS-MS) (carntine, choline and phosphate)- on serum from EPaNIC and ICU-FM-I will be exported as

EXCEL files and intergrated into the centeral FIlemaker 1 - 10 GB .

3. Legal and ethical issues

Will you use personal data? If so, shortly describe the kind of personal data you will use. Add the reference to your file in KU Leuven's Register of Data Processing for Research and Public Service Purposes (PRET application). Be aware that registering the fact that you process personal data is a legal obligation.

- No

Vital parameters, drugs and organ support administered, clinical outcome and premorbid data are analysed for efficacy and safety purposes. **Privacy commission notification:** not applicable at the date of study approval by the EC UZ/KULeuven, no longer applicable today as replaced by central KULeuven registry (as confirmed by Toon Boon –KULeuven, juridische dienst) by mail on 08-05-2018)

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? If so, add the reference to the formal approval by the relevant ethical review committee(s)

- Yes

These experiments are conducted on patients most often unable to give consent due to coma. This vulnerable population is included because it wouldn’t be possible to answer these important therapeutic questions based on similar experiments in non-comatose patients.

The Ethical Committee Research UZ/KU Leuven (Belg. Regnr. B322201629914) approved the protocol and consent forms:

for ICU-FM-I (S59328)

for EFECTS (S61665)

for EPaNIC (ML 4190 S50404)

The ICU_FM_PLUS protocol design will be finalized based on the results of the first packages and submitted thereafter

Does your work possibly result in research data with potential for tech transfer and valorisation? Will IP restrictions be claimed for the data you created? If so, for what data and which restrictions will be asserted?

- No

Do existing 3rd party agreements restrict dissemination or exploitation of the data you (re)use? If so, to what data do they relate and what restrictions are in place?

- No

4. Documentation and metadata

What documentation will be provided to enable reuse of the data collected/generated in this project?

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All clinical characteristics and particularly baseline data can be used as metadata in the structured filemaker crf to retrieve specific patients or samples.

Data is exported as EXCEL files analyzed most often in JMP. Lab results (mostly in EXCELl) are transferred to the same filemaker system after accuracy checks and linked to the applicable experiment and time point. Microscopy images, raw and processed are stored as TIFF files and a registry of the TIFF file names is linked to the adequate time point in the experiment.

Standing operating procedures and study protocols describing data collection

Info labels in the structured file maker specifying any further definition or productional information established during data gathering or processing

Moreover, for this project we will keep a separate registry documenting the names and locations for raw and processed data exports as used for every step in the project. All intermediary

datafiles and temporary copies (serving among others as double checks during the analysis process) will be destroyed once the results of that study phase are published in order to avoid confusion and avoid different copies circulating within the research group. In case a posteriori analyses are required the data will be exported from the central data management system

Will a metadata standard be used? If so, describe in detail which standard will be used. If no, state in detail which metadata will be created to make the data easy/easier to find and reuse.

- No

All clinical characteristics and particularly baseline data can be used as metadata in the structured filemaker crf to retrieve specific patients or samples.

Microscopy images, raw and processed are stored as TIFF files and a registry of the TIFF file names is linked to the adequate time point in the experiment.

5. Data storage and backup during the FWO project

Where will the data be stored?

The research database (eCRF) will be hosted on the University Hospitals Leuven servers. This closed network is only accessible for employees and affiliated persons which have to use a personal login and password to log into the system. Equipment can only have access to the network after registration/installation by the central ICT service. The hospital network is protected by a firewall but authorized research staff can access the network over the internet using a secure SSL-solution with one-time passwords (using a Vasco Digipass or Google Authenticator).

The firewall and external access procedure has been audited and approved by Ubizen and Deloitte

How is backup of the data provided?

The research database resides on the central servers with mirrored or RAID5 system disks and has hourly backups. The database is written in FilemakerPro and is login/password protected. An access log and audit trail are available.

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

UZ Leuven Servers

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

The data systems mentioned here above are UZLeuven based. We have no separate estimations for the cost of storage and Back-Up of 100 - 270 GB in this system. No costs will be charged to our Department for data storage.

