CSA JPI HDHL 2.0

Evaluation of Joint Funding Actions

Intestinal Microbiomics 2015 (IM 2015)

Content

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 on 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.[1] 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, MaNuEl) a final conference has been organized by the consortia itself without participation of SAB, SHAB or former reviewers.

[1] The data collection for the specific indicators as part of the final report was not possible for the first three JFAs (DEDIPAC, ENPADASI & MaNuEl) 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: Intestinal Microbiomics 2015 (IM 2015)

3.1 Aim of the call

The Strategic Research Agenda (SRA) of the JPI HDHL described the importance of the link between diet, intestinal microbiomics and health. The Implementation Plan 2014-2015 listed "Intestinal Microbiomics" as one future priority topic. It was highlighted that "**microbiome analysis is a new and rapidly developing area**, there is a perceived need to not only learn from the different projects that are funded by the member states but also to benchmark the progress and develop common approaches. What is currently missing are studies that specifically and systematically address the **role of the diet and dietary constituents on the microbiome** including the effects of food matrix and food processing measures which at various levels can modulate microflora composition".

The main objective of the Joint Action "Intestinal Microbiomics" (IM) was to increase knowledge on the effects of diet on human intestinal microbiota and on the impact of diet-related variations in the intestinal microbiota on health and/or on chronic diseases in order to support health promotion and prevention of non-communicable chronic diseases. The call was initiated to support multidisciplinary transnational research consortia using innovative and scientific approaches to increase knowledge on:

- the short-term and long-term functional effects of diet, dietary patterns and dietary constituents on human intestinal microbiota.
- the functional impact of diet-related variations in the intestinal microbiota on human health and/or the development of non-communicable chronic diseases.

The overall vision was to develop dietary interventions or guidance for modulation of the intestinal microbiome to promote health and/or prevent the development of non-communicable chronic diseases. The program should generate new knowledge to support health maintenance and/or new treatments.

3.2 Peer-review Procedure and Results

The IM Joint transnational call was launched on 19th of March, 2015 and was coordinated by the Call Secretariat ZonMw (The Netherlands Organisation for Health Research and Development). The implementation process was organized in a two-stage procedure with submission of a pre-proposal and a full proposal.

Deadline for submission of the pre-proposal was the 28th of April 2015. 41 pre-proposals were submitted from which 40 passed the eligibility check. Each pre-proposal was evaluated on a written basis by at least 3 international experts according to their expertise in the substantive area of the proposed research. Evaluation criteria were:

1. relevance to the aim(s) of the call

2. potential scientific excellence of the pre-proposal (innovation potential, methodology) and

3. quality of the transnational collaboration (added value of the research consortium, on both scientific and transnational levels, multidisciplinary approach).

As result of the pre-proposal evaluation, 21 projects were invited to submit a full-proposal before 1st of September 2015. The submitted full proposals were evaluated by at least three international and independent peer reviewers by using the following criteria:

1. relevance to the aim(s) of the call,

2. scientific excellence of the proposal,
3. feasibility of the project,
4. quality of the transnational collaboration,
5. international competitiveness of participating research groups in the field(s) of the proposal and
6. translational impact of the expected results for future clinical and other health relevant applications.

In total, 31 reviewers participated in the written review assessment. During the evaluation panel meeting on the 16th and 17th of November 2015, the full proposals and the written assessments were discussed by 8 reviewers. A ranking list was agreed and funding recommendations were made to be considered for the final funding decision of the Call Steering Committee. 9 full-proposals were recommended for funding by the evaluation panel.

On the 3rd of December 2015, the final funding decision was made to fund 6 consortia:

1. **ArylMUNE** – Aryl hydrocarbon receptor and immunity: Activation by diet, microbiota and probiotics
2. **DINAMIC** – Diet-induced arrangement of the gut microbiome for improvement of cardiometabolic health
3. **EarlyMicroHealth** – Impact of early life diet on microbiome development and later health
4. **EarlyVir** –Influence of diet on early life gut virome – a key player in shaping the gut microbia
5. **GI-MDH** – From infancy to childhood: the intersection of gastrointestinal microbial communities, diet and health
6. **MaPLE** – Gut and blood microbiomics for studying the effect of a polyphenol-rich dietary pattern on intestinal permeability in the elderly

The transcription factor AhR is crucial for maintaining intestinal homeostasis. Therefore, the aim of **ArylMUNE** was to assess the effects of Aryl hydrocarbon receptor activation by microbiota-derived components on intestinal immunity and physiology. The consortium was coordinated by the French Harry Sokol. The consortium started in January 2016 and the runtime finished end of January 2019. A runtime extension till end of December 2019 was granted**.**

The goal of the **DINAMIC** consortium was to investigate the interaction between diet and gut microbia and the potential of modulating these interactions for the prevention of metabolic dysfunction and cardiovascular complications in humans. The consortium was coordinated by the two Germans Thomas Clavel and Dirk Haller. The funding started in June 2016. The runtime ended end of May 2019, however the consortium received for a runtime extension until end of December 2019.

Microbial colonization of the immature gut of a new-born is essential for the development of its physiological homeostasis. The aim of the **EarlyMicroHealth** project was therefore to develop early-life interventions to promote the establishment of a healthy microbiota. The consortium was coordinated by the Spanish Miguel Gueimonde. The funding started in January 2016 and the runtime of the last partner terminated end of April 2019.

Since bacteriophages (virus attacking bacteria) may play a role in shaping gut microbial in early life, the aim of **EarlyVir** was to investigate how the gut virome is influenced by diet. Furthermore, the role in the origins of chronic childhood disorders was analyzed. The consortium was coordinated by the Danish Hans Bisgaard. The funding started in March 2016 and the runtime ended end of February 2019.

The **GI-MDH** consortium aimed to study the influence of the timing and nature of solid food introduction in infancy on gastro-intestinal microbial communities and consequent health outcomes, in particular fat accretion and allergic response. The coordinator was Eileen K. Hutton from Canada. In April 2016 the consortium started to work. The runtime finished end of May 2019 and was extended until end of May 2020.

The **MaPLE** project aimed to test the hypothesis that an increased intake of polyphenol-rich food (e.g. fruits, vegetables, nuts and seeds) reduced intestinal permeability and lowers inflammogenic bacterial factors in the bloodstream, promoting a protective metabolic phenotype in the elderly. The consortium was coordinated by the Italian Patrizia Riso. The consortium started to work in January 2016. The runtime terminated end of March 2019 but was extended until end of December 2019.

3.3 Evaluation Results

3.3.1 General Indicators

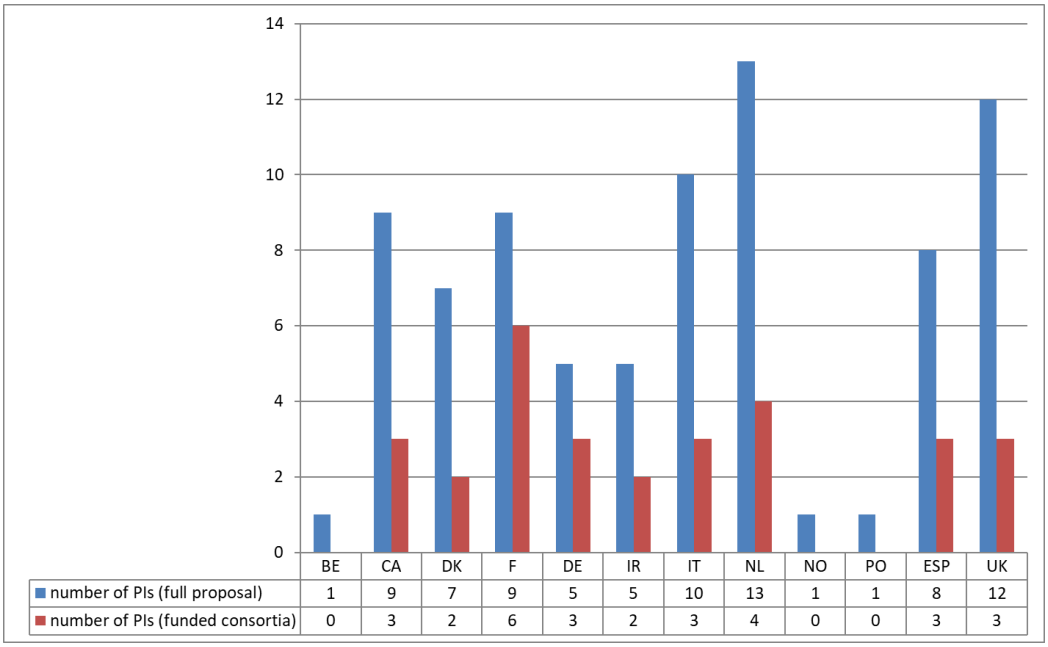
3.3.1.1 Alignment of national funding

12 JPI HDHL partner countries and 14 funding organisations participated in the call. The total *in cash* budget committed by the participating funding organisations for IM 2015 was 8.1 Mio €. In addition, the Spanish funding organisation ISCIII provided an *in kind* contribution.

