Managerial Framework for a large Multi-centre Clinical Trial within an EU-funded Collaborative Project – the "PREVIEW" Case Study

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Abstract: *A multi-centre clinical trial involves the implementation of the same clinical protocol at several independent investigational centres. Multi-centre clinical trials may be preferable to single-centre trials, but their implementation and management is more complex. EU-funded collaborative projects involve several participating organizations and countries and their consortia are typically multidisciplinary. Their coordination requires a joint effort from several actors, and an appropriate managerial structure and procedures need to be defined and established. The management of the Framework Programme 7 (FP7) PREVIEW project, whose core consisted of a clinical trial with 8 intervention centres/sites is presented as case study. PREVIEW was coordinated by the University of Copenhagen. The project management was implemented by a combination of decentralised project management, at the department level, jointly by the Project Coordinator (PC) and Project Manager (PM), and centralised, by a dedicated EU Liaison Officer from the Project Management Office (PMO). The Quality Manager role was undertaken by the PC, with support from selected consortium members. The Exploitation Manager role was assumed by*

the leader of the dissemination and exploitation work package. The Data Manager (DM) at the University of Copenhagen established and maintained a datahub for all data from the clinical trial. The General Assembly and Steering Committee were key decision bodies with regard to taking and implementing decisions. The Scientific Advisory Board (SAB) was formed by reputed external experts providing guidance and advice. The project website was the main channel to reach the general public. A password protected private section was used as internal repository for the project. Regular meetings at all levels were key to ensure good communication and collaboration among the project team. Appropriate attention to data management was given from the start. The privacy of personal data was ensured in accordance with national and EU regulations. The PC was also the Sponsor of the multi-centre clinical trial, and the PM served as the overall Clinical Trial Administrator. Each centre was led by a Principal Investigator (PI), running the trial together with the local daily responsible. The tasks and responsibilities for the clinical trial of the Coordinating Centre were shared between Copenhagen and Helsinki centres. The trial was overall led by the Clinical Trial Manager (CTM), who was the PI at the Helsinki centre. The local Independent Ethical Committees approved the protocol prior to the start of the intervention. One member of the SAB acted as Ethical Officer. The trial/study had an overall statistician. The Analyst role was shared among different people from the Copenhagen and Helsinki centres. The DM created and maintained database for the intervention and the Clinical Report Forms by using OpenClinica open source software. The staff in the intervention received training in Good Clinical Practices, the protocol and its procedures. The monitoring tasks were jointly undertaken by the Sponsor and the CTM. The documents from the Trial Master File were saved in the Internal Repository. A set of Standard Operation Procedures was defined. Meetings among all PIs, and within the Instructors' Network were key in the success of the intervention. This case study aims at serving as guidance to coordinating researchers, both during the proposal preparation and project implementation phases, as well as to provide visibility and insight into the multi-faceted role of the project managers and administrators of such projects.

Keywords: *Collaborative research projects, Multi-centre/site clinical trials, European Commission, FP7, H2020, Horizon Europe, Project Coordinator, Project Manager, Project Management Office, Clinical Trial Administrator, "PREVIEW"*

Introduction

The aim of this paper is to propose a governance structure and a set of managerial procedures and tools to be used as guidance, in order to effectively manage EU-funded collaborative projects running a multi-centre clinical trial.

Clinical trials are a key research tool in the development of new interventions to improve patient care and quality of life. Most recent interventions are a direct result of clinical research. Even

though computer simulation and animal testing can provide valuable information, they present limitations with respect to determining how a new intervention will work in the human body. Therefore, clinical trials are in most cases unavoidable and still needed.

A multi-centre clinical trial involves two or more independent investigational centres, where participants are engaged for an intervention, following the same clinical protocol (National Institutes of Health, National Heart, Lung and Blood Institute, n.d.). One centre is in charge of processing and analysing the data from all centres (Kraemer, 2000).

Multi-centre clinical trials have several advantages compared to single-centre trials. Firstly, multi-centre clinical trials generate larger sample sizes and therefore have more power to test hypotheses and estimate population parameters. This is crucial when the number of potential participants is low, if one centre alone cannot generate a large enough sample, or participants' retention is challenging (CareSearch, 2018). Secondly, the findings from multi-centre clinical trials are more generalizable than the ones obtained from single-centre trials. Participants involved in multi-centre clinical trials usually present greater variations in sociodemographic and clinical characteristics. The intervention may bring different results from one centre to another, even if it is uniformly delivered and evaluated. Thus, multi-centre studies prevent over-generalization of conclusions, since they minimize risks of idiosyncratic research findings. Thirdly, and crucially, multi-centre clinical trials can resolve belligerent conflicts in a field (Kraemer, 2000). They will often be better designed and implemented, and their results better reported than in single-centre studies (Friese et al., 2017).

The management of multi-centre clinical trials is more complicated than in the case of single-centre clinical trials (Friese, 2017). Obtaining and retaining an adequate sample while maintaining data integrity can be challenging (Forjuoh et al., 2015). Furthermore, the communication between researchers from different locations and time zones usually requires additional considerations and pre-planning. Effective communication involves adaption to various leadership styles and organizational commitment (Forjuoh et al., 2015). It is crucial to define managerial strategies, both within each clinical centre and through all centres (Kraemer, 2000).

Since 1984, the research and development activities from the European Union (EU) (European Community until 1993) have been defined and implemented by a series of multi-annual Framework Programmes (FPs): The 1st FP (1984-1987), the 2nd FP (1987-1991), the 3rd FP (1990-1994), the 4th FP (1994-1998), the 5th FP (1998-2002), the 6th FP (2002-2006), the 7th FP (2007-2013), Horizon 2020 (2014-2020) and currently Horizon Europe (2021-2028) The EU financially supports activities covering most scientific disciplines through the FPs, which are proposed by the European Commission (EC) and adopted by the European Council and the European Parliament (Eurostat, n.d.).

The EU awards grants in many different fields to organisations and, occasionally, individuals, to help them carry out projects in line with its policies (European Commission, n.d.-c). Collaborative EU-funded projects are focused research projects that are carried out by multidisciplinary consortia consisting of several participants from different countries, coming from both academia

and industry (European Commission, 2007). Support for Collaborative Projects is provided within predefined themes (topics) that are published by the EU Commission on a running basis. An exact match with a topic is needed in order to be considered for obtaining funding (top-down approach). The funding amount varies and it is specified in the topic description. The coordination of EU-funded collaborative projects is challenging, and requires a joint effort from several actors.

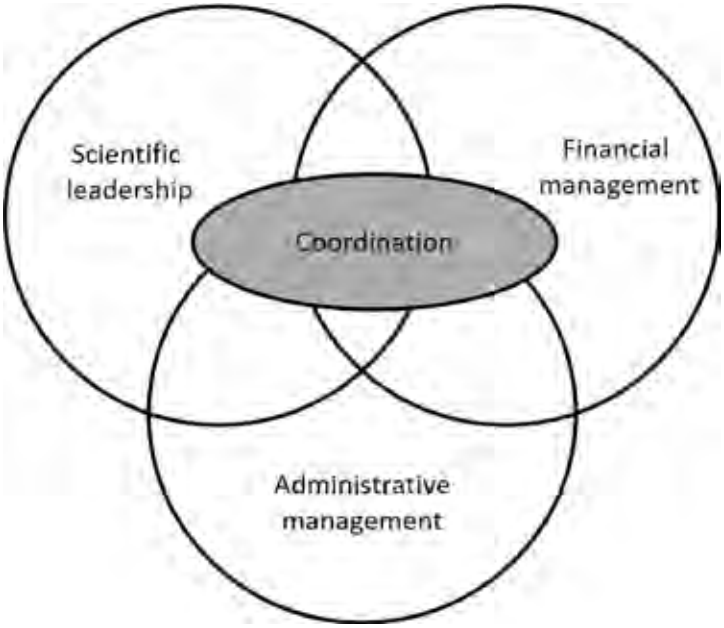

Figure 1. The three dimensions of the project coordination.

As illustrated in Figure 1, the project coordination involves three different dimensions: scientific leadership, administrative management, and financial management.

The coordinator is often the individual that has the project idea, gathers the consortium, leads the writing process, including the division of work and allocation of tasks and resources to each partner, represents the consortium towards the EC and submits the proposal. The budget of the coordinating organisation, where the coordinator belongs, includes a designated share for project management activities (Enspire.Science, n.d.-a). Once the project is running, the coordinator has many roles. He/she will be often regarded as the financial and administrative manager, as well as scientific leader, even though the last is not a contractual requirement for the coordinator.

The coordinator should monitor the project and ensure that it is implemented on time and with the expected quality. The coordinator should facilitate the communication among the consortium partners, in order to produce fruitful collaborative work. This can be challenging, given the heterogeneity of partners: by type of organization (academic vs. industrial partners), size (big vs. small organisations), previous participation in collaborative EU-funded projects (very experienced vs. new) and country of origin (with the associated cultural differences). In addition, the coordinator should be mediator between the project consortium and the EC.

