

CSA JPI HDHL 2.0

# Evaluation of Joint Funding Actions

**ENPADASI KH: Knowledge Hub on European Nutrition Phenotype  
Assessment and Data Sharing Initiative**

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## 1 Introduction and aims

Monitoring and evaluating of JPI HDHL activities is highly important to measure the success, concrete outcomes and impact of the JPI HDHL and to allow for continuous improvement and development of this initiative. Therefore, these activities are an integral part of the work plan of the current Coordination and Support Action (JPI HDHL CSA 2.0).

The evaluation activities continuously performed by JPI HDHL include:

- Monitoring and evaluation of the processes and general performance of JPI HDHL → Report on the third and fourth Process evaluation of JPI HDHL (CSA Deliverable D6.1, D6.4)
- Evaluation of the funding activities of JPI HDHL → Report on the evaluation of JPI HDHL funding activities (CSA Deliverable D6.2, the present report)
- Monitoring and evaluation the activities of JPI HDHL not related to funding → Report on the evaluation on the progress of the alignment activities (CSA Deliverable D6.3)
- Overall evaluation of the impact of JPI HDHL → Report on the evaluation of the impact of JPI HDHL (CSA Deliverable D6.5)

These tailored activities focus on different aspects of JPI HDHL presented in the consecutive published Implementation Plans (IP) and will result in publically available reports like this one.

The main aim of this report is to evaluate the monitoring data of the funded research in JPI HDHL in relation to the respective aim of the call and the IP and to analyse the output, outcomes and impact of JPI HDHL funding activities (both on call and project level). The results of the evaluations will allow the fine-tuning, refining and planning of new activities for the following IP to reach the expectations of all stakeholders and fulfill the JPI HDHL objectives. The evaluation will also assist in raising awareness for the activities performed under the umbrella of JPI HDHL and provides the basis for the communication and dissemination of JPI achievements.

## 2 Approach for the evaluation of the JFA

The evaluation is based on comparison of the objectives of the IPs and the outputs/outcomes of the different funding activities of the JPI HDHL. In addition, the Scientific Advisory Board (SAB) and Stakeholder Advisory Board (SHAB) of the JPI HDHL have been involved in the evaluation process. The evaluation of the Joint Funding Actions builds on the related work packages in the ERA-Net ERA-HDHL, in particular WP 7, dealing with monitoring and communication of the additional transnational JFAs and their results.

The present report includes evaluations of all JFAs implemented by the JPI HDHL in 2015 and earlier:

- Determinants of Diet and Physical Activity Knowledge Hub (DEDIPAC KH, 2013)
- European Nutritional Phenotype Assessment and Data Sharing Initiative (ENPADASI, 2014)
- Biomarkers for Nutrition and Health (BioNH, 2014)
- Food Processing for Health (FP4H, 2014)
- Malnutrition in the Elderly (MaNuEl, 2015)
- Intestinal Microbiomics (IM, 2015)
- Nutrition and Cognitive Function (NutriCog, 2015)

## 2.1 Methods

For this report a 'Framework for the evaluation of JPI HDHL joint funding activities' (see Annex) has been developed by the task leader and agreed with the other involved CSA partners.

In a first step, relevant indicators have been collected and defined (see chapter [2.2 Indicators](#) for details). Based on these indicators the required data from the funded projects have been collected systematically in form of project reports and oral presentations at the project symposia (see chapter [2.3 Monitoring](#) for details). If necessary, further questions were addressed to the coordinators of the research consortia. In parallel, other necessary data and information (call documents, call statistics, etc.) have been collected from the respective Call Secretariats. In addition, the success and impact of funded projects has been assessed by experts (previous or former SAB and SHAB members) based on final project reports and symposia. For the experts' assessment a specific short evaluation questionnaire, based on the elaborated indicators, has been developed. This template asked the respective expert for a short written assessment of the funded projects based on 3-4 leading questions after the attendance of the final symposium and/or reading of the final report.

The actual evaluation has then been performed by the task leader by analysing the different data available following the evaluation framework and afterwards agreed with the other involved CSA partners.

## 2.2 Indicators

The indicators used in this evaluation report have been developed in a designated task force by several CSA partners in a separate task (Subtask 6.1.1 Definition of performance indicators) within the CSA JPI HDHL 2.0. Two different types of indicators have been defined, general and specific indicators, comprising outcome, output and impact level:

### **(1) General indicators for all JFAs**

To enable the comparison between joint funding actions (at least with JFAs using the same funding instrument) a set of general indicators for all JPI HDHL JFAs has been developed. These general indicators can be grouped into six overarching categories comprising several more specific indicators: Alignment of national funding, Involvement of national scientific communities, Collaboration, Capacity Building, Data and Knowledge Sharing, and Impact.

### **(2) Specific indicators for each respective JFA**

Since the aims and objectives differ greatly between the various JFAs, the definition of specific indicators was necessary to evaluate the success of a JFA in itself and not only in comparison to other JFAs. To evaluate the success of each JFA separately, specific indicators following from the corresponding Strategic Research Agenda and IP as well as the call text as of each JFA have been developed.

## 2.3 Project Monitoring

The comprehensive monitoring of the output and outcomes of the running and finished funded projects builds the basis for the performed evaluations. The systematic and structured collection of data from all funded projects has mainly been organized within a designated work package of the ERA-Net ERA-HDHL (WP7). The monitoring activities within ERA-HDHL comprised the monitoring of

the progress and the results of the research projects of the non cofunded JFAs implemented as part of ERA-HDHL, as well as the previous calls implemented through the IP 2014-2015.

Data from all funded projects have been collected in accordance to the indicators defined in WP6 of the CSA JPI HDHL 2.0. This comprises data both on call and project level:

**(1) Call level:**

For each Joint Funding Action, the funding organisation responsible for the Joint Call Secretariat (JCS) of a JFA was in charge of the statistical analysis of the call results based on the elaborated indicators (see 2.2). In particular the geographic distribution of the scientists applying to the call, the discipline and the type of organisation, the amount of funding requested per partner/consortium and the transnational cooperation has been analysed.

**(2) Project level:**

The follow-up of funded projects was taken care of by the respective JCS. For each funded project, annual scientific progress reports and one final report have been collected.<sup>1</sup> Project coordinators were asked to submit the respective scientific reports for the joint project, on behalf of the whole consortium to the respective JCS based on a pre-defined template including the specific indicators (see 2.2). Since 2019, these reports are collected using an online submission tool.

For the calls launched 2015 and later, the progress of ongoing JFAs has also been monitored by two status symposia organized by JPI HDHL. One status symposium has been held during the runtime of the projects (midterm symposium) and one just before the project is about to finish (final symposium). The main purpose of these symposia is to provide the JCS, the Call Steering Committee and members of the former Scientific Evaluation Committee (SEC) as well as representatives from SAB and SHAB with an update on the progress of the research projects. The presentations by the project coordinators and partners PIs are followed by a plenary discussion with questions from the audience.

For most of the earlier calls (DEDIPAC, ENPADASI, FoodBall/BioNH, MaNuEI) a final conference has been organized by the consortia itself without participation of SAB, SHAB or former reviewers.

