CSA JPI HDHL 2.0

Evaluation of Joint Funding Actions

Biomarkers for Nutrition and Health (BioNH)

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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 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: Biomarkers for Nutrition and Health (BioNH)

3.1 Aim of the call

In pillar two of the strategic research agenda (SRA) that the Management Board (MB) of the JPI HDHL has adopted, the establishment of an action on biomarkers in nutrition and health has been identified as a joint funding activity to be developed over the period 2012–2014. The main objective of the Biomarkers in Nutrition and Health (BioNH) call was to support interdisciplinary research and innovative approaches for the validation of biomarkers and the investigation of intake/exposure and nutritional status of biomarkers within this scientific area. 13 JPI HDHL member countries participated as funders in the BioNH call aiming to define and harmonise the methodology necessary to prove the nutritional effects in the development of new foods.

In the call text, the most important dietary biomarkers identified to be investigated were:

- Recovery dietary biomarkers: based on the metabolic balance between intake and excretion over a fixed period of time
- Predictive dietary biomarkers: to assess the degree of measurement errors in dietary assessment methods
- Concentration and replacement dietary biomarkers: for comparison with estimated dietary intakes and estimated diet–disease risk associations.

3.2 Peer-review Procedure and Results

The BioNH Joint transnational call was launched on 14th of April, 2014. The Joint Call Secretariat was located at ZonMw (The Netherlands organization for health research and development). The implementation process was organized by a postal (20 reviewers) and a panel review. In the postal review each eligible submitted proposal was evaluated by 4 reviewers on basis of the evaluation criteria as published in the call text by at least three international experts according to their expertise in the substantive area of the proposed research. In the panel review, 6 international experts discussed the inputs of the postal peer reviews, the overall merit and priority of proposals. Evaluation criteria were (1) scientific quality of the proposal and quality of the transnational project, (2) quality and relevance of individual scientists and research groups, (3) quality and efficiency of the implementation and management of resources made available to the collaborative projects and (4) potential impact. The panels ranked the proposals and made recommendations for proposals to be considered for funding by the Call Steering Committee. Out of 20 full proposals 2 were funded. On the 10th of October, 2014 the final funding decision was made to fund the two consortia, **miRDiet** (Circulating microRNAs as markers of dietary intake) and **FoodBall** (The Food Biomarker Alliance).

The two funded consortia **miRDiet** and **FoodBall** concentrated on different biomarkers after nutritional intake. **miRDiet** aimed to identify differential responses of specific circulating microRNAs that occur during dietary interventions in individuals with various metabolic status. **FoodBall** proposed to carry out a systematic exploration and validation of biomarkers to obtain a good coverage of the food intake in different population groups within Europe.

The funding of both consortia started at the 1st of December, 2014. The **miRDiet** consortium was led by Prof. Dominique Langin and the **FoodBall** consortium by Prof. Edith Feskens. The run time of **MiRDiet** ended in December 2017[2] and **FoodBall** in July 2018.

[2] The project was not finished by then. A second final report was submitted in March 2019 since the work was still ongoing.