The coordination role is often considered prestigious and is associated with decision power and visibility for both the individual and his/her organisation. Despite these advantages, potential coordinators are often reluctant to assume this role, because the non-scientific and administrative activities may be perceived as tedious, too time-consuming and little rewarding (Enspire.Science, n.d.-a).

The benefits of applying project management to research, for funders, researchers and research managers have been previously described (Gist & Langley, 2007). In the case of coordinators coming from academia, it is especially important to have a managerial structure in place that allows coordinators to focus on their scientific tasks and scientific leadership, which are appealing to most of them, while guaranteeing that the administrative and financial management of the project is given appropriate attention.

A search in CORDIS, the Community Research and Development Information Service, for projects funded by the Framework Programmes, from FP1 up to H2020 with the search words "clinical trials" provides more than 2000 results (European Commission, n.d.-b), and many of these projects involve multi-centre clinical trials. As example, in January 2020, the EC launched an emergency call, with a budget of 48.5 M€, looking for research projects that will advance the knowledge about the novel coronavirus epidemic, contribute to more efficient clinical management of patients infected with the virus, as well as public health preparedness and response. The EC has already provided funding to 18 projects, involving 151 research teams from across the EU and beyond (European Commission, 2020d), and several will involve clinical trials. Therefore, it is expected that in the future, and during the next FP Horizon Europe (HORIZON), that will run from 2021 to 2027 (European Commission, n.d.-a) and has the largest budget so far, the EC is launching more calls for proposals on topics involving multi-centre clinical trials.

Materials and Methods

Multi-centre Clinical Trials: Managerial Roles and Structure

This section describes some of the key roles in the management of a multi-centre clinical trial. They are represented in Figure 2.

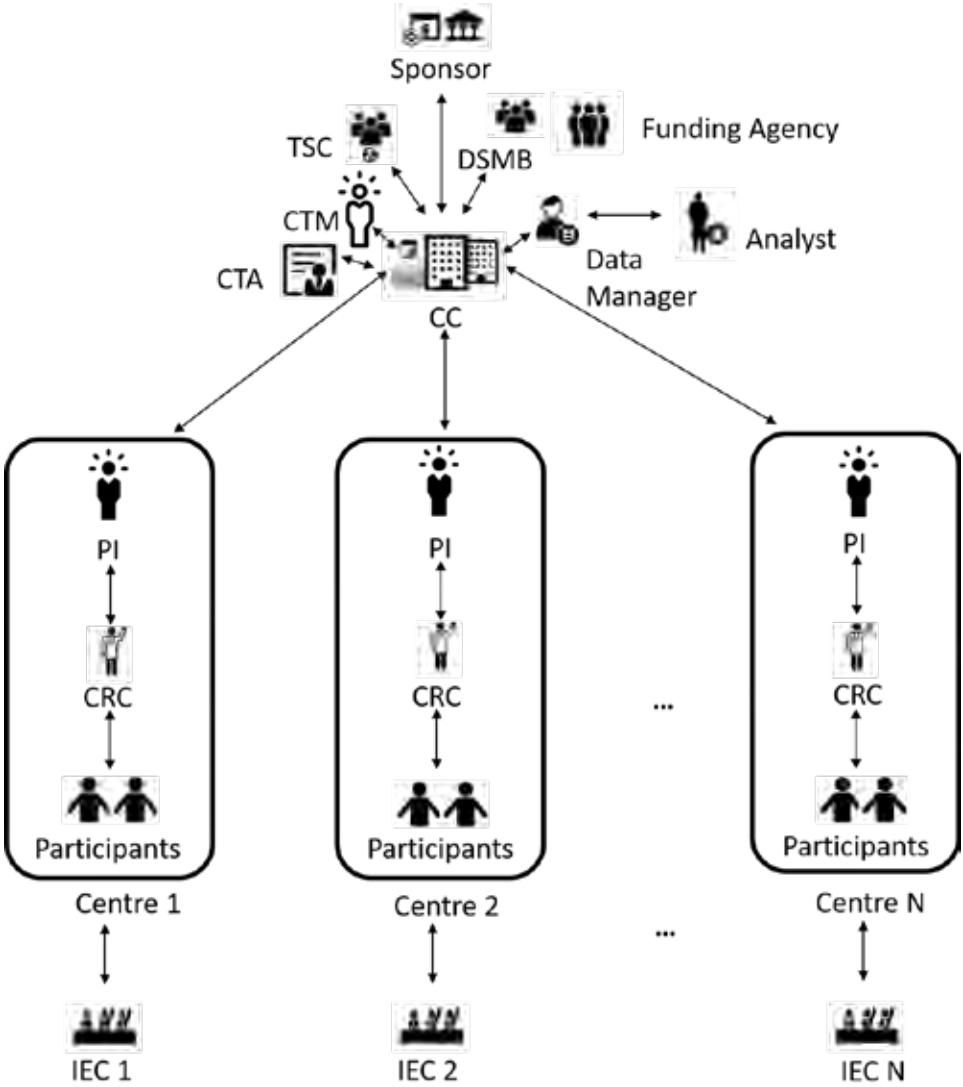

Figure 2. Managerial Framework for a Multi-centre Clinical Trial (adapted from Choudhury et al., 2019a).

Sponsor means an individual, institution, or organization that initiates and manages a clinical trial, but does not actually conduct it (U.S. Food & Drug Administration [FDA], 2020). Sponsor-investigator means an individual who both initiates and actually conducts a clinical investigation, alone or with others. The obligations of a sponsor-investigator include both the ones of an investigator and those of a sponsor (FDA, 2020).

Contract Research Organisation (CRO) is a person or an organization contracted by the sponsor to assume some of the sponsor's trial-related tasks and duties. However, the sponsor has the ultimate responsibility for the quality and integrity of the trial data (The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use [ICH], 1996). A CRO helps the sponsor to write the protocol and submit the data to the regulatory agencies. The CROs also hire their own CRAs (Clinical Research Associates), who visit and monitor the centres throughout the trial, in order to make sure that it is carried out in agreement with the protocol and good clinical practice (GCP) standards (Medium, 2015). The structure depicted in Figure 2 does not contemplate this role, but a structure with a coordinating centre instead.

Coordinating Centre (CC) is a centre that is responsible for overseeing and monitoring a clinical trial and facilitating the communication among all centres (Johns Hopkins Medicine, 2016). They are in charge of the overall data management, and maintain a central database with all data from the trial (Choudhury et al., 2019b). They generate reports based on the data collected, schedule activities for participants, and communicate them to appropriate stakeholders (JHM, 2016). This structure is key in facilitating Coordinated Collaborative Science (Rolland et al., 2017).

Clinical Research Associate (CRA) can also be known as Clinical Research Coordinator (CRC) and Clinical Trial Manager (CTM). They are responsible for the planning and coordination of medical research projects and clinical trials. In this text, we will use the term Clinical Trial Manager (CTM) to refer to the CRA working at the Coordinating Centre, and the term Clinical Research Coordinator (CRC) to refer to the person coordinating the trial on a daily basis in each one of the centres.

Clinical Trial Manager (CTM) is the chief investigator working at the Coordinating Centre, responsible for coordinating the trial among the different trial centres and monitoring the trial, on behalf of the sponsor. The CTM has in most cases a very significant contribution to the design of the trial, and the definition of the clinical trial protocol and the Standard Operating Procedures (SOPs).

Principal Investigator (PI) is the main person responsible for preparing, implementing and administering the study at each centre of a multi-centre clinical trial (Choudhury et al., 2019a). The PI takes large responsibility for the ongoing conduct of the trial and may review some or all data from a clinical point of view (McFadden, 2007).

Clinical Research Coordinator (CRC) responsibilities include preparing the Institutional Review Board submission, writing the informed consent document and developing a detailed cost analysis for their centres. The CRCs should be involved to some extent in the design and pilot testing of the Case Report Forms (CRF), as well as in the evaluation of proposed systems, software and procedures. The CRC is usually also responsible for recruiting and registering/randomising participants, scheduling visits and tests, completing the CRFs and submitting those and other data to the CC, adverse event reporting and study close-out (McFadden, 2007).

Clinical Trial Administrator (CTA) primarily manages the administrative aspects of a clinical trial, at every stage of the process. The CTA works with study protocols, prepares, distributes, tracks and files the clinical trial documents (such as the Trial Master File [TMF]). He/she may also deal with Serious Adverse Events (SAE) notifications.

Trial Steering Committee (TSC) is generally comprised of an independent chair, a minimum of two additional independent members, up to two PIs and a CTM or statistician, as appropriate. The TSC is responsible for providing overall supervision and advice and has the ultimate decision for the continuation of the trial (Molloy & Henley, 2016).