3.3.1.2 Involvement of national scientific communities

3.3.1.2.1 Participation of national scientific communities

In response to the call, 21 full-proposals were submitted involving 81 PIs (principle investigators). The decision was made to fund six consortia (**ArylMUNE, DINAMIC, EarlyMicroHealth, EarlyVir, GI-MDH and MaPLE**) including 29 PIs from 9 JPI HDHL partner countries. 27.5% of the PIs were female and 72.5% male. The same distribution was found for the coordinators (28.6% female, 71.4% male). A list of all IM 2015 partners in the funded projects can be found in Annex 1. The division of the PIs per country applied for and accepted for funding respectively are depicted in fig.1. Belgium, Norway and Poland were the three countries, which had no PIs in the funded consortia.



	BE	CA	DK	F	DE	IR	IT	NL	NO	PO	ESP	UK
number of PIs (full proposal)	1	9	7	9	5	5	10	13	1	1	8	12
number of PIs (funded consortia)	0	3	2	6	3	2	3	4	0	0	3	3

Figure 1: Numbers of PIs per country in the implementation of IM 2015

3.3.1.2.2 Distribution of national funding

Like all subsequent joint funding actions implemented by the JPI HDHL, the funding of IM 2015 was organized as „virtual common pot“ meaning that each country and/or funding organization finances the activities of their respective national scientists.

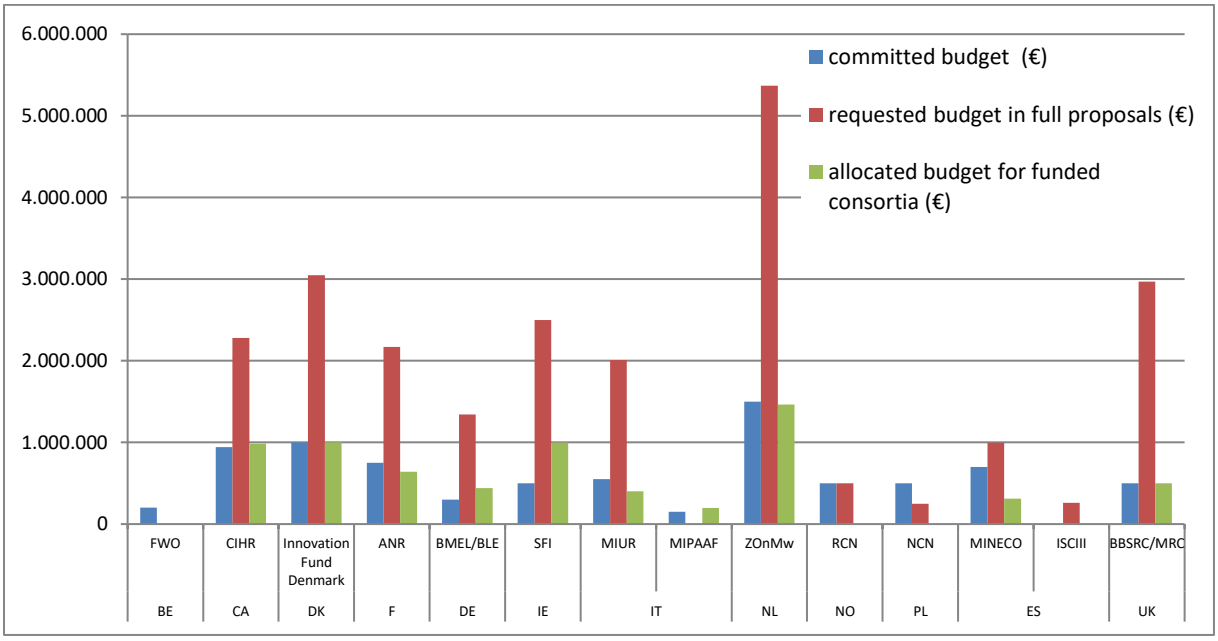


Figure 2: Committed, requested and allocated funding budget of IM 2015 consortia, distributed by countries.

The total requested budget for all full proposals submitted for the IM 2015 call was 23.7 Mio € *in cash* resulting in an oversubscription factor of 2.9. As shown in fig. 39 the requested budget for most of the country was substantially higher compared to the committed budget reflecting the large interest of the research community on the released call. For the six funded consortia, the allocated budget was 6.9 Mio € which is 85.7 % of the initially committed budget of 8.1 Mio €. The largest amount of allocated *in cash* money was available for applicants from The Netherlands.

Table 7 gives an overview about the final composition of the funded consortia. 3 to 7 countries are involved in the research and the budget differed between 0.8 to 2 Mio Euro depending mostly on the size of the consortium.

Table 1: Composition of funded consortia and received budget

Name of consortium	Number of PIs	Involved countries	Budget
ArylMUNE	4	3 (Canada, France, The Netherlands)	0.8 Mio. €
DINAMIC	8 + 1 collaborator (Germany)	7 (France, Germany, UK, Ireland, Italy, Denmark, The Netherlands)	2.0 Mio €
EarlyMicroHealth	5 + 1 collaborator (China)	4 (Ireland, Italy, Spain, The Netherlands)	1.3 Mio €
EarlyVir	4	3 (Denmark, Canada, France)	0.9 Mio €
GI-MDH	3	3 (Canada, Germany, The Netherlands)	0.8 Mio €
MaPLE	3	3 (Italy, Spain, UK)	0.6 Mio €

In total, 26 academic research institutions and 4 large industry partners were involved in the six funded consortia. Since the participation of private parties was required for applicants form the

Netherlands, all large industry partners were located in The Netherlands. Nevertheless, this also reflects the strength of the country in this research topic.

3.3.1.3 Success of implementing collaboration

The consortia worked under the umbrella of the Intestinal microbiomics call; however, the studies were conducted independently from each other with no planned collaboration between the consortia. All six consortia collaborated either with industrial partners, projects from other JPI HDHL calls and/or other European projects. **DINAMIC** collaborated with the JPI HDHL project ENPADASI knowledge hub and **MaPLE** initiated collaborations with the FoodBall consortium from the JPI HDHL BioNH call and with D-CogPlast consortium from the JPI HDHL NutriCog call. Furthermore, members of the **ArylMUNE** and **EarlyMicroHealth** consortium initiated a collaboration with the HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health. **DINAMIC** worked together with the "Preview project" and **EarlyMicroHealth** with the "Mami project" both funded by Horizon 2020. **MaPLE** worked together with the BACCHUS project (funded by the 7th framework program of the European Commission), the VALID project (funded by ERA-HDHL Cofund "Biomarkers for Nutrition and Health"), COST action POSITIVe (Interindividual variation in response to consumption of plant food bioactives and determinants involved) 2017, COST action hCOMET (The comet assay as a human biomonitoring tool) 2016 and COST Action Personalized Nutrition in aging society: redox control of major age-related diseases.

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

The 6 funded consortia covered various scientific disciplines like microbiomics, food metabolomics, functional genomics, microbiology, molecular biology, nutritional sciences and some more. The involved expertise of each consortium is listed in table 8.

Table 2: List of disciplines of IM 2015 funded consortia

Name of consortium	List of disciplines
ArylMUNE	microbiomics
DINAMIC	food metabolomics, functional genomics, microbiology, microbiomics, molecular biology, nutrition
EarlyMicroHealth	bacteriology, virology, next generation sequencing, nutrition, pediatrics
EarlyVir	microbiology, virology, diet, metagenomics, chronic disease
GI-MDH	biochemistry, biology, food metabolomics, microbiology
MaPLE	food metabolomics, food science, medicine, microbiomics, nutrition

3.3.1.3.2 Transnational collaboration

Most partners in the 6 funded consortia closely collaborated in the single work packages (WP) which is depicted in Figure 3 to 8. EarlyVir and MaPLe were an exception where often only one partner worked on a single work package. Reasons for this could be the very specific exertise of the partners within these consoria.

Within **ArylMUNE** the French coordinator was responsible for WP0 (management and coordination). In the other WPs, namely WP1 (*In vitro* screen of strains producing AhR agonists), WP2 (Identification of a dietary intervention activating AhR through the microbiota), WP3 (Dietary intervention in Human to modulate AhR activity) and WP4 (Identification of microorganisms acting on AhR) all partners of the consortium collaborated intensively with each other (Fig. 40).