3.3 Evaluation Results

3.3.1 General Indicators

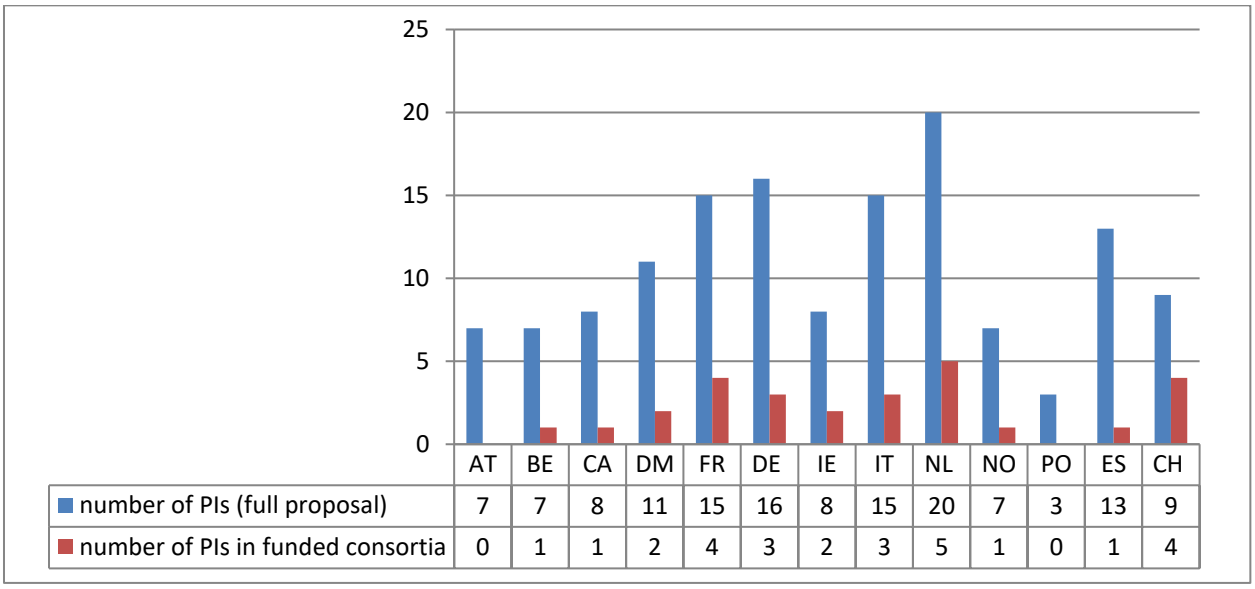
3.3.1.1 Alignment of national funding

13 JPI HDHL partner countries and 16 funding organisations participated in the call. The total *in cash* budget committed by the participating funding organisations for BioNH was 5.74 Mio €. In addition, Italy, France, The Netherlands and Spain provided an unspecified in kind budget.

3.3.1.2 Involvement of national scientific communities

3.3.1.2.1 Participation of national scientific communities

In response to the call, 20 full-proposals were submitted involving 139 PIs (principle investigators). The decision was made to fund two consortia (**miRDiet** and **FoodBall**) including 27 PIs from 11 JPI HDHL partner countries. With 12 female and 15 male PIs in the funded consortia the distribution between the sexes was almost equally. A list of all BioNH partners in both 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. Austria and Poland were the two countries which had no PIs in the funded consortia.



	AT	BE	CA	DM	FR	DE	IE	IT	NL	NO	PO	ES	CH
number of PIs (full proposal)	7	7	8	11	15	16	8	15	20	7	3	13	9
number of PIs in funded consortia	0	1	1	2	4	3	2	3	5	1	0	1	4

Figure 1: Numbers of PIs per country in the implementation of BioNH

3.3.1.2.2 Distribution of national funding

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

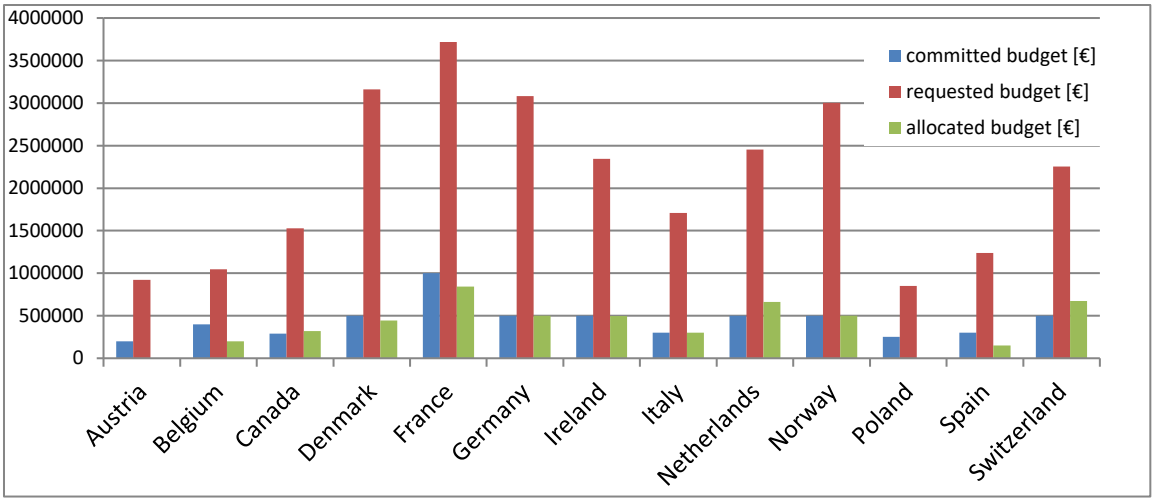


Figure 2: Committed, requested and allocated funding budget of BioNH call, distributed by countries.