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<sup>1</sup> The data collection for the specific indicators as part of the final report was not possible for the first three JFAs (DEDIPAC, ENPADASI & MaNuEI) since the specific indicators have only be defined after the projects where finished. The project coordinators have been contacted retrospectively to answer those indicators.

### 3 JPI HDHL Joint Funding Action: Knowledge Hub on European Nutrition Phenotype Assessment and Data Sharing Initiative (ENPADASI KH)

#### 3.1 Aim of the call

The ENPADASI Knowledge Hub (KH) was the second joint funding action that has been implemented by the JPI HDHL in March 2014 and the first joint funding action within Research Area 3: “Diet-related chronic diseases”. **The aim of this funding action**, in which twelve funding organisations from nine JPI HDHL member states participated, was to **provide a standardized framework for human intervention studies on food and health and their health outcomes with an open-access reference database**. To achieve this, a Knowledge Hub was to be formed and to carry out joint trans- and multidisciplinary activities aiming at the standardisation of data collection, storage and management through the development of a common methodology and a shared Information and Communication Technology (ICT) infrastructure.

ENPADASI KH was established to offer an **open access tool** for all future mechanistic, intervention and epidemiological studies; providing the highest level of standardisation of all phenotypic information of study subjects with regard to diet, physical activity levels and all biological, clinical and physiological measurements that define human body responses in health and disease states.

The implementation of the joint action focused on three areas:

- **Database development.** The ambition was to make ENPADASI the leading system for big-data storage assessment and sharing in nutritional research in Europe. Investments to develop the system encompassing functions such as shared analysis modules, sharing of images, etc were required.
- **Integrating existing databases in the ENPADASI.** In order to make full use of the system, datasets from nationally and European funded research projects were to be linked
- **Training sessions for young researchers.** Researchers were to be trained to learn how to work with the system.

The following main goals were given in the call text:

- a) Defining the standardised phenotypic information with regard to diet, physical activity levels and all biological, clinical and physiological measurements (including large scale approaches)
- b) mapping the different existing data sharing initiatives in the field of nutrition and closely related fields (e.g., nutrition-related diseases) at EU and national levels.
- c) defining specifications and requirements for a shared database from technical (including back-up), scientific and ethical points of view.
- d) evaluating the compatibilities between existing systems and possibilities of using various end user applications.
- e) evaluating sustainability and maintenance costs and planning corresponding resources.
- f) standardizing methods and data. Agreements on standardized methods and data handling, interoperability, assembling of the database and embedding of standardization in global developments. The database should allow all European established and future nutritional studies to interact on common methodology and procedures.

- g) Integrating existing databases in the area of human intervention studies and mechanistic models in ENPADASI. Testing of integrated database with research questions reflecting both existing data as well as data newly integrated in the system.
- h) Building a European governance structure for the database maintenance and development, data duration and data pipelining, with adequate 'rules of engagement'.
- i) Defining procedures to safeguard ethical issues and privacy protection of ENPADASI to meet international and legal standards for the use of personal data for research purpose
- j) Training for researchers on how to work with the system.

## 3.2 Peer-review Procedure and Results

The call for the ENPADASI Knowledge Hub was **launched on the 31<sup>st</sup> of March, 2014**. The drafting of the call text was coordinated by Italy. The Joint Call Secretariat was located at the Netherlands Organisation for Health, Research and Development (ZonMW).

The implementation process was organised as a three-step procedure.

- 1) Researchers in all participating countries were asked to submit an **Expression of Interest -letter** (Eol), stating their expertise and scientific excellence in the relevant field, personal and institutional capacities and infrastructures and the potential contribution to the activities of the KH. In the following **national evaluation processes**, each participating funding organisation selected their ENPADASI KH members according to national eligibility criteria as well as agreed criteria as stated in the "Terms of Reference" (i.e. call text) document. After finishing the national evaluation, the funders represented in the ENPADASI Steering Board discussed and adapted the overall selection of candidates to ensure sufficient scientific and geographical balance of the network partners<sup>2</sup>. Subsequently, the applicants were informed on the outcome of the process.
- 2) The partners selected for the ENPADASI KH met for the first time at the **networking meeting on the 13<sup>th</sup>-14<sup>th</sup> of May 2014 in Rome**. At this meeting, the background and specific objectives of the initiative were presented and discussed. Furthermore, the networking meeting was the starting point for concept development and drafting of one transnational **ENPADASI programme proposal**. During the course of this networking meeting a coordinator was elected. During the next four months, a full joint proposal was developed and the programme proposal was submitted by the coordinator on 1<sup>st</sup> of September, 2014.
- 3) The ENPADASI programme proposal was evaluated in a **peer-reviewed process** by an evaluation panel consisting of 3 internationally renowned experts in the field from Sweden, Norway and Switzerland, according to the criteria that were described in the terms of reference document. The Evaluation Panel (EP) discussed the network proposal in an **evaluation meeting** on the 13<sup>th</sup> of October 2014 in Bonn, including a hearing of the knowledge hub coordinating team. As a result of that meeting, the hub coordinator was invited to revise and re-submit the programme proposal according to recommendations from the EP. The revised proposal was again evaluated by the EP and based on the positive result, the Call Steering Committee decided to fund the knowledge hub (November 2014).

**In December 2014** the ENPADASI KH officially **started its work**. Some of the partners only received a final acceptance of funding more than a year after the start of the project which delayed the work,

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<sup>2</sup> „Partners“ refers to Principal Investigators (PI). Most research institutions were involved in ENPADASI with one partner, only few with two partners. See Annex 1.

especially in WP4. The project was coordinated by Jildau Bouwman (Netherlands) and Duccio Cavalieri (Italy) as deputy. An external advisory board (AB) and a knowledge management committee (KMC) were established and have supported the project by regular meetings.

In total, 51 PIs from 46 institutions across all nine participating European countries were involved in the ENPADASI KH: Belgium, Denmark, Estonia, Germany, France, Ireland, Italy, Spain, The Netherlands. A list of all ENPADASI Knowledge Hub partners can be found in Annex 1. One partner (University Maastricht) joined the consortium later.

The ENPADASI KH officially ended in summer 2017. The final report was submitted on the 16th of December 2017. In February 2018, an article was published in “The Journal of Nutrition” on the outcomes of the project “Joint Data Analysis in Nutritional Epidemiology: Identification of Observational Studies and Minimal Requirements”.

### **3.3 Evaluation Results**

#### **3.3.1 General Indicators**

##### ***3.3.1.1 Alignment of national funding***

Nine JPI HDHL countries and 12 funding organisations participated in the call. The total *in cash* budget committed by the participating funding organisations for the Knowledge Hub was 1.62 Mio. € plus approx. 1.7 Mio. € *in kind*.

##### ***3.3.1.2 Involvement of national scientific communities***

###### **3.3.1.2.1 Participation of national scientific communities**

In response to the call 26 EoI letters were submitted, of which 15 were selected as hub members in the national selection processes (step 1) and invited to attend the networking meeting (step 2). In the submitted network proposal 46 institutions were involved (step 3). A total of 51 partners contributed to the 15 EoIs and wrote the joint research proposal together.