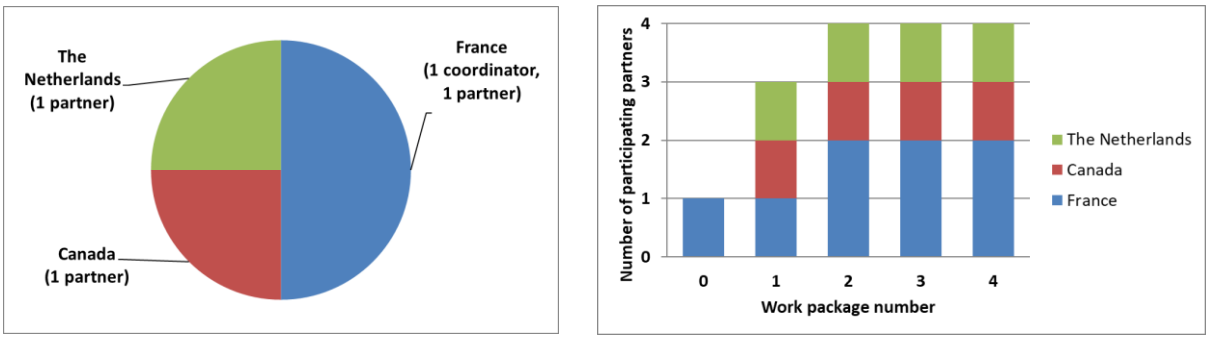


Figure 3: Transnational composition and number of participating partners per work package in the consortium ArylMUNE

All partners of the consortium **DINAMIC** were involved in WP1 (management and coordination) and WP4 (Meta-omics). Also, in WP2 (diet-microbiome analysis of prospective cohorts) and WP3 (dietary interventions) were 6 to 7 partners, respectively, involved demonstrating a very strong collaboration (Fig. 41).

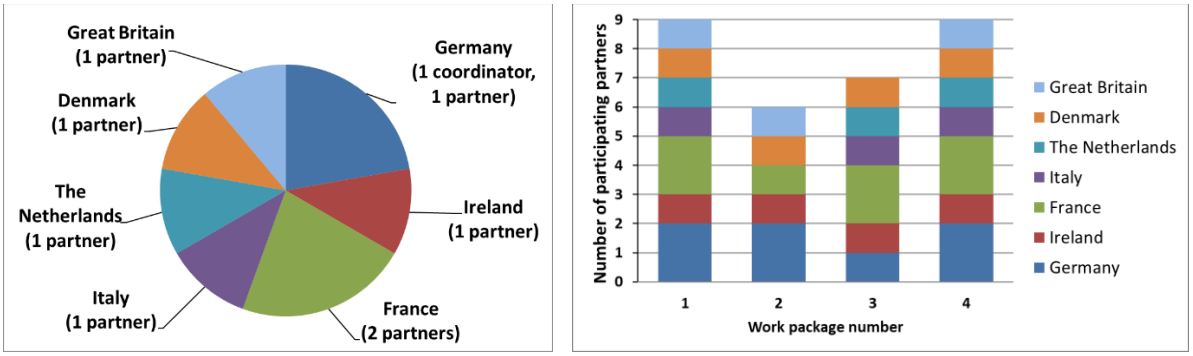


Figure 4: Transnational composition and number of participating partners per work package in the consortium DINAMIC

The project of **EarlyMicroHealth** consisted of 7 work packages and all partners including the Chinese collaborator worked together in WP1 (Standardization/harmonization of procedures, protocols and method) and WP4 (Microbial community analyses). 4 partners were involved in WP6 (nutritional analysis) and 3 partners each in WP2 (longitudinal cohort study), WP5(clinical analyses) and WP7 (data integration, database development and maintenance). Only WP3 (dietary intervention study) was managed by the two Spanish partners alone (Fig. 42).

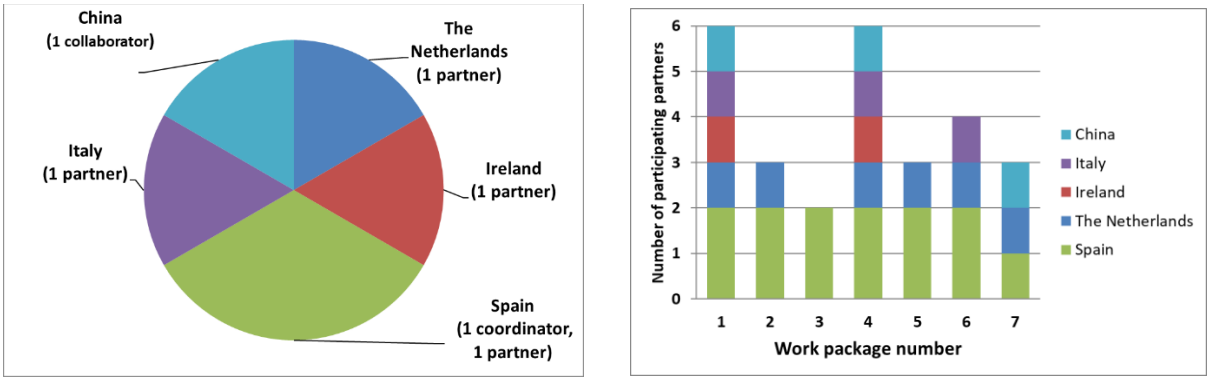


Figure 5: Transnational composition and number of participating partners per work package in the consortium EarlyMicroHealth

In **EarlyVir** both WP 1 (virome characterization) and WP2 (identification of phage-host pairs) 2 to 3 partners, collaborated. WP3 (identification and characterization of CRISPR-Cas systems in the early life GM) and 4 (data integration) were mainly covered by one partner (Canada or Denmark) (Fig. 43).

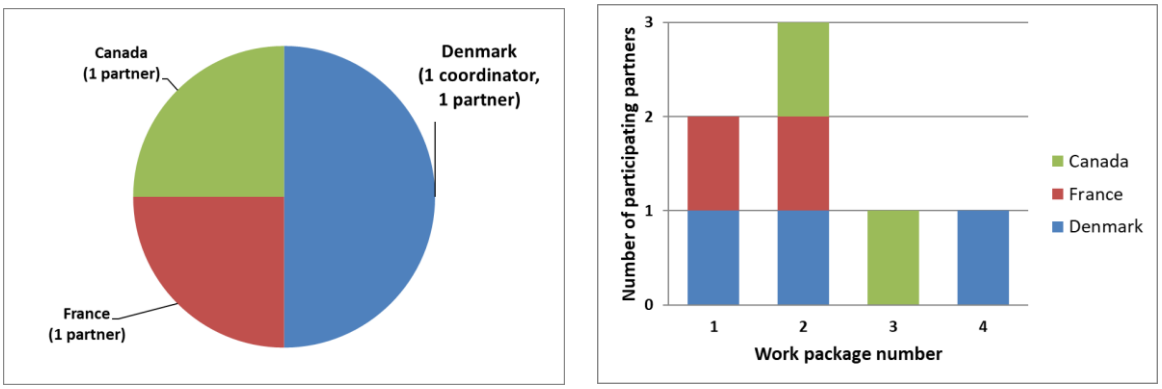


Figure 6: Transnational composition and number of participating partners per work package in the consortium EarlyVir

All 3 partners of the **GI-MDH** consortium collaborated closely in all WPs, namely WP1 (coordination of cohort studies), WP2 (microbiome analyses), WP3(measures of chronic inflammation in obesity and atopy), WP4 (data integration) and WP5(project coordination, management and time plan) (Fig. 44).