The total requested budget for all proposal submitted for the BioNH call was 27.3 Mio € *in cash* resulting in an oversubscription factor of 4.8. As shown in fig. 19 the requested budget for each country was substantially higher compared to the committed budget reflecting the large interest of the research community on the released call. For the two recommended consortia, the allocated budget was 5.1 Mio € which is 88.7 % of the initially committed budget of 5.74 Mio €. The largest amount of allocated *in cash* money was available for applicants from France, The Netherlands and Switzerland. Therefore, these countries had the most PIs working in the consortia. The projects were led by a French coordinator (**miRDiet**) and a Dutch coordinator (**Foodball**).

However, the requested and granted budget of the two funded projects differed substantially, which to some extent arises from the divergent size of the two consortia: for **miRDiet, 6 PIs/groups of PIs** were funded with 0.7 Mio €; whereas for **FoodBall, 22 PIs/groups of PIs** received 4.4 Mio €. Partners in both consortia also allocated additional in kind contributions to their granted budgets: within **miRDiet** approx. 96 Person Months were provided in kind and for **FoodBall** two partners provided approx. 550.000 € as own contributions to the project.

From 28 PIs in the two consortia, only one partner came from large industry (Nestlé R&D as partner in **miRDiet**) and the other 27 PIs were from academic and food and health research institutes. This indicates a stronger interest by academia although results should be interesting for food industry, too.

3.3.1.3 Success of implementing collaboration

The main objective of the BioNH call was to support interdisciplinary research and innovative approaches for the validation of biomarkers and the investigation of intake/exposure and nutritional status of biomarkers within this scientific area. The two consortia worked under the umbrella of the BioNH call; however, the studies were conducted independently from each other with no planned collaboration in between. However, both BioNH consortia collaborated with ENPADASI KH (research area 3 of JPI HDHL).

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 partners and 8 co-applicants (colleagues of the partners) of the **miRDiet** consortium were experts in nutrition, “omics” techniques and clinical interventions. The consortium included basic

labs, hospital groups and the Nestlé Institute of Health Science demonstrating a clear interdisciplinarity.

The **FoodBall** consortium included expertise and facilities in nutrition, metabolomics, epidemiology, clinical science, analytical chemistry, molecular biology, food sciences, bioinformatics and statistics. The 22 partners as well as the 37 co-applicants (colleagues of the partners) and the 4 collaborators of the consortium reflected a complementary interdisciplinarity in their skills, competence and knowledge. This composition was also highlighted by the four reviewers of the proposal.

3.3.1.3.2 Transnational collaboration

MiRDiet, as the smaller consortium, consisted of 6 partners from 3 different countries (France, The Netherland and Switzerland). The transnational composition of **miRDiet** is depicted in Fig. 20. With 3 partners, France was the strongest represented part in the consortium.

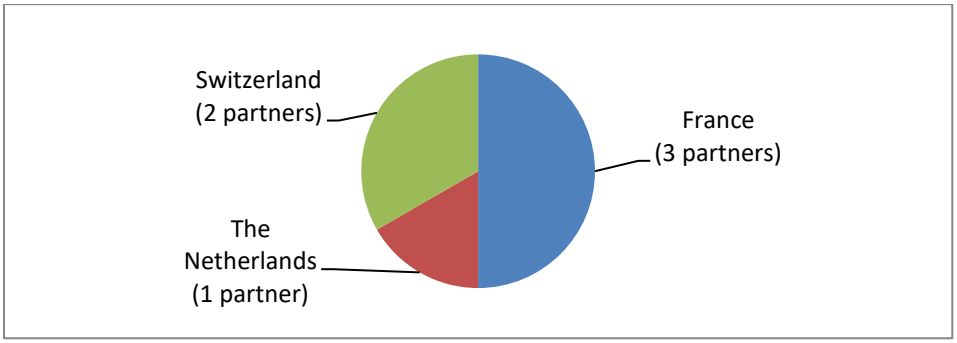


Figure 3: Transnational composition of miRDiet

The number of participating partners in the single work packages (WP) (Fig. 21) clearly demonstrated the transnational collaboration in the **miRDiet** consortium.