The distribution of the submitted EoI letters and selected hub members over the nine participating countries is shown in figure 1. Per country, 1 - 8 EoI letters were submitted in response to the call and research groups and/or scientists were selected to join the knowledge hub.



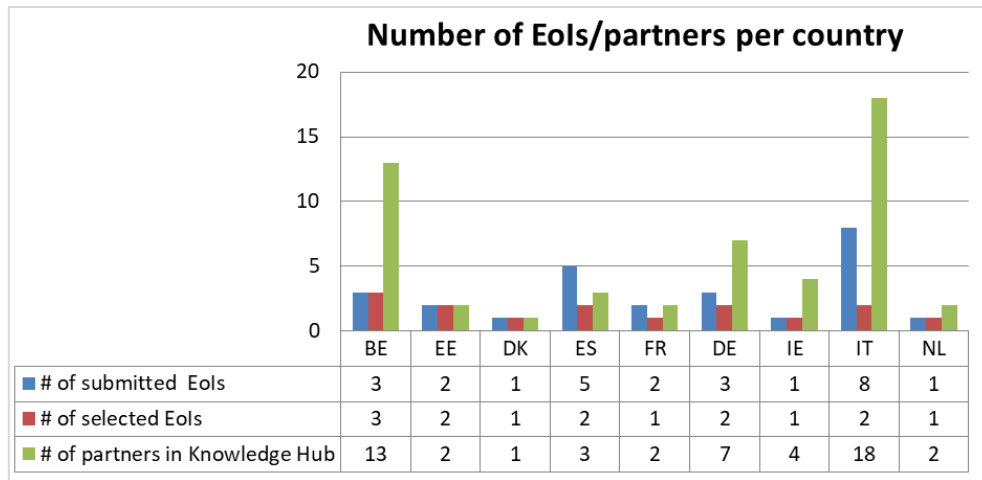


Figure 1: Numbers of Eols and partners per country in the implementation of ENPADASI KH (BE: Belgium, DK: Denmark, EE: Estonia, DE: Germany, FR: France, IE: Ireland, IT: Italy, ES: Spain, NL: The Netherlands)

It should be also noted that the Eols were handled quite differently in the different countries. In some countries, only single research groups were behind one Eol (e.g. Denmark, The Netherlands), whereas in other countries a group of researchers formed a national consortium which together wrote an Eol for the knowledge platform (e.g. Belgium, Italy). Therefore, the numbers given in the statistics should be interpreted with some caution.

### 3.3.1.2.2 Distribution of national funding

Like all subsequent joint funding actions implemented by the JPI HDHL, the funding of the ENPADASI KH was organized as a “virtual common pot“, meaning that each country and/or funding organization financed the activities of “their“ national scientists.

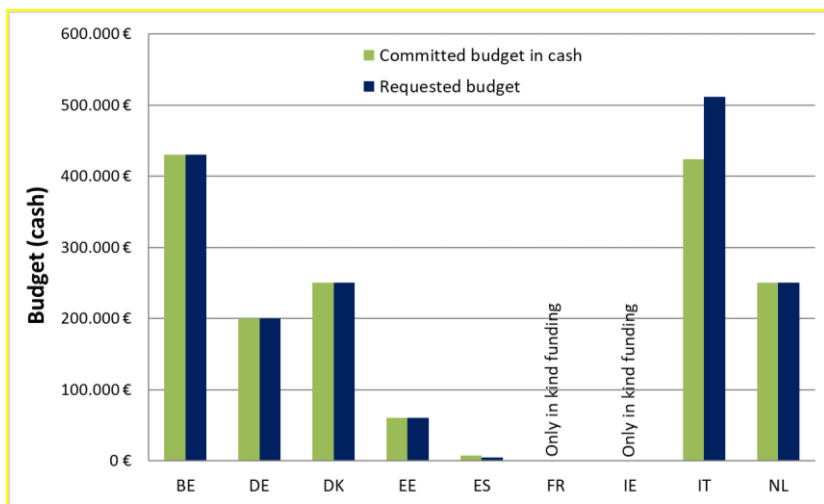


Figure 2: Committed funding budget in cash and requested budget of the ENPADASI KH distributed by countries. (BE: Belgium, DK: Denmark, EE: Estonia, FR: France, DE: Germany, IE: Ireland, IT: Italy, NL: The Netherlands).

A total of almost 3.3 Mio. € of in cash and in-kind funding was committed to the KH by the nine countries. Out of that, 1.6 Mio. € were committed in cash. As shown in figure 12 the available funding budget differed substantially between the participating countries. The largest budget was available for Italian applicants. Accordingly, Italian researchers comprised the largest group of partners in the network and took over a large number of tasks and work packages.

**All ENPADASI KH partners were scientists/research groups from research institutions. No industry partners or other types of institutions were involved reflecting the academic nature of this project.**

### *3.3.1.3 Success of implementing collaboration*

The ENPADASI KH was specifically designed to boost transnational co-operation, multi- and interdisciplinary collaboration and communication. The aim was to bring together research groups from different disciplines to contribute to establishing the open access reference database.

Thus, the joint funding action was conducted as a joint Knowledge Hub with its members addressing one research challenge together, in contrast to a classical competitive call in which several smaller research consortia address several research questions in parallel. The success of the established collaboration on transnational and scientific level is being assessed in the following subchapters.

#### *3.3.1.3.1 Interdisciplinary collaboration*

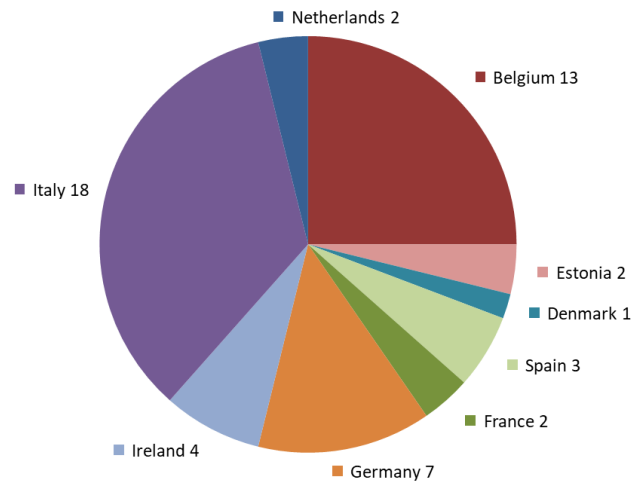
**Almost 30 different scientific disciplines were involved in the ENPADASI KH**, including Nutrition Sciences, Computational and Systems Biology, Biomedicine, Public Health, Epidemiology (see fig. 13). However, due to the non-centralised national selection procedure it was difficult to ensure a good balance among scientific expertise in the KH. One measure that was taken to achieve this goal was a meeting of the Call Steering Committee after finalisation of the national selection processes to discuss and, if needed, adapt the composition of the network. This turned out to be difficult since the national priorities and country balance proved to be as important as the scientific balance for most of the funders. **However, a good balance of expertise could still be achieved in the final selection of hub members.**