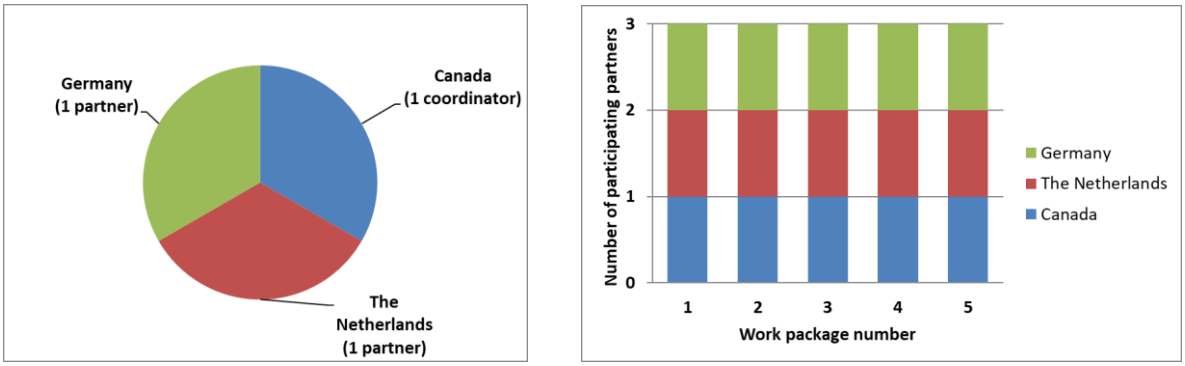


Figure 7: Transnational composition and number of participating partners per work package in the consortium GI-MDH

The Italian partner (coordinator) in the **MaPLE** consortium was involved in 4 out of 6 WPs. WP1 (project coordination and management), WP2 (intervention study), WP3 (biomarker evaluation), WP4 (mechanistic study) and WP5 (data elaboration) were covered only by one partner of the consortium. For dissemination (WP6) all partners worked together (Fig. 45).

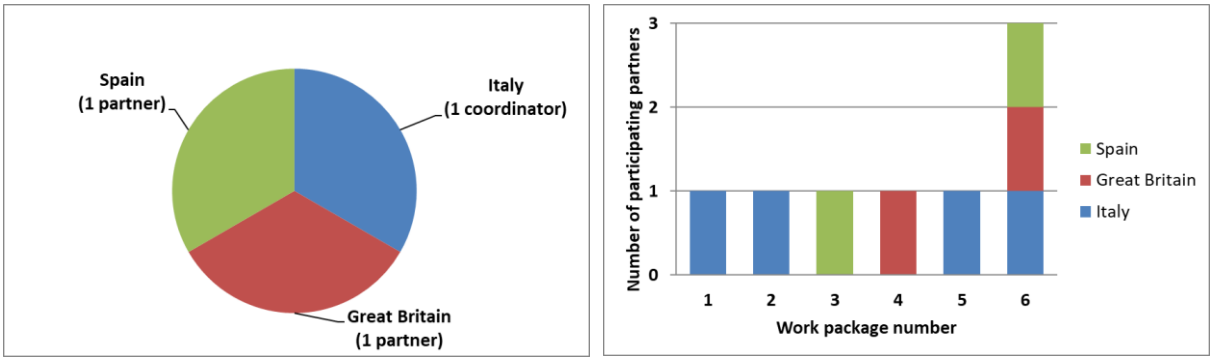


Figure 8: Transnational composition and number of participating partners per work package in the consortium MaPLE

3.3.1.3.3 Intensity of Collaboration

The intensity of collaboration varied between the different consortia. During the 4 years of research in the **ArylMUNE** consortium each year 3 phone call meetings were arranged, but no further lab exchanges.

The partners of the **DINAMIC** consortium meet 4 times physically in Munich, Naples, London and Copenhagen. Furthermore, they organized a final symposium in December 2019 in Amsterdam. 4 lab

exchanges were arranged for 3 PhD students and 1 associated Professor for the duration of 1 month up to 1 year.

During the runtime of **EarlyMicroHealth** the partner met 4 times physically in Madrid, Parma and Amsterdam and two lab exchanges were organized for a month each.

Out of the 6 physical meetings arranged by **EarlyVir** 4 meetings took place with all partners. Additionally, 22 telephone conferences with all partners were realized during the runtime of the consortium. Furthermore, one master student got the chance to participate on a lab exchange for 4 months.

All partners of the **GI-MDH** met in the first year of funding 4 times and regular meeting according to the WPs were organized. Two physically meetings were arranged in 2017 and 2018. Furthermore, monthly digital meetings corresponding to the different work packages took place for the whole funding period.

The **MaPLE** consortium organized 12 physical meetings in Milan, Norwich, Canada, Cesena, Barcelona, Lisbon, Brussels, Dublin and Japan in addition to 10 telephone conferences. During the runtime 11 lab exchanges for master students, graduate students and PhD student were arranged for 1, 3 or 6 months.

Although the work packages in **EarlyVir** and **MaPLE** were handled mostly by only one partner, both consortia organized, compared to all consortia, the most meetings ensuring a close collaboration.

3.3.1.4 Success of scientific collaboration

3.3.1.4.1 Scientific Output

All consortia published their results during the runtime and afterwards however the published number per consortium differed between 2 up to 42 publications. One reason for the different number of publications could be due to the submission of patents (see section “Activities towards innovation”). Furthermore, the consortia presented their results orally or by posters to different targets groups like scientists, physicians, general public, industry and some more. The number of publications and presentations per consortium are depicted in table 9.

Table 3: Publication, oral and poster presentations of IM 2015 funded consortia

Name of consortium	No. of publications	No. of oral presentations	No. of poster presentations	Target groups
ArylMUNE	2	3	/	Scientists and physicians
DINAMIC	15 + 2 in preparation	23	7	Diabetes researchers, internists, dieticians, scientists, industry, policy makers
EarlyMicroHealth	42	22	9	Scientists, general public, policy makers, end users
EarlyVir	6 + 1 in preparation	9	3	Scientists, journal editors, general public
GI-MDH	3 + 1 in preparation	19	10	Scientists, health care providers, academia, industry, clinicians, physicians, nutritionists
MaPLE	18	20	16	Scientists, physicians, nutrition professionists, food industry, PhD students

The **MaPLE** consortium furthermore prepared dissemination materials for the communication to the general public and presented their results to “CAT.AL” (Lombardy High Tech Agrofood Cluster) whose

aim was to support enterprises, universities and research bodies in Lombardy in their process of developing collaborative networks and needs of innovation in the agro-food sector.

3.3.1.4.2 New funding obtained

All consortia applied for or obtained additional funding by utilizing their results. **ArylMUNE** wrote a proposal to a CIHR[2] project grant to translate findings into a phase 1 clinical trial in celiac disease. The **DINAMIC** consortium received a CDRF[3] grant from January 2019 to June 2022 (Assessing the Role of Long and Short-Term Food Choices on Gut Microbiome-induced Visceral Fat Mass Accumulation; £142,923), from January 2020 to January 2021 (Targeted metabolomics of urine samples to understand the role of the gut microbiota in food polyphenol metabolism; £9,990) and a Diabetes UK Small grant from September 2020 to September 2021 (Metabolomics of faecal samples to identify markers of type 2 diabetes incidence; £12,447). Furthermore, one partner successfully applied to the Novo-Nordisk Foundation for new funding on food-related effects on the microbiota (PRIMA project). After joining the HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health in 2019, **EarlyMicroHealth** consortium aimed to apply for a future joint project, like the EU calls Digital transformation in Health and Care (SC1-DHT-02-2020) or Food and Natural Resources (FNR-12-2020). The **EarlyVir** consortium received a grant from Capital Region of Denmark's foundation for health research (€ 330.000) and NNF[4] grants in basic biomedicine (€ 200.000) and the study of phage sensitivity profile for the *E. coli* isolates was transferred to the Université Laval's team under the Sentinel North 3.7 thematic project (transdisciplinary research program funded by Canada First Research on Excellence Fund). The **GI-MDH** consortium received an internally sponsored research grant at McMaster (Canada) and planned to apply for additional funding to continue the follow up to the preterm cohort. Between 2016 and 2018, the **MaPLE** consortium received a grant in the innovation by design program which was supported by COOK2HEALTH through the European Institute of Innovation and Technology (EIT) HEALTH. The program should bring together leading businesses, universities and research organizations. Furthermore, proposals were submitted to the ERA-HDHL Call "Biomarkers for Nutrition and Health", to the Cranberry Institute Request for Health Research and to the International Nut and dried fruit Council, however no funding was obtained.

3.3.1.5 Involvement in other JPI HDHL activities

The 6 consortia participated at different activities organized by the JPI HDHL. The level of participation differed between 1 (**DINAMIC**) up to 6 (**MaPLE**) activities. A detailed overview about the attendance to the JPI HDHL activities is listed in table 10.

Table 4: Participation of the IM 2015 funded consortia on JPI HDHL activities

JPI HDHL activities	ArylMUNE	DINAMIC	EarlyMicro Health	EarlyVir	GI-MDH	MaPLE
JPI HDHL Mid-term symposium Sept. 2017	**X**		**X**	**X**	**X**	**X**
Workshop for the ERA INTIMIC call/ Knowledge & Research Platform on Diet, Intestinal Microbiomes and Health – Sept. 2017					**X**	

[2] Canadian Institutes of Health Research
[3] Chronic Disease Research Fund
[4] Novo Nordisk Fund

Workshop "FOODBALL Finals" May 2018						X
JPI-HDHL Strategic Research Agenda (SRA) National consultation workshop Rome, Ministry of Health, Sept. 2018						X
JPI HDHL conference Dec. 2017		X			X	X
JPI HDHL conference Feb. 2019	X		X	X	X	X
Final Symposia of ERA-HDHL projects Feb. 2019	X	X	X	X	X	X

3.3.1.6 Capacity Building

All consortia generated new positions and with the exceptions of **ArylMUNE** and **EarlyVir** training activities for young scientists were offered in all projects.