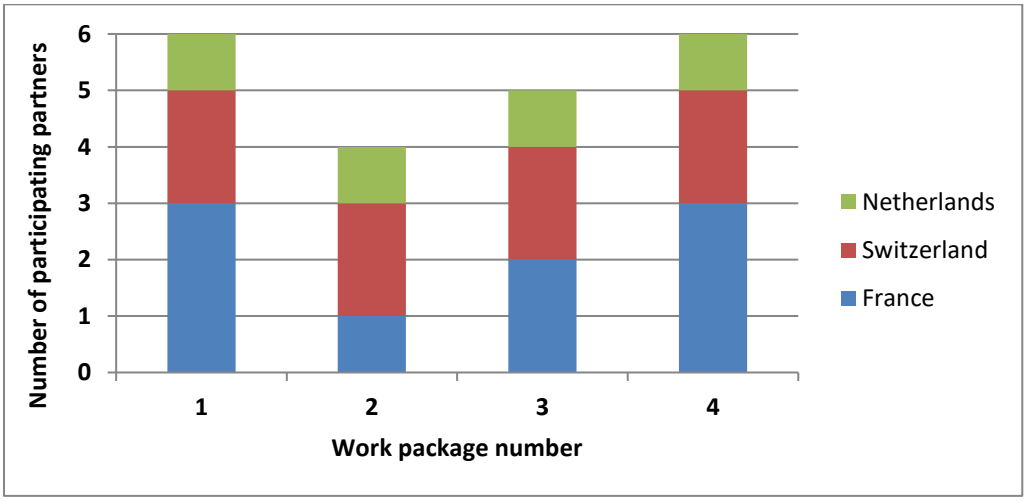


Figure 4: Number of participating miRDiet partners in working tasks

FoodBall consisted of 22 partners from 11 countries (Belgium, Canada, Denmark, France, Germany, Ireland, Italy, Norway, Spain, Switzerland and The Netherlands). The transnational composition of **FoodBall** is depicted in Fig. 22. During the funding period two additional partners were brought into the **FoodBall** consortium. To cover the work Chalmers University (Sweden) and University of Eastern Finland (Finland) were invited to the consortium.

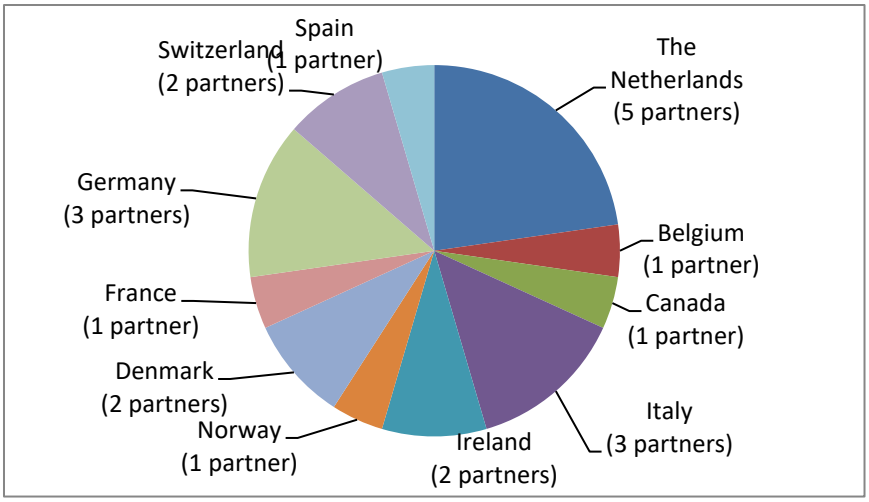


Figure 5: Transnational composition of FoodBall

The 22 partners of the consortium closely collaborated in the single work packages (Fig. 23). They focused on developing, harmonising and testing methodology for discovery and validation of biomarkers of food intake (WP1-4); developing and testing new technologies such as dried blood spots and mid-infrared spectroscopy (WP1 and 2) and joining data from metabolome and transcriptome to understand metabolic pathways (WP5). WP 6 and 7 included policies and coordination of the consortium. The leading roles in the 7 WPs are depicted in Figure 24.