*Table 1: List of different scientific departments involved in ENPADASI KH*

Biomedicine	Food and Nutritional Sciences	Nutrition, Exercise and Sports
Biotechnology and Biopharmacy	Food Quality and Nutrition	Nutritional Behaviour
Chemistry	Health development	Physical education & Physiotherapy
Clinical & experimental endocrinology	Medical Genetics	Physics
Clinical Physiology	Medicine and Life Sciences	Preventive Medicine
Computational and Systems Biology	Molecular Epidemiology	Public Health
Environmental Risk and Health	Molecular Nutrition	Technology and Food Science
Epidemiology	Nutrition and functional food	Veterinary Public Health & Food Safety
Food and Health	Nutrition, Environment and Health	

#### *3.3.1.3.2 Transnational collaboration*

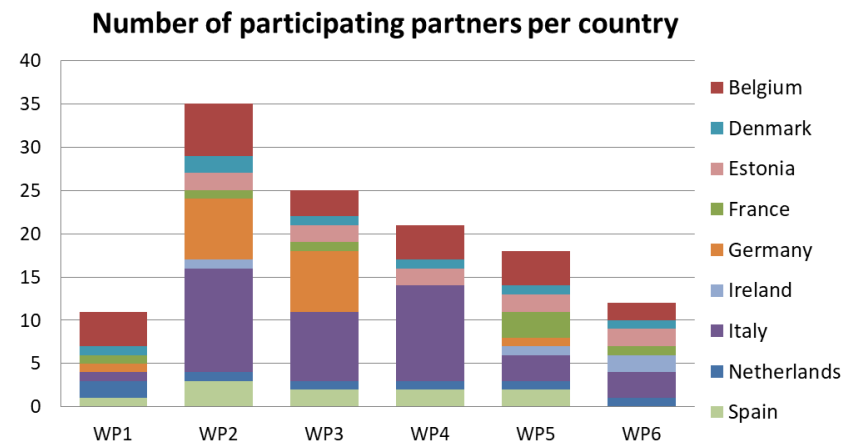
The transnational composition of the Knowledge Hub is depicted in figure 13.



*Figure 3: Transnational composition of ENPADASI KH (Number of partners)*

There was some geographical unbalance within the hub composition, partially due to the differences in funding budgets and eligibility rules. Approximately one third of the 51 partners originated from Italy and a quarter from Belgium. The remaining seven countries were represented by one to seven partners (figure 13).

The ENPADASI program consisted of six work packages (WPs). In each work package, partners from at least six countries were involved indicating a very good degree of transnational collaboration (Fig. 4A). The total number of partners collaborating in each work package ranged from a minimum of 11 partners in WP1 and a maximum of 35 partners in WP2. The six work package leaders came from five different countries with Italy leading two of them (Fig. 4B).

**A****B**

### Workpackage leaders per country

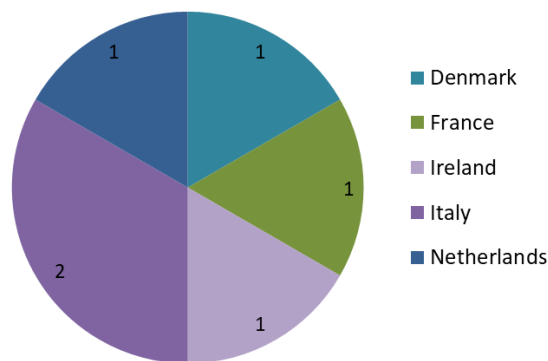


Figure 4: Country distribution of partners in the work packages (A) and of work package leaders (B)

#### 3.3.1.3.3 Intensity of Collaboration

A kick-off meeting, the first annual consortium meeting and regular Executive Committee meetings were held. An annual consortium meeting was held in September 2016.

#### 3.3.1.4 Success of scientific collaboration

##### 3.3.1.4.1 Scientific Output

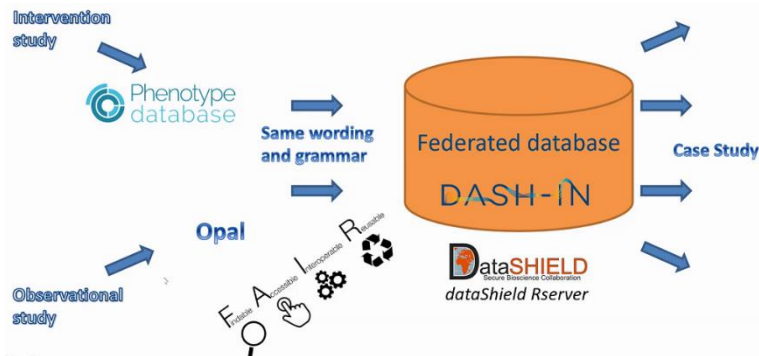
The major output of the ENPADASI KH consists of a new and optimized infrastructure for sharing data. For an overview, please see figure 15.

- The DASH-IN (data sharing in nutrition) system (<https://dashin.eu/interventionstudies/>), an open access research infrastructure (RI) for all nutritional studies that is an integration of the Phenotype database and Opal / DataShield was developed. In this database, experimental and observational data can be combined facilitating further exploitation of research data (hypothesis testing, scenario analysis, secondary analysis and modelling).
- Three templates for data collection were designed. Hence, a very broad range of study designs was made available in a format to fit into the common database.
- 85 interventional studies and 23 observational studies were entered into the templates and/or the database (approximately 40 studies were added to the database during the

funding period of ENPADASI KH (see <https://dashin.eu/interventionstudies/>); 28 studies were made open access.

- A new ontology for nutritional studies (ONS) was created which is openly shared: <https://github.com/enpadasi/Ontology-for-Nutritional-Studies>.
- A broad consent and data sharing statement for future consortia was outlined together with CORBEL (Coordinated Research Infrastructures Building Enduring Life-science Services). See [http://www.enpadasi.eu/deliverables\\_final\\_pdf/D5.1.pdf](http://www.enpadasi.eu/deliverables_final_pdf/D5.1.pdf) (Pages 11, 12)

All deliverables and material developed can be found on the ENPADASI website.

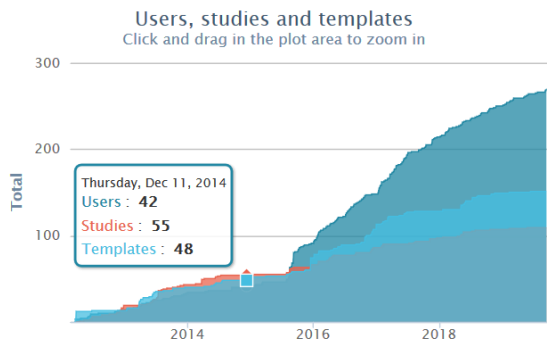


([www.enpadasi.eu](http://www.enpadasi.eu)).

