



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Success factors, lessons learned and
recommendations for infrastructure
and organisation of joint research
between consortia

Harmony Covid-19 vaccine studies



Lessons learned

The Dutch National Institute for Public Health and the Environment (RIVM) worked with academic hospitals and a general hospital, providing ten studies, in the Harmony partnership to study the immune response brought on by COVID-19 vaccinations.

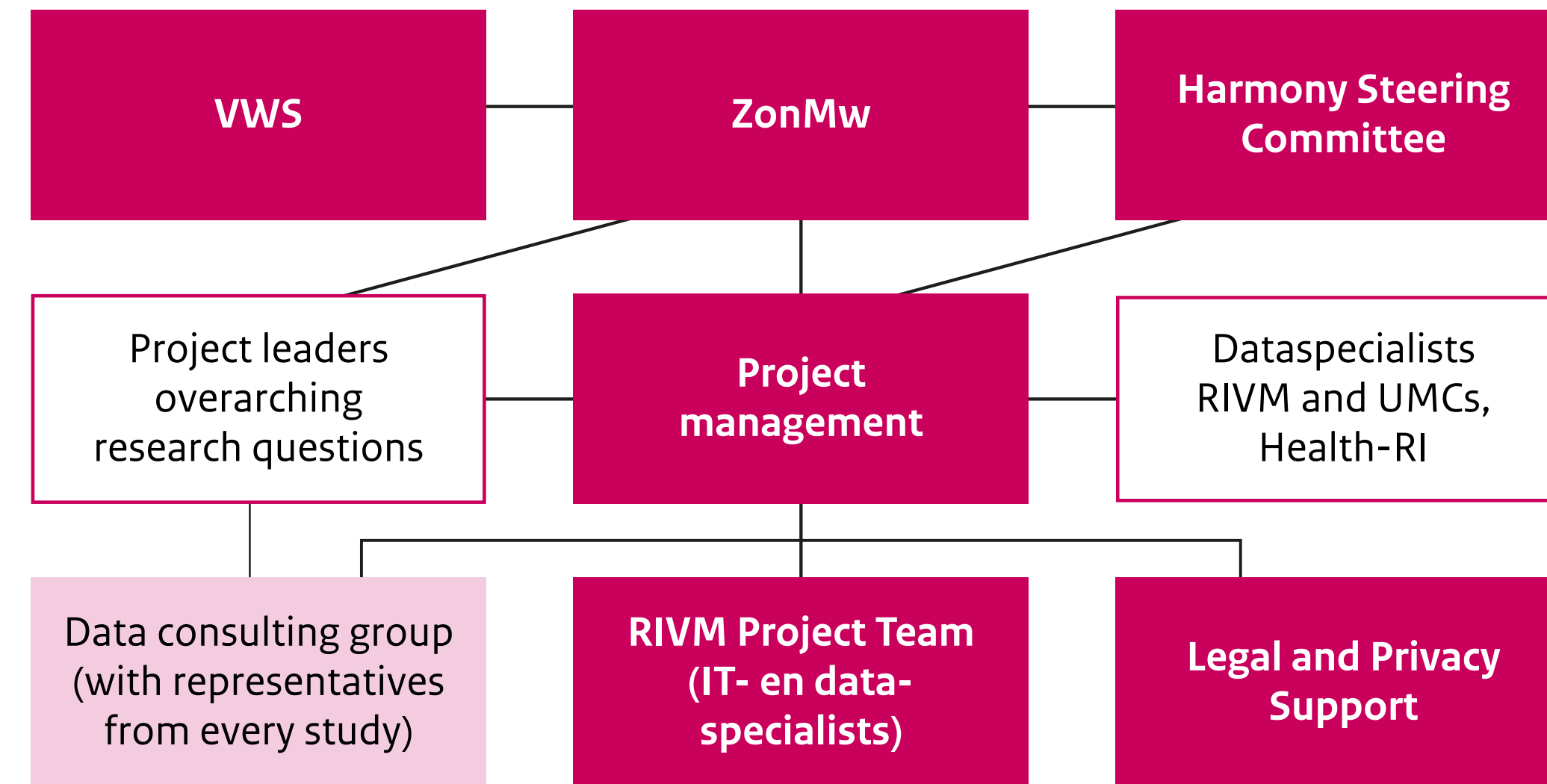
This memorandum includes success factors, lessons learned and recommendations for researchers and policy makers who are about to combine knowledge from all the studies to provide the best treatment for their patients through joint research and shared data.

About the HARMONY partnership

In 2021, a large portion of the Dutch population was vaccinated against COVID-19. The vaccination triggers an immune response in the body, boosting the body's immunity. RIVM and Erasmus MC studied the immune responses of healthy people. Ten Dutch research groups studied the immune responses of patients with reduced immune function. The Netherlands Organisation for Health Research and Development (ZonMw), the grant provider, requested to align the dates for evaluation and the final dates for the COVID-19 vaccine studies, so the results from the various studies (among different patients) can be compared, an overarching analysis can be carried out and overarching research questions can be answered. The Harmony consortium was established to enable data to be shared in a safe and efficient manner and to ensure uniform language. The goal of the Harmony project was to build an organisation and infrastructure for overarching analyses. The overarching research project pilot of Erasmus MC was used to test whether it was working.