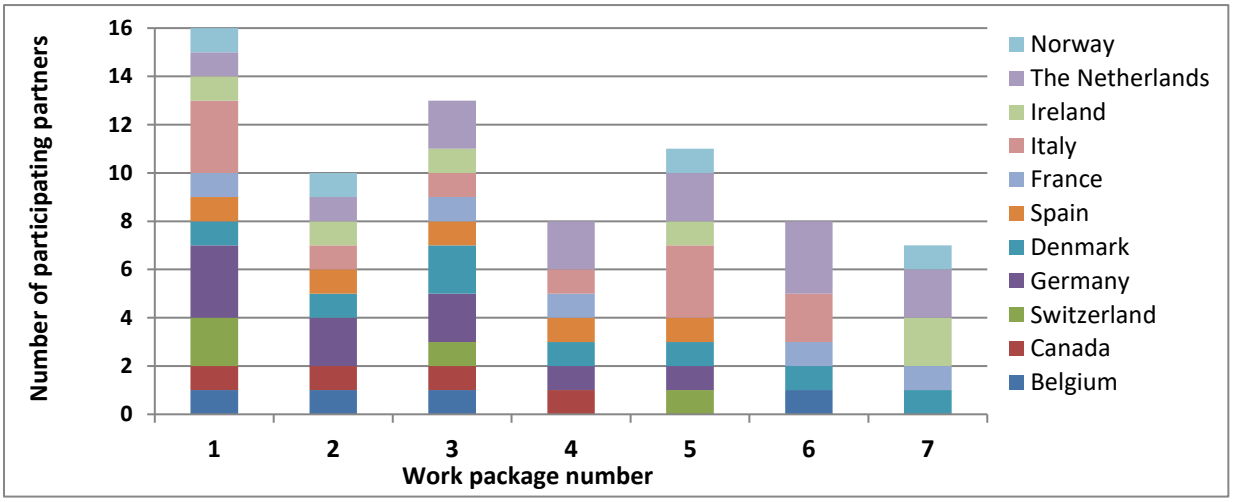


Figure 6: Number of participating FoodBall partners per work package.

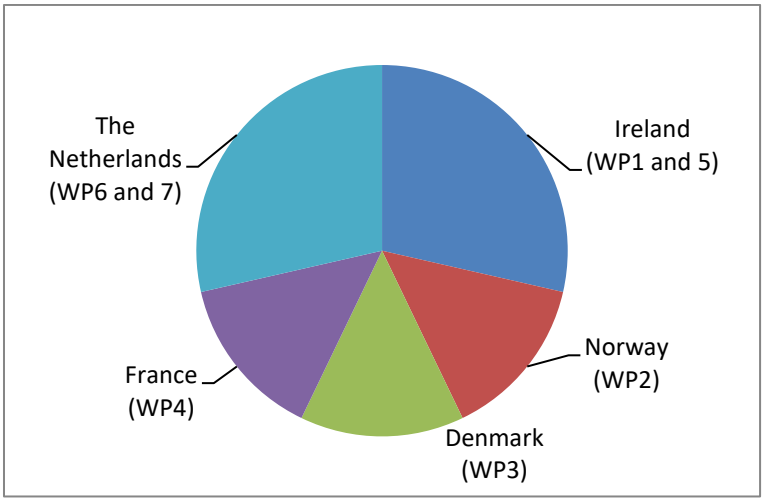


Figure 7: Distribution of Leading Roles within the network.

Collaboration with other JPI funded projects was implemented in both consortia. **miRDiet** and **FoodBall** collaborated both with the ENPADASI KH and **miRDiet** furthermore with the DEDIPAC KH. Although **miRDiet** had already one collaboration partner from the industry (Nestlé R&D) no further collaboration with the industry was obtained in both consortia. **FoodBall** initiated collaboration with the COST Action "POSITIVe", a network focused on inter-individual variation in response to consumption of plant food bioactives. During a US workshop organized by the National Institute of Health (NIH), 4 scientists from **FoodBall** had the chance to present their results and get in touch with American scientists.