ArylMUNE generated 4 Postdocs and 2 clinical fellow positions.

The **DINAMIC** consortium generated several new positions including 2 master students, 3 PhD students, 6 Postdocs and 3 assistant scientists or nurses. Furthermore, a workshop on 16S rRNA amplicon analysis as well as the personnel training "The intestinal microbiome and diet in human and animal health" were offered to young scientists.

EarlyMicroHealth generated 8 master student positions, 2 PhD student positions, 6 Postdoc positions as well as 2 positions for research assistants. 5 personnel training activities like GDPR practice, ethical research, statistics, R software and new data protection regulation were organized for young scientists.

The **EarlyVir** consortium generated positions including 2 bachelor students, 3 master students, 2 PhD students and 4 Postdocs.

The **GI-MDH** consortium generated 9 master student positions, 3 PhD student positions, 1 Postdoc position and 2 positions for research coordinators. Three large workshops with 40-100 participants were offered about the topics "The microbiome: a new frontier", "Maternal and infant predictors of the gut microbiome" and "Tools for stools: studying the gut microbiome and its establishment during early life". A training activity for health care professionals ("microbiome in health and disease") and for general practitioners, infectious disease specialists, municipal health service employees, pediatricians and midwives ("impact of the microbiome on allergy development") were organized as well as the possibility for biomedical students to attend to a training at the MOSA conference ("with a little help from your little friends").

MaPLE generated 19 positions for master students, 3 positions for PhD students, 8 positions for Postdocs and 2 positions for assistant professors. 7 Personal trainings (for PhD students or Postdocs) were organized with topics like "analysis of 16s rRNA gene sequencing datasets", "speech like Obama", "techniques to improve research", "safe and legal handling of human samples", "bioinformatics tools for analyzing shotgun metagenomics datasets". Furthermore, 2 workshops for research in pharmacy and food science, a summer school about eating for healthy aging, a training for open access research outputs and a course about nutrition and health ("research, development and innovation applied to healthcare") were offered to young scientists. Master students, PhD students and Postdocs got the chance to participate at the EURO-GEROSCIENCE Conference 2019 as well as to the Ecotrophelia Europe Silver prize 2019 (mentoring of the team from master in master in Food Research, Development and Innovation).

3.3.1.7 Data and Knowledge Sharing

All consortia stated to work according to the FAIR (**F**indable, **A**ccessible, **I**nteroperable and/or **R**eusable) data principle. An overview about the used data sources in the different consortia can be found in table 11. Most of the consortia gave an outlook of their plans for data and knowledge sharing but since some data were not published yet, these plans could not be fully realized until now.

Table 5: Handling of data source in the IM 2015 funded consortia

	ArylMUNE	DINAMIC	EarlyMicro Health	EarlyVir	GI-MDH	MaPLE
FAIR principles	yes	yes	yes	yes	yes	yes
use of samples from existing cohorts and / or other epidemiological studies	no	yes	yes	no	yes	no
use of existing data or pooled data	no	yes	yes	yes	yes	no
creation of new or further development existing tools and/or infrastructure	no	no	yes	yes	yes	yes
use of samples from bio-bank or/and other disease register sample collections	no	no	no	yes	yes	no

The **ArylMUNE** consortium stated that the project was managed according to the developed project data management plan ensuring transparent research and widely available data to the research community. The data were published in peer review journals and the raw data in particular microbiota sequencing and transcriptomics data are planned to be uploaded in public databases which should be fully free accessible for other researchers.

DINAMIC used the existing cohorts KORA and TwinsUK for their studies. 16S rRNA sequencing data and food frequency questionnaires available from 2,700 volunteers were pooled from TwinsUK as well as microbiome data form KORA and TwinsUK. All datasets were submitted to public repositories whenever possible (e.g. https://www.ebi.ac.uk/ena/data/view/PRJEB33500me restrictions existed due to the informed consent given by the cohort study participants not allowing the deposit of data in public databases. However, data are available upon request by means of a project agreement as well as of the FoCus-cohort. The German partner has developed a database for integration of amplicon sequencing data (http://www.imngs.org/o NFDI4Microbiota in Germany (https://nfdi4microbiota.de/) will support the microbiology community with access to data, analysis services, data/metadata standards and training.

Originally, the **EarlyMicroHealth** consortium planned to pool previously available data, however the analyses of the methods used and the lack of harmonization and standardization avoided the combination of data from different partners. Therefore, only different subsets of data were used. Furthermore, a next generation sequences analysis tools (METAnnotatorX) and a cohort were created with the infants (DIMISA Asturias). **EarlyMicroHealth** decided to upload the data into the phenotype database developed by ENPADASI (https://dashin.eu/interventionstudies/) at the end of the project. After the upload the data will be made openly available also to the JPI-HDHL INTIMIC Knowledge Platform which aims at improving data sharing and management.

In the **EarlyVir** project feces samples of 1-year old children were used form the COPSAC2010 mother child cohort consisting of 700 children. Furthermore, existing data originated from their own cohort were pooled (16S sequencing data, exposome data, clinical phenotyping, metagenomic (bacteriome)

data). All data were collected and stored in a data warehouse (nc.copsac.com) and all project participants have access. Key viruses (and their bacterial hosts) isolated are permanently stored in Félix d'Hérelle Reference Center for Bacteria Viruses in Canada. The center has expertise in shipping biological materials around the world as well as in signing material transfer agreements. All sequence data along with necessary meta-data will be deposited in public databases prior to publication. Furthermore, a web interface was developed for anyone interested to graphically inspect the virus genomes (e.g. graphics for virus family number 1684: http://crispr.dk/data/EarlyVir/svgs/1684.svg). The viruses discovered in this project were new to science, despite already being found inside the bodies of most humans, so making this information widely available was paramount to the success of the project.

GI-MDH consortium used data and samples which were previously collected in a random controlled trail from the PAPS cohort. Furthermore, two new cohorts were created by the consortium named LucKi cohort (The Netherlands) and Baby&Mi-cohort (Canada). The data will be made available to all partners of the Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health and a deposit of all data will be stored online repository allowing it to be accessed and reused by other researchers.

The **MaPLE** consortium contributed to the development of an ontology called FOBI (Food-Biomarker ontology, https://github.com/pcastellanoescuder/FoodBiomarkerOntology) composed of two interconnected subontologies consisting of raw foods and prepared foods as well as food intake biomarkers classified by their chemical classes. The new developed ontology allows the visualization in a bi-directional way going from metabolomics to nutritional data or vice versa. Furthermore, a database was developed including nutritional characteristics of recipes considered in the menus provided to older people in the nursing home as well as the newly obtained polyphenol data. All data and outcomes generated within the project were deposited in a dedicate section of the Dataverse repository platform at the University of Milan (Dataverse-UNIMI, https://dataverse.org) ensuring the sharing, storage, citation, exploration and analyzation of the research data. Additionally, all sequencing data generated by 16S rRNA gene profiling analysis of blood and fecal samples were deposited into the open access dedicated repository European Nucleotide Archive (ENA) of the European Bioinformatics Institute (EBI) at the European Molecular Biology Laboratory (EMBL). The data will be made open access once scientific manuscripts including such data are accepted for publication. i.e. to the American National Center for Bioinformatic Information (NCBI) and the DNA Data Bank of Japan (DDBJ). Collaboration with the HDHL INTIMIC Knowledge Platform resulted among others in the use of **MaPLE** data to disentangle the role of baseline gut microbiome on the response to fiber and polyphenol rich diets considering a large number of individual characteristics.

3.3.1.8 Impact

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

The **ArylMUNE** consortium identified alterations in the gut microbiota function in humans suffering from Celiac disease characterized by an impaired production of aryl hydrocarbon receptor (AhR) agonists. These alterations could be corrected in a mouse model by using a pharmacologic approach or intestinal bacteria naturally producing AhR agonists which alleviated the severity of the gluten immunopathology. Due to their research topic, the consortium could not contribute to standardisation of methods but provided their obtained knowledge by publishing of the results.