Data Safety and Monitoring Board (DSMB) is also called Data Monitoring Committee (DMC). The DSMB is an independent group of experts that periodically review and evaluate the accumulated study data concerning the study progress and participant safety and make recommendations concerning the continuation, modification, or termination of the trial. Its main duty is to monitor safety of the trial, in particular to review SAEs, especially the Suspected Unexpected Serious Adverse Reactions (SUSAR) and mortality, per arm of the trial and overall. The DSMB provides recommendations to the TSC, the CTM and the sponsor regarding the continuation or early stopping of the trial based on safety or ethical issues (Molloy & Henley, 2016).

Institutional Review Boards (IRBs)/Independent Ethical Committees (IECs) have the aim to protect the rights, safety, and wellbeing of human participants participating in a clinical trial. This board reviews all aspects of a trial, before and during the study. They should approve/provide favourable option to the protocol, as well as other study material such as the informed consent documents and investigator brochures, before the trial can start (FDA, 1998; ICH, 2016).

Participant is an individual that takes part in a research study and from whom data are collected through intervention or interaction with the individual (Choudhury et al., 2019a).

Funding agencies provide financial resources for carrying out a research study. The term often connotes funding obtained through a competitive process, in which potential research projects are evaluated and only the most promising receive funding.

Analyst is a researcher or statistician who gathers and analyses trial data throughout the study and organizes trial results. He/she participates in the study design, calculates the sample size and defines the statistical methodology to be used in the analyses, which is described in the Statistical Analysis Plan for the trial (Choudhury et al., 2019a; McFadden, 2007).

Data Manager (DM) (also called Data Coordinator and Data Specialist) is in charge of quality control of data in the Coordinating Centre. He/she should be involved in the design of Case Report Forms (CRFs), review of the protocol document and development and testing of some of the trial SOPs. The DM randomizes participants, maintains all study CRFs and generates queries upon data requests. The DM assists the Analyst in preparing data sets for analysis and he/she is the main contact with the trials personnel at the participating centres. The DM usually also performs a Database Administrator (DBA) role, being responsible for designing, and setting up the trial database, ensuring its security and integrity and maintaining a backup of all the electronic

files and database(s). Additionally, he/she is often also performing tasks corresponding to a System Analyst, such as the design, development, testing, documenting and validation of the trials software (McFadden, 2007).

Multi-centre Clinical Trials: Managerial Procedures and Tools

This section describes the main managerial procedures that need to be taken into consideration and applied in a multi-centre clinical trial.

Good Clinical Research Practice (GCP) is a process that applies established ethical and scientific quality standards for the design, conduct, recording and reporting of clinical trials involving the participation of human participants. Compliance with GCP ensures that the rights, safety and well-being of research participants are protected and respected, in agreement with the principles enunciated in the Declaration of Helsinki and other internationally recognized ethical guidelines, and ensures the integrity of clinical research data (World Health Organization [WHO], 2005). Some renowned institutions from the USA also provide resources and advice on how to design, plan and implement clinical trials according to GCP principles (Multiregional Clinical Trials Center [MRCT] of Brigham and Women´s Hospital and Harvard 2021; Clinical Trials Transformation Initiative, 2021).

Monitoring is a process that is an integral part of GCP and ensures that a trial is conducted in compliance with international regulations, standards and guidelines. The sponsor is responsible for ensuring that the trial is adequately monitored, even though the task can be delegated (Molloy & Henley, 2016).

Protocol is a document that describes how a clinical trial will be conducted (the objectives, design, methodology, organization and statistical considerations of a clinical trial) and ensures the safety of the trial participants and integrity of the data collected (Clinical Research Resource Hub [HUB], University of California San Francisco, 2017). In the case of a multi-centre clinical trial, it is crucial that the protocol is common and shared among all the clinical centres.

Trial Master File (TMF) refers to the collection of essential documents from the clinical trial that facilitate evaluation of the trial's implementation and the quality of data, and therefore compliance with GCP guidelines and applicable law (GCP-Enhederne, 2021).

Case Report Form (CRF) "is a printed, optical or electronic document designed to collect the data that is described in the protocol for each trial participant". Before designing the CRF, it is advisable to consider how the data will be handled and stored in the database, as these decisions may impact the data collection process (GCP-Enhederne, 2021).

Standard Operating Procedures (SOPs) are detailed, written instructions aimed at ensuring that a procedure is conducted in a uniform manner and according to plans. Furthermore, SOPs are useful tools when training new trial staff (GCP-Enhederne, 2021). Ensuring uniformity in the procedures is even more crucial in multi-centre clinical trials.

Meetings: Regular internal meetings within the staff involved in a clinical trial are crucial for the good planning and implementation of the trial. In the case of a multi-centre clinical trial, regular meetings among the centres are as well needed for alignment, discussion of clinical practices, etc.

Collaborative EU-funded projects: Managerial Roles and Structure

The next paragraphs will describe some of the key roles in the management of an EU-funded project.

Project Coordinator (PC): During the project's life time, and in addition to the scientific tasks that the coordinator may have as a consortium partner, there is a line of mandatory responsibilities that the coordinator is obligated to perform, such as: "1) monitor that the action is implemented properly; 2) act as the intermediary for all communications between the beneficiaries and the EC; 3) request and review any documents or information required by the EC and verify their completeness and correctness before passing them on to the EC; 4) submit the deliverables and reports to the EC; 5) ensure that all payments are made to the other beneficiaries without unjustified delay and 6) inform the EC of the amounts paid to each beneficiary, when required under the Agreement" (European Commission, 2019).

Project Manager (PM) oversees the project on a daily basis, in collaboration with the PC, in order to ensure timely and high-quality results within the budgeted resources. Other responsibilities include project communication, stakeholder management as well as risk management (PM^2 Alliance, 2018). The PM needs to have excellent administrative and financial management skills, but also a certain degree of understanding of the science behind the project in order to efficiently collaborate and provide support to the scientific coordinator (Enspire.Science, n.d.-b). Therefore, the scientific-leadership and the administrative and financial management roles in the project are not completely independent of each other. Some of the administrative tasks of the PM are as follows: 1) provide administrative support to the project; 2) define requirements for reporting and communication; 3) administer project meetings and draft related minutes; 4) support the PC in planning, monitoring and controlling the project; 5) advise on project management tools and administrative services; and 6) manage the project documentation (versioning, archiving, etc.) (PM2 Alliance, 2018).

Project Management Office (PMO) is a management structure that standardises the project-related governance processes and facilitates the sharing of resources, methodologies, tools and techniques. It provides support to one or more projects, and may be established as a separate entity within the organization. A primary function of a PMO is to support the PC and the PM by: 1) managing shared resources across all projects administered by the PMO; 2) identifying and developing project management methodologies, best practices and standards; 3) coaching, mentoring and training; 4) monitoring compliance with project management standards, policies, procedures, and templates; 5) developing and managing project policies, procedures, templates, and other shared documentation; and 6) coordinating communication across projects (Project Management Institute [PMI], 2017). The PMO is well suited to the academic world and research projects where knowledge generation and dissemination is of paramount importance (Wedekind & Philbin, 2018).

Quality Manager (QM): This role is responsible for monitoring and ensuring the quality of processes and outcomes of the project. In some cases, the PC undertakes also the QM role. In some other cases, it is undertaken by another project partner(s) or representatives. In the case of projects implementing an explicit peer-review process of the main project deliverables, the QM is in charge of collecting the reviewers' comments, distributing them to the responsible deliverable authors and deciding on the final deliverable status (Nathanail et al., 2015).

Exploitation and/or Innovation Manager: This role, when it exists, focuses on identifying opportunities for exploitation of the project's research and development results in compliance with the terms and conditions of both the Grant Agreement and the Consortium Agreement. This person facilitates the process of bringing the project's innovations to the market and is responsible for defining the business model and exploitation plan and strategies. He/she also is in charge of monitoring the needs of end-user groups in order to align the products/services emerging from the project to the real needs of the market. The Exploitation and Innovation Manager monitors the potential intellectual property rights (IPR) resulting from the project, including any possible patents and facilitating the process of patent application to the parties. He/she reports to the PC in order to keep the project's innovation capacity under constant surveillance, and participates in the SC meetings, without voting rights.

Data Manager focuses on ensuring the efficient and effective treatment and use of data. In some occasions, the PC or someone in the coordinating organization will undertake this role. In other cases, a partner/person with specific IT skills will assume it. This role has acquired an increased relevance since 2017, when the EC started running the Open Research Data Pilot, aiming at improving and maximizing access to and re-use of research data generated by Horizon 2020 (European Commission, 2021a).

Project Management Team (PMT) is typically composed by the PC, the PM and the PMO representatives. In addition, it sometimes also includes the exploitation and/or innovation manager, for those projects that have such a role.