3.3.1.3.3 Intensity of Collaboration

The intensity of collaboration varied between the two consortia. Over the 3 years funding **miRDiet** had 15 project meetings including 8 telephone conferences and 2 physical meetings at the French National Institute of Health and Medical Research (Inserm) and at the Nestlé Institute of Health Science (NIHS), respectively. However there were no lab visits or exchanges of scientists during this time. During the funding period of **FoodBall**, 7 physical meetings in six different cities (Wageningen, Barcelona, Copenhagen, Karlsruhe, Varna, Bern) took place starting with the kick off meeting in Wageningen 2015 and ending with the final meeting in Wageningen 2018. One Italian scientist attended to a 6 month scholarship in Copenhagen and another scientist visit the Copenhagen lab for one month. Two scientists from Spain visited the labs in Dublin and Sweden, respectively, within the COST Action "POSITVe", a collaboration initiated by the **FoodBall** consortium.

3.3.1.4 Success of scientific collaboration

3.3.1.4.1 Scientific Output

So far no publications were released from the consortium **miRDiet** but 2 papers are in preparation. In contrast to this, 56 publications (peer review and others) were generated in **FoodBall** consortium with 13 further reports which are submitted or in preparation. At the time of drafting this report (November 2019) a total of 62 papers were published by **FoodBall**. Number of publications can be also correlated to the size of the consortium since **miRDiet** is significant smaller compared to **FoodBall**. The data of **miRDiet** have been presented at 7 conferences or symposia (including JPI HDHL activities) while 67 oral presentations and 33 poster presentations were held at international meetings, symposia and congresses by scientists of the **FoodBall** consortium.

3.3.1.4.2 New funding obtained

While **FoodBall** has not obtained any further funding, one partner of the **miRDiet** consortium INSERM Toulouse received a grant from the company Nutrition&Santé. These additional funds were related to Task 1. Both University of Lausanne (UL) and INSERM Lyon applied for additional funding to support the cost of the nutritional intervention, the analysis of specific markers and microbiota. However, these funds were not related to the **miRDiet** project directly.

3.3.1.5 Involvement in other JPI HDHL activities

As demanded in the call text, **miRDiet** built up collaboration with DEDIPAC and ENPADASI mainly for data sharing according to the ENPADASI database access rules. **FoodBall** collaborated with ENPADASI to develop a protocol for data sharing between different studies for the purposes of metabolomics data mining. One scientist has visited Copenhagen during one month to establish a joint analysis using data from an onion intake study (**FoodBall**) and observational studies in ENPADASI. Furthermore, a hands-on workshop on working with the preliminary ENPADASI database (dbNP) has been organized during the annual project meeting in Copenhagen. The work on ontology for

nutrition and adding metabolomics studies to the dbNP are significant collaborative activities with ENPADASI. In addition, a joint data analysis project has been conducted using several studies, including meal studies from **FoodBall**, to look up chicken intake biomarkers using the ENPADASI system. These activities show an example of fruitful linkage between funding activities under the umbrella of JPI HDHL.

3.3.1.6 Capacity Building

Within the **miRDiet** consortium 2 Bachelor degrees for database internship at INSERM Toulouse were allocated. In the **FoodBall** consortium young scientists attended to several training activities including:

- Statistic courses
- Online webcase course for liquid chromatography-mass spectrometry (LC-MS) or short-course on mass spectrometry
- Post-doc orientation events
- Post-graduate course 2015: Nutrigenomics studies in humans: from epidemiology to intervention organized by the NuGO
- Two days international symposium on obesity workshop organized by the Fundación Ramón Areces and CSIC
- EMBO practical course on metabolomics, bioinformatics of life scientists
- Two days workshop at MRI on multivariate data analysis
- Two days hand-on metabolomics workshop
- Training course on "Use of metabolomics in nutrition research organized by COST Action "POSITIVe"
- Course of "Introduction to Nutritional Metabolomics" (scientists form **FoodBall** teached, supervised and attended to this course)

Moreover new jobs were generated in both consortia. **miRDiet** generated 9 new positions including:

- 1 research engineer
- 2 assistant engineers
- 1 biostatician
- 1 medical research assistant
- 1 technichian
- 1 PhD student
- 2 research associates (Master degree)

Foodball consortium generated 29 new positions including:

- 11 Post-docs
- 12 PhD students
- 3 graduate students
- 2 programmer analysts
- 1 clinical research associate

The **FoodBall** consortium developed the following three databases important for the food metabolome field:

- FooDB: a comprehensive database for food constituents and their chemical and biological data.