The **DINAMIC** consortium investigated the interplay between diet, gut microbiota and the host in the context of cardiometabolic health. By using state-of-the-art prospective human cohorts, microbiota

profiling, the consortium identified specific features associated with disease states. The results were published and actively shared with the community. Furthermore, meta-omics technologies were employed, aiming at the harmonization of results and the establishment of models towards prediction of detrimental and favorable gut environments with respect to cardiometabolic health.

The aim of the **EarlyMicroHealth** consortium was to unravel the process of intestinal microbiota establishment in infants and to deduce ways to positively modulate this process. In this context, some standard procedures, questionnaires and food composition databases were developed offering the opportunity to develop new generations of infant foods and to delineate the future of infant nutrition; a nutrition targeted not just to nourish the infants but also to promote a healthy microbiome development with reduced levels of antibiotic resistance genes.

The **EarylVir** consortium developed the largest single human virome study and made their data and methods transparent for the community. 8000 diverse viruses were identified in the healthy infant gut flora and the new developed database allows a unique characterization of the virus including family and host providing a standard for all further virome analysis.

The **GI-MDH** consortium worked on the impact of early life dietary events among infants born at term and preterm on gut microbiome community structures and the subsequent association with health outcomes. They demonstrated that in the first year of life the development of the microbiome is characterized by an increasing diversity, the birth mode was a major driver of microbiota community structure only in the first month of life, while thereafter diet became the strongest driving force of microbiota composition. The results can be used in the future for standardization of dietary guidelines for infants and toddlers.

The **MaPLE** consortium tested the hypothesis that an increased intake of polyphenol-rich foods can reduce intestinal permeability and the quantity of inflammogenic bacterial factors in the bloodstream, promoting a protective metabolic phenotype. For this reason, a dietary protocol was developed to deliver three portions per day of specific polyphenol-rich foods/beverages to older participants living in a controlled setting. The polyphenol-enriched diet caused reductions in intestinal permeability. The new data will result in dietary guidelines that can be easily applied in different contexts such as nursing homes or for the support in the management of different clinical conditions associated with increased intestinal permeability.

3.3.1.8.2 Contribution to Public Health

The results of all consortia are relevant for diverse representatives. An overview about the specific target groups of each consortium is depicted in table 12.

Table 6: Target groups of the IM 2015 funded consortia

Target groups	ArylMUNE	DINAMIC	EarlyMicro Health	EarlyVir	GI-MDH	MaPLE
Patients	x	x				x
Scientists, Clinicians	x	x	x	x	x	x
Consumers		x	x		x	x
Policy maker						x
Industry	x					
Special aged groups			0-3 years	0-11 years	0-3 years	60+ years

Interestingly, the **EarlyVir** consortium plans to follow the children not only for 10 years but more likely their whole life to pattern the emergence of chronic diseases to the early life virome and to identify beneficial and harmful viruses. This research plan could be potentially used for further applications.

In addition to the already mentioned target groups the results of the **MaPLE** consortium will be of large interest for managers of food services in healthcare, residential care, nutritionists, dieticians, as well as for stakeholders involved in the promotion of a healthy aging approach.

3.3.1.8.3 Activities towards innovation

ArylMUNE received from the collaboration partner Danone 200 bacterial strains for their research. Furthermore, **ArylMUNE** and **MaPLE** collaborated with large as well as small and medium sized enterprises without specifying the single collaboration partners. Partners of **EarlyMicroHealth** initiated research contracts with the SME Clerici-Saccho from Italy, Carbery from Ireland and B-Food Science from Japan.

ArylMUNE and **EarlyMicroHealth** applied for EU patents with the topic "Methods for preventing or treating gluten-induced gasterointestinal disease" and "Composition comprising new *Lactobacillus salivarius* strain and a method for the prevention and treatment of otitis and upper respiratory infections", respectively and the **EarlyVir** consortium prepared patents for six virulent coliphages.

The **EarlyMicroHealth** consortium developed bioinformatic tools for profiling of Bifidobacterium genus species/subspecies and for phageome analyses and food composition tables for commercial foods targeted to infants between 0 and 12 months of age.

One partner of the **GI-MDH** consortium developed a bacterial profiling technique which is based upon amplifying small fragments of the bacterial DNA and focusing on specific variations in the length of these fragments, which are specific for that species.

Due to the preclinical setting of **ArylMUNE**, **DINAMIC**, **EarlyVir** and **MaPLE** no new products were developed. The obtained results are more important for dietary guidelines and the application in future interventions.

3.3.1.8.4 New strategies/applications to reduce incidence of diet related chronic diseases

Recommendations developed by **ArylMUNE** favoring vegetables naturally enriched in AhR agonists alone or in combination with bacteria naturally producing AhR might be interesting in terms of prevention and /or treatment of several diseases including Celiac disease.

DINAMIC demonstrated that the gut microbiome is important for cardiometabolic health. Evidence was provided that a Mediterranean diet is an efficient strategy to reduce inflammation status during controlled energy intake which might benefit public health by limiting people at risks of developing cardiometabolic diseases.

The **EarlyMicroHealth** consortium analyzed the infant microbiome in combination and integration with clinical and nutritional data. The obtained results of the consortium will assist in the development of better strategies for limiting the deleterious impact of early life medical treatments or diets on the microbiota development and later health.

The **EarlyVir** consortium aimed to identify viruses promoting health and reducing chronic diseases. 8000 diverse viruses were identified in healthy infants and the characterization is still in progress. The results might have a long-term societal impact in terms of decreased disease burden if it is possible to utilise viruses in the future to prevent and treat the chronic diseases.

The **GI-MDH** consortium could demonstrate amongst others, that there is an association between specific gut microbial communities and subsequent development of atopy. Specific microbial communities associated with chronic disease were identified in infants and children which can be used in the future for prevention and therapy.

Replacing low-polyphenol foods and beverages with polyphenol rich foods and beverages will reduce the incidence of and protect against the development of diet-related chronic diseases. The scientific evidences obtained in **MaPLE** could result in new dietary recommendations for older citizens but also for industry exploitation (e.g. food, pharmaceutical, medical products) to improve and develop foods, nutraceuticals or devices which contribute to the promotion of a protective metabolic phenotype in the older subjects.

3.3.1.9 Experts' assessment on general aspects and the specific aims of IM 2015

For external evaluation of **ArylMUNE, DINAMIC, EarlyMicroHealth, EarlyVir, GI-MDH** and **MaPLE** one expert form the stakeholder advisory board (SHAB) and one expert form the scientific advisory board (SAB) have answered general questions regarding the projects.

1. *Contribution of the JFA to fill relevant research gaps in the field*

Both experts agreed that the JFA filled a relevant research gap since the intestinal microbiome is an emerging area in the field of nutrition, food technology and health. The JFA stimulated the collaboration of different expert groups in microbiomics and health in the EU and beyond and contributed to the standardization of methods in this field, in particular in the quantification of microbiome species and characterization of healthy intestinal microbiome. The experts expect longstanding collaborations between institutes all over Europe based on this JFA.

2. *Contribution of the JFA to better coordination and collaboration*

From the experts' view the JFA contributed to a better understanding of the role of the intestinal microbiome in health and disease. A better understanding was established on healthy intestinal microbiome and the involved microbial species. The role of nutrition in early life was highlighted by the experts as an important topic of the JFA. Furthermore, the experts think that collaborations of consortia like in this JFA always stimulate the development of better standards and harmonized methods.

3. *(Future) Impact of JFA results for changes/improvement in the food and/or public health sector*

Table 7: Impact of funded projects

Results of JFA have or will generate	End of the project	In the coming years
New suitable strategies	**expert 1**: yes **expert 2**: yes	**expert 1**: yes **expert 2**: yes, even more than at the end of the project
Recommendations	**expert 1**: see comment below **expert 2**: yes	**expert 1**: see comment below **expert 2**: yes, even more than at the end of the project
Applications	**expert 1**: yes **expert 2**: yes	**expert 1**: yes **expert 2**: yes
Product to reduce the incidence of chronic diseases	**expert 1**: it seems important to learn about strategies of successful disease reduction by the funders **expert 2**: in some of the projects such as GI MDH	**expert 1**: no comment **expert 2**: yes and no
Induce changes/improvements in the food and drink sector	**expert 1**: improvements are always seen **expert 2**: potentially	**expert 1**: no comment **expert 2**: certainly

Induce changes/improvements in the public sector	**expert 1**: no comment **expert 2**: too short to have already effect of public health	**expert 1**: no comment **expert 2**: leads to healthier dietary guidelines

Comments: One expert mentioned that the projects are of high scientific quality. However, it was suggested that the funders should get a very clear view how to link scientific results from projects with measurable disease reduction and other public health implications. In the view of the expert the definition of recommendations and standards are issues of the whole scientific community and not of a single project.