Steering Committee (SC) is chaired by the PC and is the key-decision making and issue-resolution body for the project. Any significant decisions that may affect the project or the teams' ability to deliver on the objectives will be escalated to the SC. Approval of key documents and deliverables, resolution of important project issues or significant amendment requests will be discussed and decided upon here (PM2 Alliance, 2018; Andersen et al., 2018). In other contexts it is also referred as to Executive Board (ttopstart, n.d.).

General Assembly (GA) is usually formed by one representative of each project partner and is led by the PC. The GA typically meets several times during the course of the project, where it provides information about the progress of activities and helps resolving issues (PM² Alliance, 2018).

Advisory Board(s) (ABs) are valued groups of external experts who regularly meet with the Consortium through the project (Tsioutsia et al., 2016). They typically provide guidance on scientific, technical, ethical and legal matters. They often encourage the interactions of the project with other projects, initiatives and activities.

Collaborative EU-funded projects: Managerial Procedures and Tools

This section describes the managerial procedures and tools required for a successful implementation of a collaborative EU-funded project.

Website: In an EU-funded project, the project website is one of the main dissemination and communication channels. It ideally should present the project hypothesis and main goal, the administrative data of the project, describe the Consortium and provide access to the public deliverables of the project.

Internal Repository: In order to share internal documents among the Consortium members, it is very useful to set a file repository. There a several solutions and file hosting services, but it is important that access is protected and restricted to the Consortium.

Meetings: In order to ensure appropriate communication within the project, it is imperative that the different managerial boards meet regularly. These meetings can be either in person or remotely by use of teleconference media.

Data Management: Good research data management allows data and knowledge integration and reuse, and therefore plays a key role in knowledge discovery and innovation. The objective is to make project research data Findable, Accessible, Interoperable and Reusable (FAIR). Data Management Plans (DMPs) are a key element of good data management. A DMP describes the data management life cycle for the data to be collected, processed and/or generated by an EU-funded project (European Commission, 2021a). The General Data Protection Regulation (GDPR) is applicable since 5 May 2018. Since that date, all entities concerned must comply with the new rules when processing personal data (European Union, 2016).

Results

After presenting the managerial structure and tools for both multi-centre clinical trials and EU-funded collaborative projects, the next sections aim at describing the PREVIEW project (Raben et al., 2013), as a case study illustrating and merging both features.

Case Study, the PREVIEW project

Diabetes is a costly disease and according to WHO, the direct health care costs of diabetes range from 2.5% to 15% of annual national health care budgets. Type-2 diabetes (T2D) represents about 90% of all cases of diabetes and is mainly caused by the worldwide obesity epidemic (WHO, 2003).

PREVIEW "PREVention of diabetes through lifestyle Intervention and population studies in Europe and around the World" project (Grant Agreement no. 312057, 2017) addressed potential solutions to the massive problems associated with the global diabesity epidemic (obesity and T2D). PREVIEW aimed at increasing the knowledge on how specific lifestyle factors can help preventing type-2 diabetes (PREVIEW, n.d.).

PREVIEW started on 01-January 2013 and finished on 31-December 2018. It had a budget of 14 M€ corresponding to a maximum funding from the European Commission of 9 M€ plus national funds from the Australia, New Zealand and Canada (European Commission, n.d.-b).

The project was coordinated by Prof. Anne Raben from the University of Copenhagen (UCPH), Denmark (PREVIEW, n.d.).

PREVIEW included 15 beneficiaries, 12 of them from Europe (East, West, North and South) and 3 overseas (Australia, New Zealand, and Canada). Among them are 12 Universities, 1 research centre, 1 SME and 1 industrial partner (PREVIEW, n.d.). The project was multidisciplinary, involving experts in fields such as human nutrition and dietetics, paediatric nutrition, medicine, sport science, psychology, cooking, laboratory analyses and information and communication technologies.

The project consisted of 6 work packages (WPs): WP1: Multicentre intervention: Randomized, controlled, multicentre trial (RCT); WP2: Population studies; WP3: The role of sleep and stress in interaction with the role of diet and physical activity; WP4: Other lifestyle variables: Behavioural, sociological, environmental, cultural, socio-ecological, and socioeconomic components; WP5: Dissemination and exploitation; and WP6: Management (PREVIEW, n.d.).

Figure 3 illustrates the interrelation between the different work-packages. WP1: The clinical intervention RCT was the core element of the project.

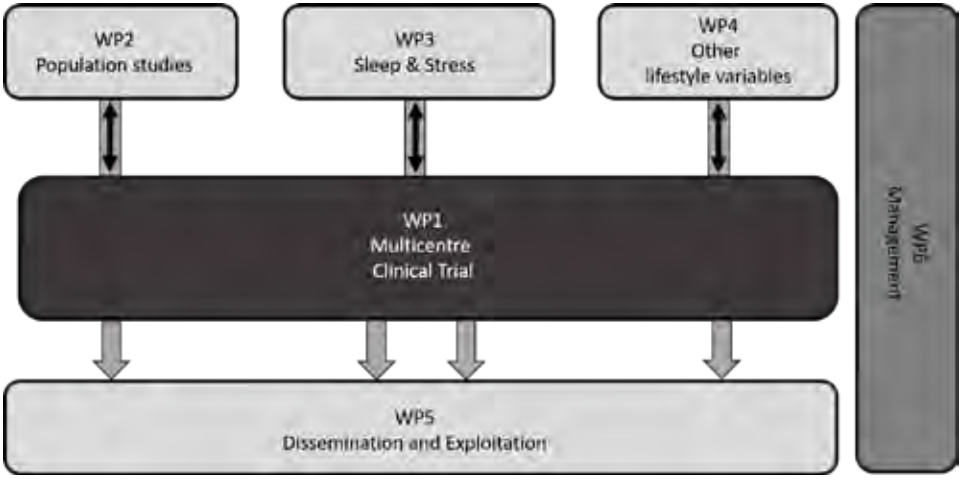

Figure 3. PREVIEW EU Project Pert Diagram (adapted from PREVIEW, 2017.)

The primary goal was to identify the most efficient lifestyle pattern for the prevention of T2D in a population of pre-diabetic overweight or obese individuals (European Commission, n.d.-b).

The project comprised two distinct lines of evidence:

1) A multi-centre, randomized, controlled intervention trial (RCT) (WP1) with participants in all ages, with overweight or obesity and pre-diabetes.
2) Large population studies (WP2) using multinational data sets from all age groups (European Commission, n.d.-b).

Focus in both lines of evidence was on diet (specifically protein and glycaemic index) and intensity of physical activity, as well as their interaction with the lifestyle factors, habitual stress, and sleeping patterns, as well as behavioural, environmental, cultural and socioeconomic variables (European Commission, n.d.-b).

PREVIEW Multi-centre Clinical Trial: Managerial Roles and Structure

PREVIEW WP1 comprised a randomised, controlled, multi-centre (multi-site) and multinational trial comparing the effect of two diets as well as two intensities of physical activity on T2D incidence and weight control in overweight pre-diabetic participants (Fogelholm et al., 2017).

A large number of participants was needed in order to aim at sufficient study power. Since different ethnic and socioeconomic groups should be represented, a collaborative international approach (in and beyond Europe) rather than a national one was needed (PREVIEW, 2017).

The intervention part of PREVIEW ran over 3 years (2 years for children and adolescents) in 6 EU countries, New Zealand and Australia, and 2,326 adults and 126 children and adolescents were enrolled (Fogelholm et al., 2017; Dorenbos et al., 2018).

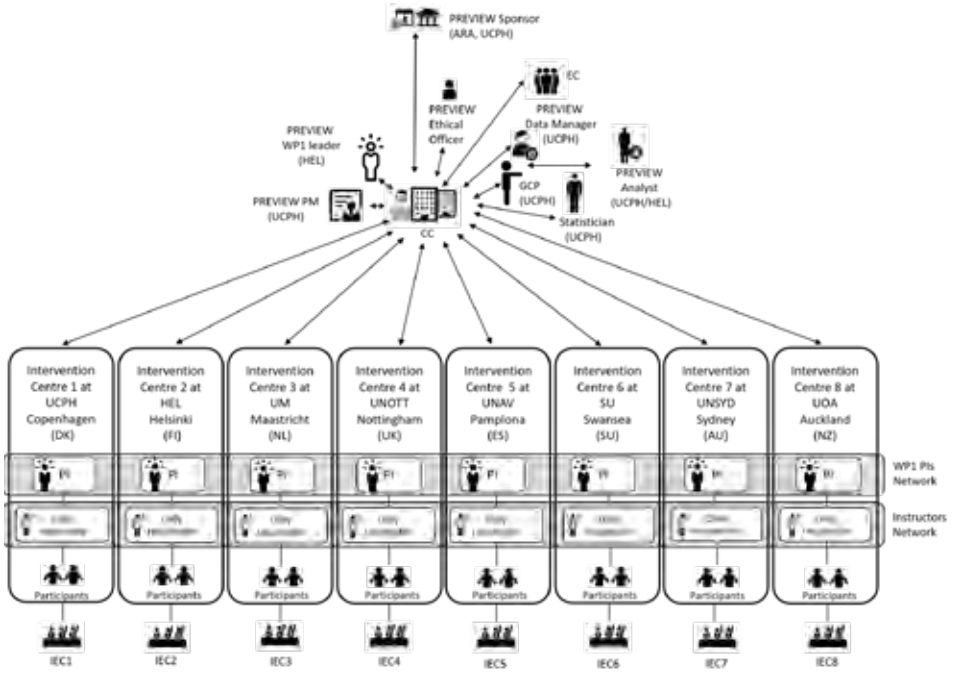

Figure 4. Managerial Structure in PREVIEW Multi-centre Clinical Trial.