- FoodComEx: a virtual library of isolated food-derived compounds (stored at different laboratories) to enhance exchange of these standards.
- PhytoHub: a database of dietary phytochemicals and their human and animal metabolites.

FoodBall also collaborated on the Exposome Explorer, the first database dedicated to biomarkers of exposure to environmental risk factors for diseases.

The data of **miRDiet** were stored in an extension of the FORCE database with a partner-specific individual access. FORCE is the Clinical research national network specialized in the study of obesities and associated pathologies, established by the French Clinical Research Infrastructure Network (F-CRIN), which is the French side of the European Clinical Research Infrastructure Network (ECRIN).

3.3.1.7 Data and Knowledge Sharing

Data for **miRDiet** were obtained from 8 different already existing cohort studies.

- DiOGenes (Diet, Obesity, and Genes)/EMIF-IMI (EMIF-Metabolic)
- MONA (Metabolism Obesity Nutrition Ageing)
- PolyNut (Polyphenols, Nutrition)
- Micro-Obes (Human intestinal microbiota in obesity and nutritional transition)
- Alpro (short term polyphenol study)
- Alpro (long term polyphenol study)
- Frumilk (Fructose-Milk protein interaction on cardiometabolic risk factors)
- Eurostarch

The results were pooled from 2-3 cohorts according to the question to be answered. All data were shared in accordance to open access strategies and FAIR principles, as defined for the ENPADASI database access rules.

In the **FoodBall** consortium 7 study centres successfully completed acute intervention studies to establish links between blood cell gene expression, clinical chemistry parameters and metabolites related disorders. A cross-sectional study from the Netherlands was analysed to compare dietary records with biomarker measurements. Four cohort studies were used to quantitatively analyse novel dietary-biomarkers and results were pooled. The collected data were stored in dbNP, the database in DASH-IN, i.e. the ENPADASI infrastructure. Furthermore, a public web portal has been launched, which provides a unique platform to share knowledge and resources with the scientific community. This web portal for instance provides open-access to the databases and spectral libraries for food compounds and their metabolites.

3.3.1.8 Impact

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

Both consortia contributed to the coordination or harmonization of research activities. Standardization of adipose tissue and blood sampling as well as the processing protocols were established in **miRDiet**. **FoodBall** developed new (FoodDB and FoodComEx) and advanced existing platforms (PhytoHub) for sharing knowledge and resources and supporting thereby the harmonization of methodologies (see 3.3.1.6). Furthermore a public website was constructed to share food derived standards produced by **FoodBall** partners.

3.3.1.8.2 Contribution to Public Health

The results of circulating miRNAs from **miRDiet** consortium may become the biomarkers of dietary intake with potential clinical use in nutritional intake or status testing of patients. The biomarkers

could be interesting for endocrinologist and show a link to obesity related comorbidities which is interesting for scientists and health professionals. Results of **FoodBall** strengthened diet-related public health recommendations and are of central importance for health professionals and for citizens around the world to understand the relationship between food intake and health as well as disease development. The recommendations on the value of biomarkers are interesting for researchers but also policy makers.

3.3.1.8.3 Activities towards innovation

Although one partner from large industry was participating in BioNH, no further industrial collaboration were established. Most innovations were made in the field of data sharing. **FoodBall** conducted 3 databases for sharing the obtained data (see 3.3.1.6) or to advance the existing platforms. Availability of the data not only to scientists but also to the public was achieved by the development of a public web portal. New sampling techniques (dried blood spots (DBS) analysis) were tested for lipidomics to facilitate sampling collection and storage.

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

The results of both consortia are of large interest but at this time point they don't indicate strategies reducing diet related chronic disease. Further research on the basis of the obtained results is necessary to achieve new strategies and applications. **MiRDiet** results are more of a basic research approach which requires further investigation. In the future the obtained results of **FoodBall** will increase the probability of detecting potential nutrient/food-based health effects in scientific studies, which will strengthen diet-related public health recommendations. Experts from the SHAB and SAB had the same opinion about the state of research in both consortia.

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

For external evaluation of **miRDiet** and **FoodBall** an expert from the scientific advisory board (SAB) and the stakeholder advisory board (SHAB) have answered general questions regarding the project.