4. *Any other comment on this funding measure:*

One expert mentioned that it was remarkable to see that nearly all recommended projects got funded and were subsequently faced with issues such as long waiting time of consortium agreements (share of data and knowledge) and ethical clearance with some proposals that even did not get full ethical approval. In the view of the expert the overall strategy of funding needs to be reconsidered and the existence of a signed consortium agreements and ethical approval of all human studies need to be a prerequisite for funding (and evaluation of the proposals).

5. *Do the results of this research project substantially contribute to the understanding of the functionality of the intestinal microbiome and its interrelation with diet and/or dietary components and host health?*
6. *Could the knowledge generated in this project lead to new dietary interventions or recommendations that promote health and/or prevent diet-related chronic diseases via modulation of the intestinal microbiome?*
7. *Any other comments on the projects*

One of the two expert did not rate the different projects since it was his/her impression that they had been similar in quality and performance without critical aspects. In the table below the comments of the other expert per project are listed.

Table 8: Experts' comments on funded projects

Name of consortium	Comment
ArylMUNE	The expert thinks that it is a very basic research-oriented project about the role of the aryl hydrocarbon receptor in relation to maintenance of intestinal homeostasis. For a generalist in the field the presentation was difficult to follow since too many technical aspects. The expert highlighted the clinical human study to test the best AhR antagonists coming out of in vivo studies with 3 different pathological models. However so far, no conclusive results were presented. The project is least linked to the other projects in terms of a better understanding of the role of intestinal microbiome in relation to health and disease. Due to the fact that no dietary interventions are tested yet, the experts had difficulties to speculate on the final value of this project.
DINAMIC	The expert evaluated the project as very active with many activities by a number of excellent clinical centers in the field of intestinal microbiome and health. A number of clinical trials are underway or finished using dietary interventions or fecal microbiota transplantations to look for targeted manipulation of the microbiome under controlled conditions. The expert thinks that the project is potentially important for valuable public health recommendations.
EarlyMicroHealth	Interesting results were presented especially on the massive effects of perinatal antibiotic use and the effects on composition of the microbiome

	later in life. The expert is sure that this will certainly have societal impact and will lead to recommendations on restricted antibiotic use early in life. The expert recommended some efforts in the development of an own database and a closer collaboration with ENPADASI.
EarlyVir	The expert stated that the project was very challenging since the dataset for bacteriophages needed still to be developed. Therefore, the objectives of this project might have been too ambitious to achieve the formulated objectives in the given time period of only three years. Nevertheless, the expert sees the very valuable work of the consortium and is convinced that this will be of benefit for future groups working on this topic. The expert assumes the consortium will continue to work together to still reach some of the objectives.
GI-MDH	The expert thinks that this was a very interesting project on the effects of cessation of breast-feeding and the start of solid food on the intestinal microbiome. However, the research of the core project was delayed due to problems to get a consortium agreement. That's why the experts suggested that that funders come with a guideline for a consortium agreement to shorten this process and alleviate the working load.[5] In the meantime, the consortium worked on the PAB data from Germany and they could show a strong effect of cessation on microbiome diversity at 8 years of age. The expert stated that this gives already good indications about the importance of the project leading to valuable guidelines to parents about weaning behavior.
MaPLE	The project tested the hypothesis that an increased intake of polyphenol-rich diets reduces intestinal permeability and lowers intestinal and systemic inflammation. This research question was studied on three levels; human, animal and cell culture. The impact of the animal and cell culture projects was unclear for the expert. The well-controlled human experiment with 51 subjects in a nursing home showed a significant effect on CRP levels as proxy for systemic inflammation confirming the given hypothesis. As a next step the expert suggested to formulate the new dietary guidelines.

3.3.2 Conclusions

The aim of the IM 2015 call was to increase the knowledge on the effects of diet on human intestinal microbiota and on the impact of diet-related variations in the intestinal microbiota. The results of the research should end in the development of dietary interventions or guidance for modulation of the intestinal microbiome to promote health or prevent chronic diseases.

During the runtime of the six consortia regularly telephone and physical meetings allowed a close collaboration of the partners within the consortia. Interestingly, the distribution of the work packages to the partners in the consortia different ranging from 1 partner per work package up to all partner involved. However, the handling of the work packages by 1 partner of the consortia did not minimize the success of the work in any way reflected by the large number of publications (in total 86 published + 4 in preparation). The consortia developed important tools like the next generation sequences analysis tools (METAnnotatorX), food composition tables, a web interface to graphically

[5] There are a few model Consortium Agreements published by the EC and JPI HDHL already recommends in all call texts to make use of those templates.

inspect the virus genomes, blood metabolomics and a new bacterial profiling technique which are important tools for further research.

Although a lot of interesting results were obtained during the research, still a lot of work will be necessary in the future. For example, the **ArylMUNE** consortium stated that especially the human intervention study testing new probiotic strains needs to be continued in the future since the project runtime was too short for the complete investigations. Also, the 8000 identified viruses by the **EarlyVir** consortium in healthy infants need to be further investigated to extract the viruses which can be used in the future to prevent chronic disease. The long-term follow up of infants and toddlers up to the adulthood will give a lot of information about the impact of bacterial populations, medical use and diet for a healthy gastrointestinal development and reduction of chronic disease. All six consortia worked on a transnational and interdisciplinary basis with a broad range of different topics like the role of a specific transcription factor for Celiac disease, prevention of cardiovascular complications and the impact of Mediterranean diet, the establishment of a healthy gut microbiota of new-born and healthy diet for children, the role of viruses for prevention of chronic diseases as well as the effect of polyphenol-rich diet for elderly. Thus, the topics cover various target groups of each age, from birth up to the retirement age and the next step will be to provide recommendations and formulate dietary guidelines which could prevent the development of chronic disease.

3.4 Annexes

3.4.1 Annex 1: List of IM 2015 partners

Due to data protection regulations the list of IM 2015 partners was removed.

3.4.2 Annex 2: Used data sources

Call Text “Joint Action: Intestinal microbiomics (IM 2015)” published via https://www.healthydietforhealthylife.eu/images/documents/Call_document_JPI_HDHL_Joint_Action_Intestinal_Microbiomics.pdf

IM 2015 full proposals submitted by 1st of September 2015.

IM 2015 final report from ArylMUNE, DINAMIC, EarlyMicroHealth, EarlyVir, GI-MDH and MaPLE were submitted on 12.03.20120, 07.08.2020, 20.06.2019, 07.06.2019, 31.08.2020 and 30.04.2020, respectively.

Written feedback to IM final symposia presentations from Stakeholder Advisory Board (SHAB) and Scientific Advisory Board (SAB) members.

3.4.3 Annex 3: Overview on general indicators

4.1.1 Alignment of national funding						
- Number of countries/partners participating in the call	12 countries and 14 funding organizations					
- total committed budget	8.1 Mio €					
4.1.2 Involvement of national scientific communities						
- Number of submitted pre/full-proposals per country/funding organisation	41 pre-proposals (40 eligible proposals) and 21 full-proposals					
- Number of accepted proposals per country/ funding organization	9 consortia recommended for funding 6 consortia funded					
- Committed budget per country	8.1 Mio € in total					
- Budget requested /allocated per country	23.9 Mio € requested / 6.9 Mio € allocated in total					
- % of the total budget spent	85.7 % (6.9 Mio € spent in total)					
-Committed budget per consortium	**ArylMUNE**: 0.8 Mio€	**DINAMIC**: 2.0 Mio €	**EarlyMicroHealth:** 1.3 Mio €	**EarlyVir:** 0.9 Mio €	**GI-MDH:** 0.8 Mio €	**MaPLE:** 0.6 Mio €
- Number and type (Research/SME/Large industry) of organisations/teams in the funded consortia	4 partners (all from research institutes and academia)	8 partners (all from research institutes and academia) +1 collaborator	5 partners (industry/academia) + 1 collaborator	4 partners	3 partners	3 partners
- Gender of Coordinators and PI's	28% female and 72% male coordinators; 28% female and 72% male PI's					
4.1.3 Success of implementing collaboration						
- Interdisciplinary collaboration						
Number of disciplines per consortium	**ArylMUNE**: 1	**DINAMIC:** 6	**EarlyMicroHealth:** 6	**EarlyVir:** 5	**GI-MDH:** 4	**MaPLE:**5
list of disciplines	microbiomics	food metabolomics, functional genomics, microbiology, microbiomics, molecular biology, nutrition	bacteriology, virology, next generation sequencing, nutrition, pediatrics	microbiology, virology, diet, metagenomics, chronic disease	biochemistry, biology, food metabolomics, microbiology	food metabolomics, food science, medicine, microbiomics, nutrition