PREVIEW Sponsor and Clinical Trial Manager (CTM): PREVIEW Sponsor was Prof. Anne Raben from the University of Copenhagen. She was furthermore the overall coordinator of PREVIEW project (PREVIEW, n.d.; Raben et al., 2013). In this case, she was a sponsor-investigator, who had the responsibility for the clinical study, but did not finance it, since the funding agency was the European Commission (National Institutes of Health [NIH] U.S. National Library of Medicine, n.d.).

In PREVIEW, both the Sponsor (in this case the same person as the PC) and the CTM (in this case the same person as the WP1 leader, Prof. Mikael Fogelholm) developed the project protocol jointly and performed monitoring tasks in the different intervention centres (Fogelholm et al., 2017).

PREVIEW Intervention Centres/Sites: The Clinical Trial Centres (CTCs) in PREVIEW received the name of Intervention Centres or Intervention Sites. There were 8 centres located in 6 European cities (Copenhagen, Helsinki, Maastricht, Nottingham, Pamplona and Swansea) and 2 overseas cities (Sydney and Auckland) (Fogelholm et al., 2017).

PREVIEW Coordinating Centre: The tasks allocated to the CC in PREVIEW intervention were shared between Copenhagen centre, run by The University of Copenhagen (UCPH) (organization of the Sponsor and overall PC) and Helsinki centre, run by The University of

Helsinki (HEL) (organization of the CTM/WP1 leader). Both the clinical protocol and the CRFs were developed together by Copenhagen and Helsinki centres.

The Data Manager at Copenhagen centre established and maintained the central database for the clinical study (WP1) in PREVIEW. The DM was also in charge of retrieving data upon demand from the intervention centres.

The Copenhagen centre was in charge of collating and analysing overall data for the study. This centre also provided the study with a statistician, who was consulted for doing the statistical calculations and statistical analysis plan.

Both the sponsor at Copenhagen centre and the CTM at Helsinki centre were performing several monitoring visits to the intervention centres and ensuring high quality and consistency of the intervention across all centres.

PREVIEW Principal Investigators (PIs): Each one of the eight intervention centres in PREVIEW had one Study Principal Investigator (often referred to simply as Principal Investigator, PI) as overall responsible for the trial and activities in their centres, reporting to the CTM.

Their names were as follows: Assoc. Prof. Thomas Meinert Larsen (Copenhagen, DK), Prof. Mikael Fogelholm (Helskinki, FI), Prof. Margriet Westerterp-Plantenga (Maastricht, NL), Prof. Ian Macdonald (Nottinhgam, UK), Prof. Alfredo Martinez (Navarra, ES), Prof. Svetoslav Handjiev (Sofia, BG), Prof. Jennie Brand-Miller (Sydney, AUS) and Prof. Sally Poppitt (Auckland, NZ).

PREVIEW Clinical Research Coordinators (CRCs): Each of the intervention centres in PREVIEW was coordinated on a daily basis by a CRC, usually with specific background in nutrition and/or medicine, on behalf of their respective PIs.

PREVIEW Clinical Trial Administrator (CTA): The role of the CTA was undertaken by the PREVIEW PM at the University of Copenhagen (UCPH), which was the organisation where the sponsor/PC belonged.

The CTA was in charge of the administrative aspects of the intervention when dealing with the protocol and its amendments, SOPs and instructions to participants. The CTA in PREVIEW maintained the overall TMF, both electronically and in paper, and was filing SAEs.

In addition, the CTA performed the data cleaning of data from all centres, in order to ensure their consistence and quality, in collaboration with PREVIEW DM.

PREVIEW Trial Steering Committee (TSC), Data Safety and Monitoring Board (DSMB) and Institutional Review Boards (IRBs)/IECs (Independent Ethics Committees): There was no TSC appointed in PREVIEW project. Instead, similar tasks were performed by the group of the eight PIs from the intervention centres, who met monthly during the recruitment period and bi-monthly afterwards, and consulted the project statistician when needed.

Any adverse events during the trial were notified to the local PI, the sponsor, the CTM and the PM. There was no DSMB in PREVIEW, but a similar role was performed by one of the members

of the SAB, appointed as Ethical Officer, who was in charge of reporting about SAEs and their occurrence.

The intervention centres in PREVIEW fully conformed to national legislation and applicable codes of conduct. Each centre obtained the ethical approval by their corresponding local IEC/IRB, prior to the trial start, namely:

1) Copenhagen centre: The Research Ethics Committee A of the Capital Region, DK;
2) Helsinki centre: Coordinating Ethics Committee Helsinki and Uusimaa Hospital District, FI;
3) Maastricht centre: Medical Ethical Committee (METC), Academic Hospital Maastricht, Maastricht, NL;
4) Nottingham centre: NHS Health Research Authority, NRES Committee East Midlands – Leicester, UK;
5) Navarra centre: Research Ethics Committee of the University of Navarra, ES;
6) Sofia centre: Ethics Committee for Scientific Research at the Medical University Sofia (KENIMUS), Sofia, BG;
7) Sydney centre: The University of Sydney Human Research Ethics Committee (HREC), AU;
8) Auckland centre: Northern B Health and Disability Ethics Committee (HDEC), Ministry of Health, NZ.

Furthermore, these IRBs/IECs approved the subsequent amendments to the protocol.

PREVIEW study participants were people with overweight or obesity (defined as Body Mass Index equal or over 25) with diabetes, belonging to the age ranges 10-18 years and 25-70 years. More detailed inclusion and exclusion criteria were defined in the clinical protocol (NIH, n.d.).

PREVIEW funding agencies: PREVIEW project (including WP1, the multi-centre clinical intervention) was funded by the 7th Framework Programme of the European Commission, under Grant Agreement no. (312057). The total funding provided by the EC was 9 M€.

In addition, funding was provided the New Zealand Health Research Council, Grant No. 14/191; and the NHMRC-EU Collaborative Grant, Australia. All Low Calorie Diet (LCD) products consumed by all participants from all centres during 8 weeks were provided by Cambridge Weight Plan®, UK.

PREVIEW Analyst and Data Manager (DM): The role and tasks of the Analyst in PREVIEW were shared among different people. The analyses of the trial data through the study and organisation of the trial results were done by both the Sponsor and the CRC at Copenhagen centre and the CTM at the CC in Helsinki. The project statistician from the University of Copenhagen participated in the study design, calculated the sample size and defined the Statistical Analysis Plan for the trial.

The PREVIEW DM was a person working at the Copenhagen centre, acting as overall data manager for the clinical intervention. The DM was involved in the design CRFs, review of the protocol document and development of the trial SOPs related to data management.

The PREVIEW DM randomized the participants and created and maintained the CRFs, which were populated by staff in each intervention centre. The DM was responsible for designing, and setting up and maintaining the trial databases. The DM also generated queries and prepared datasets upon request from personnel in the intervention centres.

PREVIEW Multi-centre Clinical Trial: Managerial Procedures and Tools

PREVIEW GCP: The work of PREVIEW was carried out in compliance with the relevant requirements of the latest version of the Declaration of Helsinki (59th WMA General Assembly, Seoul, Korea, October 2008), and the ICH-GCP, The International Conference on Harmonisation (ICH) for Good Clinical Practice to the extent that was possible and relevant considering financial and time-constraints (ICH, 1997, 2016). All participants provided written informed consent prior to commencing screening procedures in clinic. All information obtained during the trial was handled according to local regulations and the European Directive 95/46/CE (directive on protection of individuals with regard to the processing of personal data and on the free movement of such data) (Fogelholm et al., 2017). The trial is registered with ClinicalTrials.gov, NCT01777893.

All staff involved in the PREVIEW study followed specific training in Good Clinical Practices. For example, personnel in Copenhagen who had not received training previously, followed 1-h GCP training in http://www.gcp-enhed.dk/elaering/. In addition, key personnel received the GCP training offered as a PhD course at the University of Copenhagen (duration of 3 days).