Data security: how will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

The research database (eCRF) will be hosted on the University Hospitals Leuven servers. This closed network is only accessible for employees and affiliated persons which have to use a personal login and password to log into the system. Equipment can only have access to the network after registration/installation by the central ICT service. The hospital network is protected by a firewall but authorized research staff can access the network over the internet using a secure SSL-solution with one-time passwords (using a Vasco Digipass or Google Authenticator).

The firewall and external access procedure has been audited and approved by Ubizen and Deloitte.

6. Data preservation after the FWO project

Which data will be retained for the expected 5 year period after the end of the project? In case only a selection of the data can/will be preserved, clearly state the reasons for this (legal or contractual restrictions, physical preservation issues, ...).

All data initially entered in the eCRF, the patient medical files remain available in UZLeuven as source files but the link to their identity is encrypted in a separate system. This allows –among others- source file verification by the competent authorities.

The eCRF, crucial to any later interpretation of the biological samples harvested during the project will be stored for at least 25 years - in compliance with Beligan law on experimetns on Human Beings likewise for the final datafiles supporting the published data.

Where will the data be archived (= stored for the longer term)?

The research database resides on the UZ Leuven central servers with mirrored or RAID5 system disks and has hourly backups. Data will remain there for at least 20 years

What are the expected costs for data preservation during the retention period of 5 years? How will the costs be covered?

The research database resides on the UZ Leuven central servers no separate costs will be charged for the use of this servers the database in maintained by the Datamanagers of the Laboratory and Clinical Department of Intensive Care Medicine

7. Data sharing and reuse

Are there any factors restricting or preventing the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)?

- Yes. Specify:

No data will be made available unconditionally in the public space. The participant level data of this clinical experiment will not be publicly available. This would be a potential source of erroneous findings due to inadequate interpretation of the study design. The data will be stored in the research database of the Clinical Department and Laboratory of Intensive Care Medicine and request for post-hoc analyses with a clearly defined research question and methodology can be sent to the investigators. This approach to avoid misinterpretation of complex data and databases has been proposed in a recent summit on data sharing organized by the NEJM in April 2017 where Prof. Dr. Greet Van den Berghe Chair of the Clinical Department and Laboratory of Intensive Care Medicine contributed.

Which data will be made available after the end of the project?

See previous question

Where/how will the data be made available for reuse?

- Other (specify):

The data will be stored in the research database of the Clinical Department and Laboratory of Intensive Care Medicine and request for post-hoc analyses with a clearly defined research question and methodology can be sent to the investigators. Data will be available after signing a data sharing agreement and only for the predefined duration and the predefined analyses.

When will the data be made available?

- Upon publication of the research results

When requested and only after the primary analyses have been performed and published

Who will be able to access the data and under what conditions?

The data will be stored in the research database of the Clinical Department and Laboratory of Intensive Care Medicine and request for post-hoc analyses with a clearly defined research question and methodology can be sent to the investigators. Data will be available after signing a data sharing agreement and only for the predefined duration and the predefined analyses.

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

Not applicable, see above.

8. Responsibilities

Who will be responsible for data documentation & metadata?

The PI’s and the central clinical research data managers within the UZLeuven Intensive Care Department and Laboratory are responsible and both are supervised by the Chair of Clinical Department and Laboratory of Intensive Care Medicine. Doctoral students involved in study conduct and CRA’s are co-responsible for the accuracy of the data generated or transscripted on daily basis during the study and for the double checks they perform per protocol.

Who will be responsible for data storage & back up during the project?

The PI’s and the central clinical research data managers within the UZLeuven Intensive Care Department and Laboratory are responsible and both are supervised by the Chair of Clinical Department and Laboratory of Intensive Care Medicine

Who will be responsible for ensuring data preservation and reuse ?

The PI’s and the central clinical research data managers within the UZLeuven Intensive Care Department and Laboratory are responsible and both are supervised by the Chair of Clinical Department and Laboratory of Intensive Care Medicine

Who bears the end responsibility for updating & implementing this DMP?

The PI bears the end responsibility of updating & implementing this DMP.