Parties and their roles

Below is a diagram of the parties involved. The table next to it explains the partnership and each partner's role.



Party	Role
VWS	Ministry of Health, Welfare and Sport. Commissioning authority for the Netherlands Organisation for Health Research and Development (ZonMw), framework-setting role and European developments liaison
ZonMw	Netherlands Organisation for Health Research and Development. Grant provider, project conditions
RIVM	The Dutch National Institute for Public Health and the Environment. Main applicant ZonMw grant and project management
Harmony Steering Committee	Decide on joint focus on content, activities and financing, analysis and publications during the project
Project management	Organise the process, keep track of targets and deadlines, content coordination
Project leaders overarching research questions	Perform overarching analyses regarding the harmonised data, separate projects are funded by ZonMw
Dataspecialists RIVM and UMCs, Health-RI	Help organisations and researchers organise data and IT using tools, best practices and advice
RIVM Project Team dataspecialists	Data management, data harmonisation, data exchange, database including
Legal and Privacy Support	Support in drawing up a consortium agreement and DPIA (Data Protection Impact Assessment)
Data consulting group	Please note: not set up due to unavailability of dedicated data managers/stewards at the participating consortium partners

Project steps

The four project steps are discussed on the next pages.

We identify the success factors and lessons learned and provide recommendations.



1 Objective and preconditions



The ambition and urgency to achieve overarching analysis of the study outcomes were shared with the RIVM and UMC researchers involved during a kick-off meeting. Grant provider ZonMw set the frameworks. A comparable research setup is relevant in that respect. What was done in this phase and what have we learned?

Success factors

- ZonMw encouraged **co-operation** and included specific criteria and preconditions (supplemental to the general ZonMw criteria) to benefit the co-operation and overarching analyses. Some examples are shown below:
 - The project includes research into different components of the immune system, including the level and functionality of SARS-CoV-2 specific antibodies and T-cells. The outcome parameters for, inter alia, immunity and when they are determined are coordinated with the various consortia and RIVM to facilitate overarching analyses.
 - The Informed Consent will include the provision that data may be shared to facilitate overarching analyses, with due observance of personal data laws and regulations.

- All parties involved were **highly motivated** to perform overarching analyses in order to provide the best possible protection for their patient population and the healthy population, with the lowest possible burden (no extra vaccines if not needed).
- ZonMw and all the consortium partners laid down the **course and main line** early in the process, leading up to the grant application, which were used to build a consortium that would set to work together.

Lessons learned

- The grant provider plays an important role by setting conditions and criteria when assessing projects. The **more specific** the criteria and conditions, the more uniform the comparability of the study results and the possibilities for answering overarching research questions. Based on experience gained through the project, even more specific conditions may be set in the future. This could include the data model and codebooks to be used.
- It would have been useful for the consortium agreement to be drafted later on to have already **laid down** the main lines of the **intention** to cooperate and share data in the first step, including the privacy and legal conditions.

2 Preparation and organisation



At ZonMw's request, an overarching Infrastructure and Organisation project was formulated to enable overarching analyses, learning from experiences and setting up an organisation that would be useful now and in the future.

Success factors

- Setting up and providing a **grant** to an overarching project was a useful method. It made it possible to set up the organisation and infrastructure, to harmonise and prepare data for overarching analyses.

Lessons learned

- The first step in co-operation is drafting a consortium agreement between all the partners. Drafting and signing the consortium agreement took **more time** than anticipated. Building on an existing consortium agreement used by the same hospitals unexpectedly did not lead to a quicker procedure. Every agreement, including the DPIA, must be individually approved by a legal and privacy department. This, in combination with limited available staff, delayed the process. The sharing and harmonising of data could not start until after the DPIA had been completed and the agreement had been signed. Only then did the major differences between

the datasets of the studies become clear and the steps needed to achieve harmonisation. This all resulted in significant delays.

- In the project proposal, the project organisation was led by a Steering Committee and a Data consulting group. Due to a lack of dedicated data stewards and/or data managers in most studies, the Data consulting group never got off the ground. Even though such a group is **crucial** for discussing ambiguities, questions and issues concerning data and making decisions. This was now done in one-on-one discussions between the RIVM Project Team and a study contact person.