UCPH had a general GCP advisor for the project, who trained the project manager (PM) in how to build and keep the Trial Master File.

Monitoring in PREVIEW: The intervention centres received monitoring visits either from the Sponsor or from the PREVIEW WP1 Leader (as CTM), to check whether the protocol and procedures were followed, and ensured that corrective actions were taken, as appropriate.

PREVIEW study protocol was prepared before the start of the intervention, and approved by the local Human Ethics Committees (IECs) at each study centre. Amendments were issued when relevant, and a new approval obtained, when the local laws required so.

PREVIEW Trial Master File (TMF) and the Internal Repository: An electronic TMF with relevant documents was designed and maintained by the University of Copenhagen, both in paper and electronically. All written study material was uploaded and made available at a private section of the PREVIEW website, including the protocol and its amendments, SOPs, and instruction materials for the intervention participants, in order ensure that comparable methods were followed across the eight centres (Fogelholm et al., 2017).

PREVIEW Case Report Forms (CRFs): The PREVIEW CRFs were designed before the trial started. They were initially developed in paper, mainly by the Sponsor, the Copenhagen PI and the CTM/Helsinki PI, but with contribution and reviews from the PIs in all centres and involvement of the DM. The CRFs were afterwards implemented electronically by using OpenClinica (n.d.) open source software.

Some centres decided to drop the paper CRFs and directly type the data into the OpenClinica CRFs. Other centres initially gathered the data from the participants in paper, and subsequently included it in OpenClinica. Only selected people in each centre had permission and credentials to access OpenClinica.

PREVIEW Standard Operating Procedures (SOPs): Twenty-four SOPs were developed for PREVIEW project, in order to ensure homogeneity of procedures in the intervention among the centres. They covered aspects such: the Low Calorie Diet (Christensen et al., 2018), diet and physical activity, group supervision, pre-screening, screening and randomisation of participants, measurements from the participants, samples collection, data quality, CRFs and questionnaires.

PREVIEW Meetings: Specific working groups with relevant centre representatives were established. Their aim was to discuss and agree on questions related to dietary topics, physical activity, data management and other methodological and medical issues (Fogelholm et al., 2017).

During the recruitment phase, PIs from each centre, together with the PC and PM participated in a monthly teleconference, which continued at regular intervals throughout the intervention (Fogelholm et al., 2017).

In addition to regular internal meetings at each intervention centre (more frequent at the beginning of the study, i.e. once a week, and less as the intervention was progressing), representatives from all centres were meeting in person at least once a year at a three-day meeting, and in connection with the PREVIEW project GA meetings (Fogelholm et al., 2017).

An Instructors' network formed by the CRCs, together with key hands-on staff from each centre, was meeting regularly by teleconference, in order to discuss problems and challenges and share best practices.

Training in PREVIEW: Before the start of the trial, representatives from each centre participated in two training sessions, each of 2-3 days duration. One session at the University of Copenhagen focused on the study protocol, GCP, instructions for study participants, and all outcome measurements (Fogelholm et al., 2017). The other session, arranged by the University of Stuttgart, dealt with the behaviour change methods for group counselling. Attendees then trained their local staff (Kahlert et al., 2016).

PREVIEW Collaborative EU-funded Project: Managerial Roles and Structure

The project management structure of the PREVIEW project consisted of the following 7 bodies: 1) Project Coordinator (PC); 2) Project Manager (PM); 3) EU Liaison Office; 4) General Assembly (GA); 5) Scientific Advisory Board (SAB); 6) Steering Committee (SC); and 7) Work Package Leaders (WPL) (PREVIEW, 2017).

The Coordinator and the leading organisations of the respective work packages (WPs) of PREVIEW are indicated in parenthesis: Project Coordinator, University of Copenhagen (UCPH): Prof. A. Raben, WP1: University of Helsinki (HEL), leader: Prof. M. Fogelholm, WP2: Wageningen University (WU), leader: Prof. E. Feskens, WP3: Maastricht University (UM), leader: Prof. M. Westerterp-Plantenga, WP4: University of Stuttgart (USTUTT), leader: Prof. W. Schlicht, WP5: University of Sydney (UNSYD), leader: Prof. J. Brand-Miller, WP6: University of Copenhagen (UCPH), leader: Prof. A. Raben, EU Liaison Office at University of Copenhagen (UCPH): Senior Executive Consultant P. Petersen (PREVIEW, 2017).

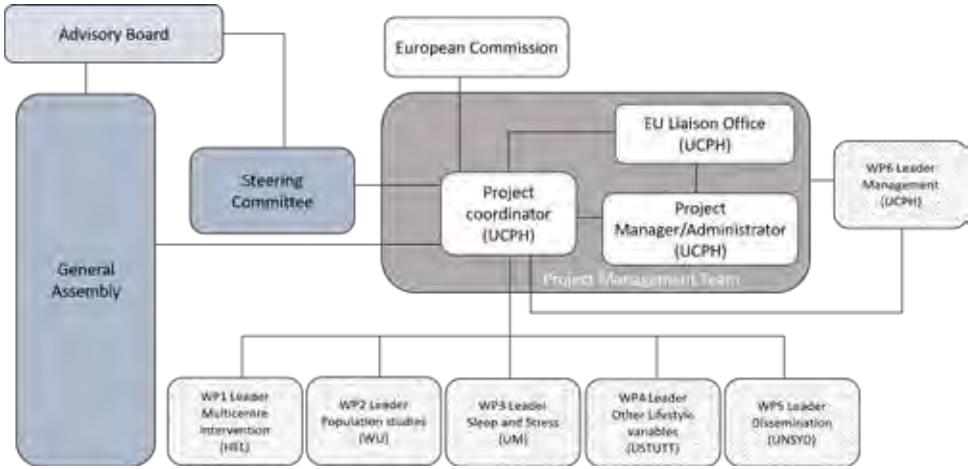

Figure 5. PREVIEW EU Project Management Structure.
UCPH: University of Copenhagen; HEL: University of Helsinki; WU: University of Wageningen; UM: University of Maastricht; USTUTT: University of Stuttgart and UNSYD: University of Sydney (adapted from PREVIEW, 2017).

PREVIEW Project Management Team (PMT): The PREVIEW PMT was formed by the Project Coordinator (PC), the Project Manager (PM) and the PMO. The managerial responsibilities with regards to the project were shared among them, as described below:

PREVIEW Project Coordinator (PC): In addition to the overall scientific coordination of the project, the responsibilities of the PC in PREVIEW were: 1) to act as the intermediary between the Consortium and the EC; 2) to ensure that the other partners duly signed the contract with the Commission in good time; 3) to distribute the funds among the partners, keep accounts and inform the EC accordingly; 4) to collect all deliverables, from the responsible partners, do a quality review of them and forward them to the Commission; and 5) to prepare periodic reports to the Commission (PREVIEW, 2017).

Even if all these responsibilities stayed with the PC, some of the related tasks were delegated to the PM or the PMO.

PREVIEW Project Manager/Administrator (PM): The daily management was carried out by the PM, under responsibility of the PC and in close collaboration with the EU-Liaison Office at the University of Copenhagen (former EU Office, currently Office of Research Services, Department of Research and Innovation), functioning as a PMO (PREVIEW, 2017).

The PM belonged to the same department as the PC (Department of Nutrition, Exercise and Sports –NEXS, Faculty of SCIENCE, University of Copenhagen), and was hired on demand and for the specific purpose of the PREVIEW project. The tasks of the PM were: 1) to manage the project on a daily basis, in agreement with the PC; 2) to arrange and prepare meeting agendas (kick-off, SC and GA meetings) and communicate decisions/prepare minutes; 3) to ensure and facilitate communication within the project partners; 4) to communicate with the EC, on behalf of the PC; 5) to collate, revise, format and submit deliverables to the EC; 6) to prepare Periodic and Final Reports, together with the PC, and with contribution from the SC members (and eventually from other partners); 7) to design and maintain the internal repository with all the project-related documents; 8) to prepare dissemination material; 9) to participate in Technical Reviews with the European Commission; and 10) to track and keep an updated list of synopses for publication.

PREVIEW Project Management Office (PMO): The PC and the PM in PREVIEW were in close contact with the central EU-Liaison Office at the University of Copenhagen. The University of Copenhagen has extensive experience in managing EU Projects. In FP7, the University of Copenhagen coordinated 21 collaborative projects and participated in total in 410 projects. In H2020 it participates in total in more than 689 projects, coordinating so far 14 collaborative projects (European Commission, 2021b).

The post-award team at the EU-Liaison Office was in charge of the following tasks: 1) support to the PC with regard to contractual matters between the Coordinator and the European Commission); 2) receipt of pre-financing and payments from the EC; 3) distribution of pre-financing and payments to the partners according to procedures agreed upon; 4) communication with the EC regarding administrative matters (such as eventual amendments) and financial reporting; 5) collation of financial reports (Form Cs and Certificates of Financial Statement; 6) provision of legal and financial advice to project partners; 7) participation in GA meetings and specific SC meetings upon request; and 8) participation in Technical Reviews in front of the EC, when deemed needed.