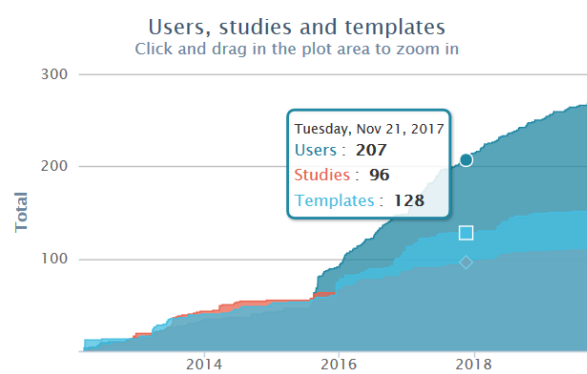
Figure 5: Summary of major output of the ENPADASI KH

Within the runtime of ENPADASI, the number of users of the infrastructure as well as the number of studies and templates made available has increase strongly: For the users from approximately 40 to 200, for the templates from 50 to 130, and for the studies from 55 to 96 (see figure 16, A versus B).

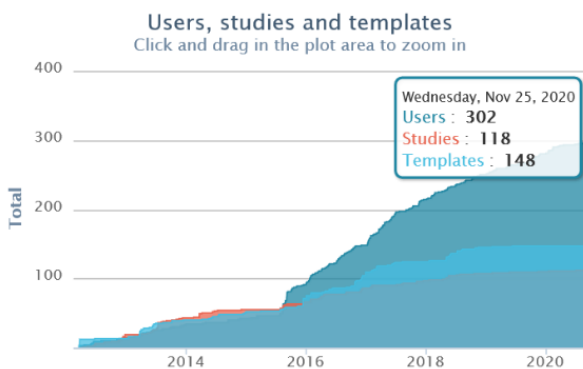
**A – Status December 2014**



**B – Status November 2017**



**C – Status November 2020**



*Figure 6: Strong increase in number of Users, studies and Templates in the Phenotype Database (now: DASH-IN database) over the course of the project and beyond. Screenshots by DLR from: <https://dashin.eu/interventionstudies/>*

All three numbers increased even further from the end of the runtime to today (end of 2020). Users now over 300, templates almost 150, and studies almost 120 (see figure 16 C).

There are two scientific publications that summarize the work done by ENPADASI KH and were published in peer-reviewed international journals:

*Pinart M, Nimptsch K, Bouwman J, Dragsted LO, Lachat C, Perozzi G, Canali R, Lombardo R, D'Archivio M, Guillaume M, Donneau A-F, Jeran S, Linseisen J, Kleiser C, Nöthlings U, Barbaresco J, Boeing H, Stelmach-Mardas M, Heuer T, Laird E, Walton J, Gasparini P, Robino A, Castaño L, RojoMartínez G, Merino J, Masana L, Standl L, Schulz H, Biagi E, Nurk E, Matthys C, Gobetti M, de Angelis M, Windler E, Zyriax B-C, Tafforeau J, Pischon T (2018). Joint data analysis in nutritional epidemiology: Identification of observational studies and minimal requirements. *J. Nutr.* 148(2):285-297*

*Yang C, Pinat M, Kolsteren P, Van Kamp J, De Cock N, Nimptsch K, Pischon T, Laird E, Perrozz G, Canali R, Hoge A, Stelmach-Mardas M, Dragsted LO, Palombi SM, Dobre I, Bouwman J, Clarys P, Minervini F, De Angelis M, Gobetti M, Tafforeau J, Coltell O, Corolla D, De Ruyck H, Walton J, Kohoe L, Matthys C, De Baets B, De Tré G, Bronselaer A, Rivellese A, Giacco R, Lombardo R, De Clerq S, Lachat (2017) C. Perspectives: Essential study quality descriptors for data from nutritional epidemiological research. *Adv. Nutr.*, 8(5):639-651.*

In total, more than **10 presentations were held at international meetings, symposia and conferences**, presenting the ENPADASI KH results (not including the presentations at ENPADASI-organised events).

#### 3.3.1.4.2 New funding obtained

They have applied to become an ELIXIR (<https://elixir-europe.org/>) use case. Several partners of the consortium have successfully applied to the Horizon 2020 “Food Cloud demonstrators” call ([https://cordis.europa.eu/programme/id/H2020\\_DT-SFS-26-2019](https://cordis.europa.eu/programme/id/H2020_DT-SFS-26-2019)) which explicitly builds on the ENPADASI project among others.

For further information on sustainability of the ENPADASI platform see 3.3.1.8 e).

#### 3.3.1.5 Involvement in other JPI HDHL activities

The ENPADASI KH presented at various events organised by JPI HDHL: JPI HDHL conference in June 2015, JPI HDHL workshop “Data sharing & Data stewardship” in February 2017, and the JPI-HDHL meeting in September 2017.

In addition, a workshop was organised by the JPI HDHL in March 2018 to follow up on both, the DEDIPAC KH and ENPADASI KH and their results and discuss possible future developments in the research field of determinants of dietary and physical activity behaviours. In this workshop, the DEDIPAC consortium presented a concept for a future joint action that builds on the needs and gaps identified by DEDIPAC KH. The goal of this suggested action would be to work towards the establishment of a pan-European cohort study, with thorough and longitudinal assessment of behaviours and behavioural determinants, with a particular focus on contextual determinants. This study should be based on a coherent, standardised and validated pan-European protocol that builds on the results of DEDIPAC is continued in the PEN network<sup>3</sup>, and takes advantage of the achievements of ENPADASI with respect to data sharing and harmonisation infrastructure. The

<sup>3</sup> Policy Evaluation Network funded by JPI HDHL/ERA-HDHL in 2017, for further details, see <https://www.healthydietforhealthylife.eu/index.php/call-activities/calls/98-calls-site-restyling/515-pen-2017-site-restyling>

concept “establishing a pan European cohort study” was presented to the management board of the JPI HDHL, but was not prioritized high enough to be included in Implementation Plan 2019-2021.

The ENPADASI database has been and is being used in subsequent JPI HDHL funded projects. It was used to integrate, for instance data from the FOOTBALL project (funded within the biomarker call launched in 2014) and FiberTAG (funded within the biomarker call launched in 2016).

### 3.3.1.6 Capacity Building

Different training activities on the use of the database were offered by the ENPADASI KH for nutritional researchers within and outside of the consortium:

- 1) Face-to-face database trainings:
  - a. September 2015 at the University of Barcelona, Spain
  - b. September 2016 at NuGOweek in Copenhagen, Denmark
  - c. September 2016 at the JPI HDHL Football meeting in Copenhagen, Denmark
  - d. January 2017 in Zaandam, Netherlands
- 2) Small-group online meetings
- 3) Training material available on the webpage (still available), including
  - a. 48-minutes tutorial video outlining all steps of the registration, data upload and export process for new users
  - b. Quick-start guide
  - c. Sample data files for different fields, e.g. genetics, biochemistry, physiology
  - d. FAQ based on actual questions

[http://www.enpadasi.eu/deliverables\\_final\\_pdf/D6.6.pdf](http://www.enpadasi.eu/deliverables_final_pdf/D6.6.pdf)

There is no information on new jobs generated in the project. In the final report, it is stated that the funding of the ENPADASI project was mainly used for the consolidation of the appointment of already hired post-docs.