Recommendations for UMCs, RIVM and ZonMw

- A **template consortium agreement** for this kind of research – its main points agreed by UMCs, RIVM and similar organisations in advance – could greatly speed up these kinds of processes. It is recommended that such a template be developed, together with the legal and privacy departments. VWS and ZonMw could develop and provide frameworks to that end.
- Start with the DPIA early in the process by gathering all the privacy lawyers involved. A **pre-filled/standardised template DPIA** can speed up the process.
- **Data stewards/managers** or trainee research assistants who performed the data analyses in this project play an essential role in these kinds of projects. ZonMw may set conditions for including data stewards/managers in project proposals.

3 Data collection, harmonisation and analysis



Project management has assembled a team consisting of an RIVM IT architect, data engineer and data stewards. This team works on the infrastructure and data harmonisation, has been in contact with all the research groups, has set up the infrastructure and performed the data harmonisation in consultation with the researchers. The team has learned many lessons, some specific to this project, others more uniform. In addition, the project was a pilot project in the RIVM Data Use Programme. The lessons learned from Harmony thus also benefitted the organisation and the developments in the Data Use Programme and vice versa.

Success factors

- **Many things are learned** in the process, for example about data, data quality, codebooks, data models and architecture. The Digital Research Environment (DRE) of anDREa is used as a secure space for sharing data and performing analyses. Federated analyses, the dot on the horizon to be attained in the future, was not feasible for this data set.
- Creating a template in which the data could be uploaded according to a **fixed structure** speeded up the harmonisation considerably.

Lessons learned

- Data quality at the source, using the same codebooks, one proper codebook (description of the variables) per study, one data model and establishing requirements with regard to data delivery, are an absolute necessity for harmonisation and answering overarching research questions. The fact that the studies were geared towards endpoints and times of vaccination proved insufficient for performing overarching analyses. It is **essential** that **agreements** are made right at the beginning. Now manual harmonisation was needed, which took a lot of time.

Recommendations for researchers

- Establish guidelines in advance for codebooks, data models and data quality. Involve data stewards **early on** to set these guidelines.

4 Completion and administration



The consortium agreement contains all the elements relevant in both the co-operation phase and upon completion. It contains the organisation of the consortium, the publication plan and how to process data after the ZonMw funding has ended. To ensure that lessons learned and experiences gained are properly safeguarded and further developed, agreements have been made with the Ministry of Health, Welfare and Sport and ZonMw. There have been talks with data departments of the organisations involved (RIVM and Health-RI regional head of nodes) and others (such as Health-RI, DANS, Statistics Netherlands). For RIVM, the Harmony project was one of the pilots of the Data Use Programme, a four-year programme aimed at optimal data use (see step 3).

There were numerous developments in data during the project, both at European (the establishment of an HDAB¹ to anticipate the EHDS²) and national level (VWS, Health-RI³, CumuluZ⁴) and in the UMCs and RIVM.

¹ Health Data Access Body

² European Health Data Space

³ Health-RI is a Dutch national initiative to facilitate and stimulate data driven research, policy and innovation with an integrated health data infrastructure. It will be accessible for researchers, citizens, care providers and industry. This will enable optimal re-use of health data, samples and images to foster a learning healthcare system and accelerate personalised health. Health-RI has received funding from the European Union's NextGenerationEU and the National Growth Fund.

⁴ CumuluZ is an open platform for Dutch care. The main purpose of this care platform is to create a life course file (a document containing an individual's health and social care history). This will grant care providers and patients access to all the health data they need to decide on the most ideal form of care. CumuluZ makes this data available through a national network of data hubs, which makes it easier to make data available for scientific research. CumuluZ was initiated in 2023 and is currently under construction.

Success factors

- The area of optimal data use is seeing rapid advances and huge strides were made during the project that could not have been anticipated beforehand. Many things were learned in the process. The lessons learned from Harmony and elsewhere contributed to **concrete products** for RIVM, such as the Checklist research project, in which the entire cycle to be followed by researchers is described, including everything in the field of data. These concrete lessons are now being developed further by RIVM, and at national and international level, so that we will be better prepared for any future pandemic.

Lessons learned

- Obstacles are made visible in a concrete project, providing an understanding of what is needed at a strategic level. This requires **communication** on lessons with various parties. Acknowledging the fact that not everyone speaks the same language and that it is a meeting of different worlds is important in that regard.

Recommendations for researchers, VWS and ZonMw

- Now is the time to prepare a **roadmap** for other co-operation projects where data from different projects must be shared. Or for the next pandemic, knowing that a tailored solution will be required.
- Make agreements on codebooks, uniform nomenclature, such as use of SNOMED or LOINC, making data uniform, registration systems to be used, etc., which is what Health-RI and CumuluZ are also working on, as will be the case going forward in the EHDS. These are steps towards **Consistent Language** for this professional field, building on the lessons learned from this project.

Recommendations for the Ministry of Health, Welfare and Sport, and grant provider ZonMw

The role and involvement of frame-setting parties, such as the Ministry of Health, Welfare and Sport and ZonMw, is crucial. This concerns initiating research and promoting co-operation and setting preconditions and providing templates (for consortium agreements, DPIA and Consistent Language).

Contact

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