In addition, the EU-Liaison Office at the University of Copenhagen was involved in the preparation of the proposal (pre-award team), and during negotiation by reviewing the Grant Agreement (GA) and Consortium Agreement (CA) (legal team).

PREVIEW Quality Manager (QM) and Exploitation/Innovation Manager: PREVIEW did not have a QM appointed. This role was undertaken jointly by the PC and the PM, with involvement from selected internal Consortium members, when needed.

PREVIEW also did not have an Exploitation/Innovation Manager. However, the leader of WP5: Exploitation and Dissemination, Prof. Jennie Brand-Miller (USTUTT) undertook this role and developed together with Prof. Wolfgang Schlicht (USTUTT) an IPR Policy document,

promoting exploitation of project results, awareness of IPR and knowledge transfer.

PREVIEW Data Manager (DM): The PREVIEW multicentre clinical intervention (WP1) appointed an overall DM working at the University of Copenhagen. In addition to the previously described Data Management tasks related to the clinical trial, the DM was in charge of the following: 1) setting up and maintaining the PREVIEW datahub, a central structure collecting all study data and 2) providing data sets to researchers, after approval from the SC of the relevant synopsis for publication.

PREVIEW WP Leaders (WPLs): Every WP (1-6) was led by a WP Leader (WPL). The WPLs were responsible for the scientific coordination of their WP and tasks, including also the coordination of the workflow between their WP and others. The WPLs provided written input to all reports on activities when requested (e.g. Periodic Reports and Final Report) and collated deliverables and other information (PREVIEW, 2017). The specific allocation of responsibilities within WP1, PREVIEW Intervention/Multi-centre clinical trial, is illustrated in Figure 4.

PREVIEW Steering Committee (SC): The SC in PREVIEW was the decision-implementing body of the project. It was formed by the work package leaders (WPLs) and chaired by the PC. The PC in cooperation with the SC was in charge of the operational management of all the activities of the PREVIEW project. The SC facilitated exchange of information, enabling the PMT to make important decisions regarding the direction of a given WP. The SC was meeting four times a year. The SC consisted of: Prof. Anne Raben (UCPH), Project Coordinator, WP6 leader; Prof. Mikael Fogelholm (HEL), WP1 leader; Prof. Edith Feskens (WU), WP2 leader; Prof. Margriet Westerterp-Plantenga (UM), WP3 leader; Prof. Wolfgang Schlicht (USTUTT), WP4 leader and Prof. Jennie Brand-Miller (UNSYD), WP5 leader (PREVIEW, 2017).

PREVIEW General Assembly (GA): The GA in PREVIEW consisted of the partners' representatives, chaired by the PC. The GA was the final decision-making authority within the project. The GA was able to make overall decisions concerning the PREVIEW project.

Formal exchange of information largely took place as part of the GA annual meeting. The PC was ultimately responsible for the content of these meetings and was largely assisted by the members of the SC regarding both scientific content, as well as practical details (PREVIEW, 2017).

PREVIEW Scientific Advisory Board (SAB): The GA and the SC in PREVIEW were assisted by a Scientific Advisory Board (SAB) consisting of independent renowned experts in the fields of obesity and diabetes (PREVIEW, 2017).

The SAB was consulted on specific strategic matters regarding the scope of the project activities and to ensure that the direction of the PREVIEW project kept in touch with ongoing international diabetes research (PREVIEW, 2017).

Exchange of information between PREVIEW and SAB largely took place as part of the GA annual meetings, and in some occasions via mail communication. Travelling and living expenses for this Board were covered by the project management budget. The SAB in PREVIEW consisted of the following members: Prof. Louise Dye, Prof. Richard L. Atkinson, Prof. Lauren Lissner, Prof Boyd Swinburn, and Grethe Andersen (Fogelholm et al., 2017).

PREVIEW EU-funded Collaborative Project: Managerial Procedures and Tools

PREVIEW Website: A project website was established at the start of the project. It was developed by the University of Sydney, by using the ning.com platform (http://preview.ning.com/) (Fogelholm et al., 2017).

The project website was the main means to reach the general public and currently is still active. It contains information about the project objectives, WPs structure and Consortium. It includes project-specific dissemination material, such as the project flyer and the 6-monthly newsletters and a list of dissemination activities and publications derived from the project. It also gives access to the project e-learning material and some multimedia material, such as project-related videos.

PREVIEW Internal Repository: A password-protected repository of documents was established early in the project, as an internal part of PREVIEW website for only Consortium members (Fogelholm et al., 2017).

It contained project related documents, such as the Grant Agreement, Consortium Agreement, deliverables, reports, meeting agendas and minutes, approved synopses for publications and project publications. As previously described, it also gave access to documents related to the multi-centre clinical trial/intervention, such as the TMF, including the protocol and its amendments, ethical approvals from the IRBs/IECs, SOPs and instructions to participants. The PM was in charge of granting access to only Consortium members and maintaining contents up to date.

Project Meetings in PREVIEW: The partners in the PREVIEW communicated and shared information by email and conference calls, in order to reduce travel cost and improve use of executive time. When possible, the annual GA meetings or SC 3-monthly meetings were held in connection with relevant international scientific conferences.

The kick-off meeting was of special relevance. It was held during M2 of the project, at the coordinator premises at the University of Copenhagen, Copenhagen, Denmark. This meeting was the first occasion where all project partners met in person. The project coordinator chaired the meeting, and the project manager was introduced. The project scene was settled, and the managerial structure and procedures were explained to all participants. Subsequent GA meetings were hosted each time by one Consortium partner.

Table 1 provides an overview of the general management procedures, including the frequency of meetings (PREVIEW, 2017).

Table 1. PREVIEW EU project Management procedures (PREVIEW, 2017.)

WHO	WHEN	WHAT
The Project Coordinator/ Project Manager	Daily	Performing the day-to-day management of the project
Partners	Monthly	Reporting to WPLs, through progress report and meetings
WP leaders	Every three months	Reporting to PC, in connection to the SC meetings
Project Coordinator	At the end of each reporting period (M12, M30, M48, M72)	Reporting to the EC, through the periodic activity report and final report
Project Coordinator	At project start, and after approval of periodic reports	Distribution of pre-financing and project payments to the Consortium
Project Coordinator / Steering Committee	Annual	Reporting to the GA Minutes of meeting circulated to all partners
Project Coordinator/ General Assembly	Annual	Presenting for the SAB
Scientific Advisory Board	Annual	Reporting to the GA Providing feedback about the project
All partners	Annual	Participating in the annual GA meeting Kick-off meeting hosted by the coordinator Rest of meetings hosted by turns by different project partners
All partners	Annual	Researcher's forum: arranged in connection with the GA meeting

During the project, in addition to regular meetings among the Consortium partners, the project went through 3 technical reviews upon request from the EC. During these, independent experts analysed the status and challenges of the project, and provided a set of recommendations and action points to which the Consortium should provide a response, and eventually react and adjust the project accordingly.

Data Management in PREVIEW: Appropriate attention to Data Management in PREVIEW was ensured from the start. However, a formal Data Management Plan was not officially issued, since it was not a requirement under FP7 (vs. H2020 projects participating in the Open Research Data Pilot).

Personal data included aspects of health, ethnicity and information related to lifestyle variables such as dietary preferences and habits and physical activity habits as well as sleep, stress, habitual behaviour, social environmental influences, cultural habits, as well as socio-ecologic and socioeconomic information. The project did not collect data on political opinions, religious or philosophical convictions. None of the data collected were disclosed to third parties and the information collected was only used within the project (PREVIEW, 2017).

Each partner in PREVIEW should ensure the confidentiality of any personal data held or transmitted on paper, files, manual or electronic systems or any other manner, for example by protecting access to databases and buildings (PREVIEW, 2017).

The clinical samples obtained were treated as confidential and labelled with a trial code number. For additional privacy protection, the trial code number was replaced by a unique new identifier, which was used in all subsequent work. The key linking both identifiers was kept safely locked at each intervention centre (PREVIEW, 2017).

The privacy of personal data was ensured during handling, storage and transfer of data, in accordance with national regulations and EU regulations such as the Data Protection Directive 95/46/EC, which was superseded by the GDPR from 2016.

PREVIEW EU-funded Collaborative project including a large Multi-centre Clinical Trial

Previous sections 3.2 and 3.3 have focused on PREVIEW multi-centre clinical trial, while sections 3.4 and 3.5 have presented PREVIEW seen from the perspective of an EU-funded collaborative project.

It can be challenging to understand the interrelation between both scenarios, as well as to comply with the rules and requirements of both as the same time.