### 3.3.1.7 Data and Knowledge Sharing

The major objective of ENPADASI was to develop an open access research infrastructure for all nutritional mechanistic, interventional and epidemiological studies. For that purpose, 85 interventional studies and 23 observational studies were entered either into the templates generated in the course of the project and/or entered into the database (approximately 40 studies were added to the database during the funding period of ENPADASI KH (see <https://dashin.eu/interventionstudies/>); 28 studies were made open access.

No new data were generated in the project, i.e. no samples were used. ENPADASI closely collaborated with ELIXIR on the FAIR standards, ontologies and vocabularies.

### 3.3.1.8 Impact

The impact analysis for ENPADASI was performed by analysing the project results with respect to the main steps of the original work plan (call text). The following main steps of the envisaged work plan were:

*a) Defining the standardised phenotypic information with regard to diet, physical activity levels and all biological, clinical and physiological measurements (including large scale approaches)*

ENPADASI worked on a common ontology language, based on controlled vocabularies using ontologically correct terms in order to describe each biological process, experiment, example or result in an unambiguous way. The ontology was named “Ontology for Nutritional Studies” (ONS). ONS builds on the subset of the “Ontology for Biomedical Investigations” (OBI) (Bandrowski et al.

2016<sup>4</sup>) that was created using the “ONTODOG” tool (Zheng et al. 2014<sup>5</sup>) and is composed of all terms relevant to nutritional investigations, and extended also in accordance to the bioinformatics infrastructure of ENPADASI. Terms related to food description were also included by importing a subset of terms from the “FOODON” list ([www.foodon.org](http://www.foodon.org)).

In the final report, the authors point out that the work done here is just a basis for future work to optimize the ontology. To address this, the team has begun to design a resource, which will likely be in the form of a Wiki, to collect contribution from experts in all the aspects of nutritional sciences on all parts of the ontology with the objective of continuously improving the ontology and its representation of nutritional sciences.

*b) Mapping the different existing data sharing initiatives in the field of nutrition and closely related fields (e.g., nutrition-related diseases) at EU and national levels.*

The consortium consolidated the mapping work of the FP7 project EuroDISH of available infrastructures for data sharing and investigated the data resources available within and relevant to this consortium. The following data sharing initiatives were compared:

- "Bioshare/Datashield"
- "Bioshare/Opal"
- "Bioshare/Molgenis"
- Phenotype database
- Observational dietary survey database Nutridata
- Lucille

based on the following criteria:

- Infrastructure
- Meta Data, Clean Data (individual), Raw Data (not processed)
- Data analysis
- Harmonization, Normalization, Implementation
- Development /Sustainability
- License
- Suitability for use in nutritional studies
- Type of data
- Security/ safety

*c) Defining specifications and requirements for a shared database from technical (including back-up), scientific and ethical points of view.*

The following specifications and requirements for the database were defined by the ENPADASI consortium:

- An atlas with the main features of each resource, access policies, where the data are collected, data representation and available pipelines should be included.
- The automated querying systems should recognize the access level of the study.
- The system should adhere to FAIR standards to make connections to other infrastructures possible.

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<sup>4</sup> Bandrowski, Anita, et al. The Ontology for Biomedical Investigations. PloS one 11.4 (2016): e0154556.

<sup>5</sup> Zheng, J., Xiang, Z., Stoeckert, C. J., & He, Y. (2014). Ontodog: a web-based ontology community view generation tool. Bioinformatics, btu008.



- Relevant for the design of the infrastructure will be the selection and management of metadata associated with molecular and clinical data in relation to nutrition research (e.g. Individual phenotype, geographic origin, diet, physiological or pathological state, etc.).
- To ensure that there is no data loss a backup plan needs to be implemented: Both for data and metadata backups will be made regularly another location to prevent data loss.
- The resulting system should be able to link out to other repositories (e.g. BBMRI<sup>6</sup>) as relevant data for nutritional questions may be available from those repositories and connected to relevant pipelines.

d) *Evaluating the compatibilities between existing systems and possibilities of using various end user applications.*

It was shown that the Phenotype database can be used for data sharing of intervention studies and observational studies that are anonymized and the opal/Datashield system for studies that are non-anonymized.

In order to be able to combine data from intervention and observation studies, a “dbNP connector” was developed to allow the “Rserver” to analyze both Phenotype database and OPAL database (see figure 16). Analyses are done on the local instances so that raw data are never shared therefore enabling a complete federate data analysis network.

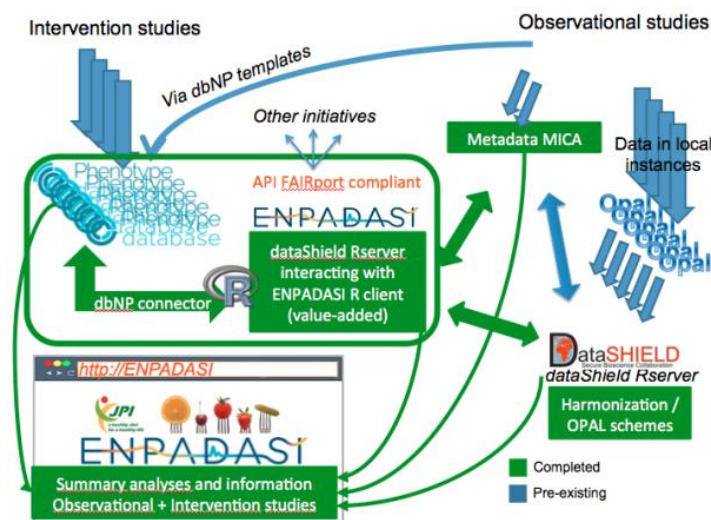


Figure 7: *Technical description of the DASH-IN system: ENPADASI used pre-existing (shown in blue) infrastructure and combined it into a new version of the Phenotype database. ENPADASI contribution is shown in green.*

e) *Evaluating sustainability and maintenance costs and planning corresponding resources.*

In the final report, the ENPADASI consortium emphasizes that funding is urgently required to keep the infrastructure up and running: “The partners in ENPADASI that host servers as part of DASH-In have indicated that they will keep the current system running as it is now for the coming 5 years on their own funds. However, the system will require updates to accommodate new versions of web browsers, due to bug reports and new uploads of studies may result in new feature requests. [...] A full support and maintenance of the system per year will require 100 - 500 k€ annually, depending on the service level and the amount of data included in the database. This includes the server costs, salary of a programmer and support for the usage of the system. A minimal service level will include

<sup>6</sup> Biobanking and Biomolecular Resources Research Infrastructure, for further details see <http://www.bbmri.nl/>

only the costs of the servers, online support and resolving of crucial bugs, whereas a higher level of service will include workshops on location and further development of the infrastructure based on feature requests.”

*f) Standardizing methods and data. Agreements on standardized methods and data handling, interoperability, assembling of the database and embedding of standardization in global developments. The database should allow all European established and future nutritional studies to interact on common methodology and procedures.*

Templates were developed that allow a very broad range of study designs to be entered into a common database format for DASH-IN. Study designs cover both experimental (mechanistic and interventional) as well as observational studies (epidemiological). The templates have been developed in such a way that they can be used directly for batch uploading of studies into the DASH-IN database.