- Success of transnational collaboration						
Number of new collaborations with academia	**ArylMUNE:** /	**DINAMIC**: 1	**EarlyMicroHealth: 1**	**EarlyVir:** /	**GI-MDH:** /	**MaPLE:** 5
Number of collaboration with other JPI funded projects	**ArylMUNE:** HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health	**DINAMIC**: ENPADASI	**EarlyMicroHealth:** HDHL-INTIMIC Knowledge Platform on Food, Diet, Intestinal Microbiomics and Human Health	**EarlyVir:** /	**GI-MDH:** /	**MaPLE:** Foodball, D-CogPlast
- Number of project coordinators/partner per country	**ArylMUNE:** see Figure 3	**DINAMIC**: see Figure 4	**EarlyMicroHealth:** see Figure 5	**EarlyVir:** see Figure 6	**GI-MDH: see** Figure 7	**MaPLE:** see Figure 8
- Intensity of Collaboration						
Number of Meetings	**ArylMUNE:**12 telephone conferences	**DINAMIC**: 4 physical meetings	**EarlyMicroHealth:** 4 physical meetings,	**EarlyVir:** 4 physical meetings, 22 telephone conferences	**GI-MDH:** 2 physical meetings, regular telephone conferences	**MaPLE:** 12 physical meetings, 10 telephone conferences
Number of mobility/lab visits within a consortium	**ArylMUNE**: /	**DINAMIC**: 4 lab exchanges	**EarlyMicroHealth:** 2 lab exchanges	**EarlyVir:** 1 lab exchange	**GI-MDH:** /	**MaPLE:** 11 lab exchanges
4.1.4 Success of scientific collaboration						
- Number of new publications related to the project	**ArylMUNE:** 2	**DINAMIC**: 15 +2 in preparation	**EarlyMicroHealth:** 42	**EarlyVir:** 6 + 1 in preparation	**GI-MDH:** 3 + 1 in preparation	**MaPLE:** 18
- Number of presentations related to the project	**ArylMUNE:** 3 oral presenations	**DINAMIC**: 23 oral and 7 poster presentations	**EarlyMicroHealth:** 22 oral and 9 poster presentations	**EarlyVir:** 9 oral and 3 poster presentations	**GI-MDH:** 19 oral and 10 poster presentations	**MaPLE:** 20 oral and 16 poster presentations
- New funding obtained	**ArylMUNE:** /	**DINAMIC**: 4	**EarlyMicroHealth:** /	**EarlyVir:** 2	**GI-MDH:** 1	**MaPLE:** 1
4.1.5 Involvement in other JPI HDHL activities	**ArylMUNE:** 3	**DINAMIC**: 2	**EarlyMicroHealth:** 3	**EarlyVir:** 4	**GI-MDH:** 5	**MaPLE: 6**
4.1.6 Capacity Building						
- Training activities	**ArylMUNE:** /	**DINAMIC**: 2 (1 workshop and 1 personnel training)	**EarlyMicroHealth:** 5 personnel trainings	**EarlyVir:** /	**GI-MDH:** 5 (3 workshops, 2 activities for health care professionals)	**MaPLE:** 14 (7 personnel trainings, 3 workshops, 1 summer school, 2 conferences)

- New jobs/positions generated in the project	**ArylMUNE:** 6 (4 Postdocs, 2 clinical fellows)	**DINAMIC**: 14 (2 masters, 3 PhDs, 6 Postdocs, 3 assistant scientists or nurses)	**EarlyMicroHealth: 18 (**8 masters, 2 PhDs, 6 Postdocs, 2 research assistants)	**EarlyVir:** 11 (2 bachelors, 3 masters, 2 PhDs, 4 Postdocs)	**GI-MDH:15 (**9 masters, 3 PhDs, 1 Postdoc, 2 research coordinators)	**MaPLE:** 32 (19 masters, 3 PhDs, 8 Postdocs, 2 assistant professors)
- Use of existing tools and/or development of new capacities or resources (e.g. a transnational database, biobanks, animal models, cohorts)	**ArylMUNE:** no	**DINAMIC**: no	**EarlyMicroHealth:** yes (NGS analysis tool METAnnotatorX)	**EarlyVir:** yes	**GI-MDH:** yes	**MaPLE:** yes (Food-Biomarker ontology)
4.1.7 Data and Knowledge Sharing						
- Use of existing data: Has existing data been used / pooled for the project?	**ArylMUNE:** no	**DINAMIC**: yes	**EarlyMicroHealth:** yes	**EarlyVir:** yes (COPSAC2010 mother child cohort)	**GI-MDH:** yes (PAPS cohort)	**MaPLE:** no
- Has the consortium used samples from existing cohorts and / or other epidemiological studies?	**ArylMUNE:** no	**DINAMIC**: yes (KORA, TwinsUK)	**EarlyMicroHealth: yes**	**EarlyVir: no**	**GI-MDH:** yes	**MaPLE:** no
- To perform the project, have you used samples (omics-based) from bio-bank or/and other disease register sample collections?	**ArylMUNE:** no	**DINAMIC**: no	**EarlyMicroHealth:** no	**EarlyVir:** yes	**GI-MDH:** yes	**MaPLE:** no
- FAIR-Data principles: Has the data generated in the project made available by following the FAIR principles?	**ArylMUNE:** yes	**DINAMIC**: yes	**EarlyMicroHealth:** yes	**EarlyVir:** yes	**GI-MDH:** yes	**MaPLE:** yes
4.1.8 Impact						
- Contribution of the project to the coordination/harmonization of research activities (standardisation of methods and protocols, data harmonisation, data and knowledge sharing)	**ArylMUNE:** no	**DINAMIC**: yes (meta-omics technologies aiming at the harmonization of results)	**EarlyMicroHealth:** yes (standard procedures, questionnaires and food composition databases)	**EarlyVir:** yes (web interface of virus genomes)	**GI-MDH**: yes (standardization of dietary guidelines for infants and toddlers)	**MaPLE:** yes (standardization of dietary guidelines for elderly)

- Activities towards innovation	**ArylMUNE:** yes	**DINAMIC**: yes	**EarlyMicroHealth:** yes	**EarlyVir:** yes	**GI-MDH:** yes	**MaPLE:** yes
New industry collaboration	**ArylMUNE:** Danone, small, medium and large enterprises	**DINAMIC**: /	**EarlyMicroHealth:** SME Clerici-Sacchoform Italy, Carbery from Ireland, B-Food Science from Japan	**EarlyVir:** /	**GI-MDH:** /	**MaPLE:** small, medium and large enterprises
Development of new methods/research tool/products	**ArylMUNE:** /	**DINAMIC:** /	**EarlyMicroHealth:** bioinformatic tools for profiling of Bifidobacterium genus species/subspecies and for phageome analyses, food composition tables	**EarlyVir:** /	**GI-MDH:** bacterial profiling technique	**MaPLE:** blood metabolomics
Patents: number and geographical scope	**ArylMUNE:** 1 (EU patent)	**DINAMIC**: /	**EarlyMicroHealth:** 1 (EU patent)	**EarlyVir:** 6 (EU patents)	**GI-MDH: /**	**MaPLE:** /
- Contribution to public health	**ArylMUNE:** yes	**DINAMIC**: yes	**EarlyMicroHealth:** yes	**EarlyVir:** yes	**GI-MDH:** yes	**MaPLE:** yes
Target groups	**ArylMUNE:** patients, scientists, industry	**DINAMIC:** patients, scientists, consumers	**EarlyMicroHealth:** scientists, consumers	**EarlyVir:** scientists	**GI-MDH:** scientists, consumers	**MaPLE:** patients, scientists, consumers, policy makers
Interaction with End-Users (e.g. consumers, patients in intervention studies)	**ArylMUNE:** no	**DINAMIC**: yes (dietary intervention)	**EarlyMicroHealth:** yes (patient interventions)	**EarlyVir:** no	**GI-MDH: yes** (interventions with infants and toddlers)	**MaPLE:** yes (interventions with elderly)
- New strategies/applications to reduce incidence of diet related chronic diseases)	**ArylMUNE:** no	**DINAMIC:** yes (Mediterranean diet to reduce inflammation status)	**EarlyMicroHealth:** yes (reduction of early life medical treatment and increasing of health)	**EarlyVir:** yes, but in the future (use of viruses to prevent or treat chronic disease)	**GI-MDH:** yes, but in the future (specific microbial communities for prevention and therapy)	**MaPLE:** yes **(**polyphenol rich foods and beverages to reduce development of diet-related chronic diseases)