Table 2 aims at establishing, when applicable, a parallelism between the managerial roles of both scenarios in PREVIEW.

Table 2. Summary of Managerial Roles, Structure, Procedures and Tools in Multi-centre Clinical Trials (Left) and in Collaborative EU-funded Projects (Right).

Managerial roles and structure	
Multi-centre Clinical Trials	**Collaborative EU-funded projects**
Sponsor	Project coordinator (PC)
	Exploitation and/or Innovation Manager
-	General Assembly (GA)
Contract Research Organisation (CRO)	Quality Manager (QM)
Coordinating Centre (CC)	Coordinating organisation
Clinical Research Associate (CRA)	-
-	Project Management Team (PMT)
Clinical Trial Manager (CTM)	Project Manager (PM)
Principal Investigator (PI)	Principal Investigator (PI)
Clinical Research Coordinator (CRC)	Daily responsible from each beneficiary
Clinical Trial Administrator (CTA)	Project Management Office (PMO)/
	Project Administrator
Trial Steering Committee (TSC)	Steering Committee (SC)
Data Safety and Monitoring Board (DSMB)/	Advisory Boards (ABs)
Data Monitoring Committee (DMC)	
Institutional Review Boards (IRBs)/	Ethics Manager
Independent Ethical Committees (IECs)	
Working Group Leader	Work package leader (WPL)
Participants	Users, stakeholders
Funding Agencies	European Commission (EC)
Analyst	Data Manager (DM)
Data Manager (DM)	

Managerial Procedures and Tools	
Multi-centre Clinical Trials	**Collaborative EU-funded projects**
Good Clinical Research Practice (GCP)	Quality Management
Register in Clinicaltrials.gov	Project website
Monitoring	Periodic Reporting and Project Reviews
Data Management	Data Management
Protocol	Description of Work (DoW)
Standard Operating Procedures (SOPs)	
Case Report Form (CRF)	-
Trial Master File (TMF)	Internal repository
Principal Investigator (PI)	Principal Investigator (PI)
Data hub	Data hub, central database
Meetings	Meetings
Training	Training

Figure 6 is a timeline aiming at providing an integrated overview of the procedures and time events for both scenarios in PREVIEW.

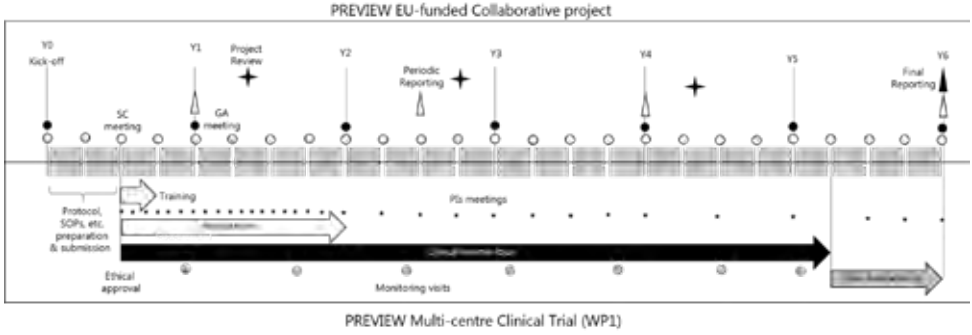

Figure 6. Timeline for the PREVIEW EU-funded Collaborative project (above) and the PREVIEW Multi-centre Clinical Trial (below).

Discussion and Conclusion

PREVIEW was a collaborative EU-funded project that involved a large multi-centre clinical trial (WP1). The Sponsor was a sponsor-investigator, and at the same time, the overall PC. This helped maintaining the overview and compliance with the demands for both contexts.

The tasks associated to the CC for WP1 were shared between Copenhagen and Helsinki centres, where the Sponsor and the CTM belonged, respectively. This approach made sense as the Sponsor and the CTM could complement and collaborate with each other. In addition, this helped balancing the distribution of efforts and responsibilities within the project.

Each of the 8 intervention centres had a PI, as overall responsible, and a daily responsible (CRC). This structure worked well, as the CRCs were in many cases, staff dedicating full-time or a significant part of their time to PREVIEW, in an operative role, while the PIs often could devote part-time to the project, and their role consisted in giving direction and strategy to the intervention.

The CTA role was undertaken by the PM, after receiving appropriate training in GCP. This approach worked well, as the PM was already dealing with the several documents from the project, where the trial belonged. This structure allowed shared use of resources, and helped the PM to acquire new knowledge and skills.

There was no TSC, and a similar role was assumed by the group of the PIs from all centres, counting with the advice from the SAB members. No DSMC was employed, although there was an Ethical Officer, responsible for monitoring and reporting about the safety of the trial. This role was undertaken by one of the members of the SAB. This configuration was cost effective, and made sense given the financial constraints of the project and the trial.

The analyst role in PREVIEW was shared among the sponsor, the CRC in Copenhagen centre, the CTM and the project statistician. The DM was hired by the University of Copenhagen, and was assuming the overall data management of the multi-centre clinical trial. This decision was logical, because of the expertise present at the University, as well as the datahub (placed at UCPH), which needed to aggregate data from all centres.

The monitoring of the trial was done internally by the CC instead of by an external monitor. Although this compromise made sense from the financial point of view, such a task should ideally be done by an external party, not involved in the trial. Therefore, in the future, it is important to include a financial contribution for this in the budget from the start.

Specific WP1 working groups (e.g. for dietary plans, questionnaires and medical issues), with relevant centre representatives were established very early in the project. This was deemed necessary, since WP1 constituted about 75% of the project and a huge workload was put on the WP1 leader and the Sponsor. It would not have been possible to fulfil the WP1 goals without delegation of some the tasks to the other partners. For similar projects in the future, it is advisable to define several thematic working groups for the clinical trial prior to the start date. Clear responsibility needs to be established, or have separate WPs dedicated to each area. It is though

important to ensure that the project does not become unmanageable because of being broken down into too many WPs.

PIs from all WP1 centres met regularly, with high intensity during the recruitment period. An instructors' network formed by the CRCs, together with key hands-on staff from each centre, also met regularly by teleconference, to discuss problems and challenges, as well as to share best practices. Such regular meetings were crucial to enhance collaboration, monitor progress and communicate in a transparent manner among partners.

The coordination of PREVIEW consisted of a combination of centralised and de-centralised project management. The PC, the PM and the PMO formed together the PMT, and jointly ensured that the coordination and administration of the project was done correctly and efficiently, while releasing the PC from some of the administrative burden.

The GA was formed by representatives from all beneficiaries, chaired by the PC, and the SC consisted of all work packages' leaders. The GA and the SC were key with regard to reviewing and implementing decisions. The PC alone would not have been able to undertake these tasks. The SAB was formed by reputed external experts, who provided independent advice.

The project website was the main channel to reach the general public. It served as a resource providing information about project objectives and progress. A password protected private section was used as internal repository, which was very useful to share project related documents among the Consortium members, including those from the TMF from the intervention in WP1. Regular meetings at all levels (WP, SC, GA, other ad-hoc meetings) were key to ensure good communication and collaboration among the project team.

Multi-centre clinical trials have several advantages with respect to single-centre trials, however, the management is more complex. Furthermore, the management of collaborative EU-funded projects is usually regarded as challenging, time consuming and demanding. This article has presented PREVIEW FP7 project, as a combination of those two managerial scenarios. A robust managerial structure and a set of managerial procedures and tools have been designed for each of them, with an optimal use and reutilisation of resources.

PREVIEW is not the first, nor the last EU-funded project that includes a multi-centre clinical trial. The authors hope that the structures, tools, and reflections gathered, described, and proposed in this paper will help future coordinators to plan and manage multi-centre clinical trials in the framework of collaborative EU-funded projects, as well as other multi-partner complex projects, in a successful way.

Authors' Note

PREVIEW project received grants from the EU 7th Framework Programme (FP7-KBBE-2012), grant agreement No. 312057; the New Zealand Health Research Council, Grant No. 14/191; the NHMRC-EU Collaborative Grant, Australia and Le Ministre De L' Enseignement Supérieur, de la Recherche, de la Science et de la Technologie, Canada (PSR-SIIRI-837). All LCD products were provided by Cambridge Weight Plan®, UK.

The authors would like to thank Malene Roost Lytsen, MSc., EU Liaison Officer, and Poul Petersen, Senior Executive Consultant, both from the Office of Research Services, Research and Innovation, University of Copenhagen, Denmark; Myhanh Nguyen, MSc., previously EU-Liaison Officer for PREVIEW at the University of Copenhagen and Stéphanie Maria Palombi, MSc. and Kateryna Kolkova, PhD., both previously affiliated to the Department of Nutrition, Exercise and Sports (NEXS) from the University of Copenhagen, PREVIEW Project Managers during 2015 and 2017, respectively, for their contributions to the management of PREVIEW.

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