Minimal requirements for intervention and observational studies to be incorporated into the database were identified so that data can be shared in future research proposals within the ENPADASI consortium. For this task, the hierarchical structure developed by the ISA Commons (<http://www.isacommons.org/>) was followed. The results for observational studies were published in the Journal of Nutrition (Pinart et al. 2018; Joint Data Analysis in Nutritional Epidemiology: Identification of Observational Studies and Minimal Requirements; J. Nutr. 148:285-297).

A new interface to improve ease of data upload has been developed and tested. Using this interface, the number of studies available has increased considerably (see figure 16).

*g) Integrating existing databases in the area of human intervention studies and mechanistic models in ENPADASI. Testing of integrated database with research questions reflecting both existing data as well as data newly integrated in the system.*

A new more user-friendly version of the Phenotype database was developed and the upload of additional studies resulted in the identification of bugs and new features that have been fixed and/or implemented. ENPADASI has delivered the DASH-IN (data sharing in nutrition) system, an open access research infrastructure (RI) for all nutritional studies. DASH-IN is an integration of the Phenotype database and Opal / DataShield, so that experimental and observational data can be combined. The RI contains secured-access user-friendly web-based pages for uniformly searching, selecting and combining multiple studies in joint analysis (pooled or federated), facilitating further exploitation of research data (hypothesis testing, scenario analysis, secondary analysis and modeling).

ENPADASI partners have tested the possibility to retrieve and analyse data within the ENPADASI infrastructure. They have performed data integration on results from human intervention and observational studies. The relation between duration of the interventions and the age of participants and levels of HDL, LDL, total cholesterol, triglycerides and glucose has been analysed. This pilot data fusion analysis shows that integrative analyses are possible.

A more complex study (FP7: MyNewGut<sup>7</sup>) has been funded after completion of ENPADASI to provide a data fusion study on metabolomics studies across different human study designs.

*h) Building a European governance structure for the database maintenance and development, data duration and data pipelining, with adequate ‘rules of engagement’.*

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<sup>7</sup> <https://www.mynewgut.eu/research>

Table 2: The DASH-In infrastructure is a federated system. The final release is shown below:

Institution	Country	Server type	Server Address
COSBI The Microsoft Research - University of Trento Centre for Computational & Systems Biology	Italy	Dash-IN	<a href="https://dashin.cosbi.eu">https://dashin.cosbi.eu</a>
Copenhagen University	Denmark	DBNP	<a href="http://enpadasi.science.ku.dk/">http://enpadasi.science.ku.dk/</a>
Gent University	Belgium	OPAL	<a href="https://bw07srv7.ugent.be:8443">https://bw07srv7.ugent.be:8443</a>
Gent University	Belgium	MICA	<a href="http://www.dietdatabase.ugent.be">http://www.dietdatabase.ugent.be</a>
Politecnico di Bari	Italy	MICA – authoritative for ENPADASI	<a href="http://mica.cloud.ba.infn.it/">http://mica.cloud.ba.infn.it/</a>
Politecnico di Bari	Italy	OPAL	<a href="http://opal.cloud.ba.infn.it:8080">http://opal.cloud.ba.infn.it:8080</a>
Politecnico di Bari	Italy	DBNP	<a href="http://dbnp.cloud.ba.infn.it/">http://dbnp.cloud.ba.infn.it/</a>
TNO – Netherlands Organisation for Applied Scientific Research	The Netherlands	DBNP	<a href="https://dashin.eu/interventionstudies">https://dashin.eu/interventionstudies</a>
TNO – Netherlands Organisation for Applied Scientific Research	The Netherlands	OPAL	<a href="http://msb1.hex.tno.nl">http://msb1.hex.tno.nl</a>
Max-Delbrück-Centrum	Germany	OPAL	<a href="https://dsmolep.mdc-berlin.de">https://dsmolep.mdc-berlin.de</a>

*i) Defining procedures to safeguard ethical issues and privacy protection of ENPADASI to meet international and legal standards for the use of personal data for research purpose*

The new research infrastructure, DASH-IN, contains fields that indicate whether or under what conditions the data may be shared or that some measures are necessary (new permission, change of permission, consortium agreement) or that data sharing is impossible. ENPADASI (together with CORBEL - Coordinated Research Infrastructures Building Enduring Life-science Services) delivered an example of a broad consent and proposed a data sharing statement for future consortium agreements.

*j) Training for researchers on how to work with the system.*

See 4.3.1.6

### 3.3.1.8.1 Contribution of the project to the coordination/harmonization of research activities

The project coordinator (Dr. Jildau Bouwman) was asked to comment on the following questions:

*a) Q: To what degree would you consider the data available through ENPADASI being standardised? Where are still gaps, what has to be improved, what further needs exist (if any) to achieve still better standardisation?*

A: The data of the studies that are uploaded in ENPADASI are well standardized (but here are some gaps). We use templates and ontologies to do so. There are gaps in the meta-data: for many parts of the meta-data no ontologies are yet available. Many datasets are still only present in the excel sheet (or similar) of the partners.

*b) Q: Is there a common methodology and shared IT infrastructure in place and being used?*

A: Yes, the Phenotype database ([www.dbnp.org](http://www.dbnp.org)) and Opal/Mica, those are connected via Datashield. We are further developing datashield in the EU tender EASME<sup>8</sup>.

*c) Q: How many existing databases /data were integrated into ENPADASI?*

A: Templates have been developed that allow a very broad range of study designs to be entered into a common database format and at least 108 studies (23 observational and 85 others) have now been entered into the templates and/or into the web database (DASH-IN) located at TNO in the Netherlands and UCPH in Denmark. In both databases there are together uploaded at least 28 studies, with both study designs and measurements that are shared with the public (full open access). For further information, please see

[http://www.enpadasi.eu/deliverables\\_final\\_pdf/D2.1.1.pdf](http://www.enpadasi.eu/deliverables_final_pdf/D2.1.1.pdf)

#### 3.3.1.8.2 Contribution to Public Health

The contribution of ENPADASI KH to public health is indirect since no new studies or experiments were performed. The delivered infrastructure gives easier access to medically and nutritionally relevant datasets and exploitation of previously unreleased datasets as well as published ones to the benefit of the wider EU-based scientific community. On the longer term, this infrastructure will help to form better and more informed hypotheses in future studies and make it possible to actually test new hypotheses without having to conduct additional studies. See also 3.3.1.8 g).

#### 3.3.1.8.3 Activities towards innovation (new industry collaborations, development of new methods, research tools/products; patents)

In line with the aim of the ENPADASI KH and the nature of this research project, collaborations with industry, development of new methods, research tools, products, or patents were not reported.

#### **3.3.1.9 Expert's assessment on general aspects and the specific aims of the ENPADASI KH**

The outcome of the ENPADASI KH has been reviewed by a member of the JPI HDHL Scientific Advisory Board (SAB). The assessment was based on a review of some of the final outputs of the project.<sup>9</sup> In the expert's opinion the ENPADASI KH has contributed to fill relevant gaps in field of nutrition research by building a useful infrastructure. The achievements of the KH were summarized by the expert as follows: Building on existing infrastructure, the ENPADASI team were successful in developing an open access research infrastructure for nutritional studies (DASH-IN) for the structuring, reporting, storage and sharing of data from a wide range of types of nutrition studies. In addition, ENPADASI have been successful in developing a new ontology for nutritional studies (ONS) that will help in harmonizing reporting of nutrition studies. The combined use of DASH-IN and ONS is intended to facilitate the re-use of existing research data. The latter remains a major challenge for nutrition research across Europe (and globally) and solutions to this challenge will help in enhancing the quality of nutrition research and in maximizing the societal benefit from investment in nutrition research.

The expert mentioned that if DASH-IN is used as intended, it could contribute to better coordination of research activities and enhanced collaboration. In addition, the infrastructure has the potential to facilitate research on diet-related chronic diseases. According to the expert, the extent to which the work by the ENPADASI network will facilitate progress and further development in the field of

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<sup>8</sup> [https://www.ceps.eu/wp-content/uploads/2019/08/09172019-Brief\\_second\\_workshop\\_WP2\\_healthcare-1.pdf](https://www.ceps.eu/wp-content/uploads/2019/08/09172019-Brief_second_workshop_WP2_healthcare-1.pdf)

<sup>9</sup> The JPI HDHL template for the final project report was not well developed, yet, at that point in time.

nutrition and health research depends critically on whether: i) the tools developed by ENPADASI (ONS and DASH-IN) remain available, up-to-date and usable, ii) nutrition researchers choose to upload additional projects to the database and iii) researchers use the data accessible via DASH-IN to undertake new research projects or to re-analyse results from existing studies.

As a side note, the expert added that in retrospect, it was a missed opportunity not to require the network to develop and implement a (financial) sustainability plan to ensure that the investment in the project yielded societal benefit.

### **3.3.2 Conclusions**

The major output of the ENPADASI KH consists of a new and optimized infrastructure for sharing data in the nutritional field, the DASH-IN (data sharing in nutrition) system (<https://dashin.eu/interventionstudies/>). The system is an open access research infrastructure (RI) for all nutritional studies. Experimental and observational data can be combined, facilitating further exploitation of research data.

Since the launch of the platform there has been a steady increase in the use and sharing of data in the field. A majority of the research projects funded in the JPI HDHDL, have chosen ENPADASI as the platform for sharing their data.

In addition, the platform has prepared the ground for further initiatives concerning data sharing to take place in Europe. Indeed, building from ENPADASI's work, the Federation of Nutrition Society has established a working group on standards and quality, using the ENPADASI platform as a basis. The Health data.org website managed by the University of Washington which is a pool for gathering dietary data also uses ENPADASI health descriptors.

## 3.4 Annexes

### 3.4.1 Annex 1: List of ENPADASI KH partners

Due to data protection regulations the list of ENPADASI KH partners was removed.

### 3.4.2 Annex 2: Members of the external ENPADASI Scientific Advisory Board

Due to data protection regulations the names of ENPADASI SAB members were removed.

### 3.4.3 Annex 3: Used data sources

Revised Network Proposal “European Nutritional Phenotype Assessment and Data Sharing Initiative”

ENPADASI KH final report submitted on 16 December 2017.

Information from project website: [www.enpadasi.eu](http://www.enpadasi.eu), mainly from the Deliverables:  
<http://www.enpadasi.eu/deliverables.html>

Written feedback from a member of the Scientific Advisory Board of JPI HDHL.

### 3.4.4 Annex 4: Overview on general indicators

<b>4.1.1 Alignment of national funding</b>	
- Number of countries participating in the call	9 countries, 12 funding organisations
- total committed budget	1.6 Mio. € + ca. 1.7 Mio.€ in kind.
<b>4.1.2 Involvement of national scientific communities</b>	
- Number of submitted pre/full-proposals per country/funding organisation	26 Eols submitted in total
- Number of accepted proposals per country/funding organization	15 Eols selected in total, 51 groups in final proposal
- Committed budget (in cash + in kind) per country	From 0.04 to 1.2 Mio € per country, 3.3 Mio € total
- Budget requested	Requested 2.1 Mio € in total
- Number and type (Research/SME/Large industry) of organisations/teams in the funded consortia	51 research groups, no industry partners
<b>4.1.3 Success of implementing collaboration</b>	
- Interdisciplinary collaboration	
Number of disciplines per consortium	>25 scientific disciplines
list of disciplines	See Table 1
- Success of transnational collaboration	
Number of new collaborations with academia	
Number of collaboration with other JPI funded projects	
- Number of project coordinators/partners per country	1 - 18 partners per country, See fig. 3 and fig. 4
- Intensity of Collaboration	
Number of Meetings	3 meetings with all partners
Number of mobility/lab visits within a consortium	n/a
<b>4.1.4 Success of scientific collaboration</b>	
- Number of new publications related to the project	2 published papers during the active project phase
- Number of presentations related to the project	>10 at international meetings, symposia and congresses
- New funding obtained	Successful application to the Horizon 2020 “Food Cloud demonstrators” call

<b>4.1.5 Involvement in other JPI HDHL activities</b>	Collaborations with FOOTBALL and DEDIPAC
<b>4.1.6 Capacity Building</b>	
- <i>Training activities</i>	4 face-to-face training workshops; online trainings
- <i>New jobs/positions generated in the project</i>	Mainly already hired Postdocs
- <i>Use of existing tools and/or development of new capacities or resources (e.g. a transnational database, biobanks, animal models, cohorts)</i>	Existing tools - Phenotype database and the opal/ Datashield system - were combined (DASH-IN); new common language "Ontology for Nutritional Studies" developed
<b>4.1.7 Data and Knowledge Sharing</b>	
- <i>Use of existing data: Has existing data been used / pooled for the project?</i>	Data of 85 interventional studies and 23 observational studies were entered into the templates and/or the database
- <i>Has the consortium used samples from existing cohorts and / or other epidemiological studies?</i>	No experimental work.
- <i>To perform the project, have you used samples (omics-based) from bio-bank or/and other disease register sample collections?</i>	No experimental work.
- <i>FAIR-Data principles: Has the data generated in the project made available by following the FAIR principles?</i>	No new data, but existing data made available following FAIR principles.
<b>4.1.8 Impact</b>	
- <i>Contribution of the project to the coordination/harmonization of research activities (standardisation of methods and protocols, data harmonisation, data and knowledge sharing)</i>	Yes. Interventional and observational studies can now be entered into one database. Common language (ontology).
- <i>Activities towards innovation</i>	
<i>New industry collaboration</i>	none
<i>Development of new methods/research tools/products</i>	Tool: DASH-IN database
<i>Patents: number and geographical scope</i>	None
- <i>Contribution to public health</i>	
<i>Target groups</i>	n.a.
<i>Interaction with End-Users (e.g. consumers, patients in intervention studies)</i>	n.a.
- <i>New strategies/applications to reduce incidence of diet related chronic diseases)</i>	n.a.