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

For **miRDiet** both experts see the need to validate and sensitive nutritional biomarkers useful for more objective assessment of the dietary and health status of populations, for better assessment of the health effects of nutritional interventions and for an enhanced understanding of effects of specific foods/nutrients in physiology and pathophysiology. The experts agreed that **FoodBall** is a great example of project to fill existing research gaps. **FoodBall** validated biomarkers through interdisciplinary research by using innovative approaches for example, methodologies necessary to prove nutritional effect in food development, or contribution to international food metabolome database. The experts commended the funding of **miRDiet** since the topic is of very large interest and research needed to be done in this field. In general they complimented the JPI HDHL for supporting both consortia not only because of the interesting topic but also for the very successful results of **FoodBall**.

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

The experts agreed that **miRDiet** worked on the basis of an interdisciplinary approach allowing the coordination of different research centres across Europe. By the use of existing databases from previous projects, analysis for biomarkers changes in diet were possible. Methodology was adapted to the new approach and new technologies have been incorporated. Although there are few publications from this project, the experts expect more for the future time.

From the expert´s view, collaboration within **FoodBall** was truly interdisciplinary. A broad network of universities and research institutes was built up and 7 international meetings were organized. The high number of publications show that the intensive collaboration led to the development of new methods and standards, identification of new biomarkers of major interest for food and nutrients and a series of open access databases, libraries for food components, software tools, SOPs and tutorials.

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

The experts agreed about the changes and improvements of the obtained results of the consortia. The following tables indicate the overall opinion.

Table 1: miRDiet

Results of JFA have or will generate	End of the project	In the coming years
New suitable strategies	Yes	Yes
Recommendations	No	No
Applications	No	No
Product to reduce the incidence of chronic diseases	No	No
Induce changes/improvements in the food and drink sector	No	No
Induce changes/improvements in the public sector	No	No

Both experts agreed that the project was related to basic science and far away from inducing changes in the food and drink sector or contributes to reduce diet-related diseases. Such exploratory approaches may not directly translate into recommendations or product development. However, identifying biomarkers that reflect changes in the content of the diet is very appropriate and needs to be funded in the view of the experts. Even if the final results identify positive and negative markers, they suppose that further projects can benefit from the experiences and new developed strategies.

Table 2: FoodBall

Results of JFA have or will generate	End of the project	In the coming years
New suitable strategies	Yes	Yes
Recommendations	Yes	Yes
Applications	Yes	Yes
Product to reduce the incidence of chronic diseases	No	Yes
Induce changes/improvements in the food and drink sector	No	Yes
Induce changes/improvements in the public sector	No	Yes

The experts emphasised the JFA as very productive which contributed significantly to the progress of metabolomics and biomarkers of food and nutrient intake. From the result of **FoodBall** it is likely in the expert´s view that new studies arise which should be relevant to public health policy regarding health claims.

4. *Did the project successfully develop or validate suitable biomarkers that could be used to prove the nutritional effects in the development of foods?*

miRDiet identified 5 miRNA relevant for specific aspects of diet and nutrients, three of them are potentially dietary biomarkers. Two of them showing the same pattern in blood and adipose tissue and therefore could be of further interest for health professionals involved in nutrition. The experts see that the project so far is on the right way since promising results for variations in energy intake have been found. In their opinion, further research needs to be done to confirm that intervention do not lead to expand expression of downregulated miRNAs as the results indicated.

The experts concurred that the **FoodBall** consortium very successfully developed novel biomarkers of food intake and new approaches for study biomarkers of nutrient status or intake. The data are available through an online database and in a public web portal. They have performed ontology, classification, literature search strategy and validation procedures for the food and health biomarker area, which resulted in the publication of four position papers and 69 additional publications.

5. *Have innovative approaches been used and are these approaches applicable to develop/validate other biomarkers?*

MiRDiet has used innovative approaches screening for new biomarkers in the view of the experts. More than 1000 mRNAs were analyzed for relevance choosing the most significant for further validation. The low abundance of miRNAs created problems in measurement, but, in the middle of the project, the setup of new HTG Edge Seq next generation sequencing technology was emphasized by the experts. This technic allowed the researchers to analyze 200 samples.

The experts agreed that **FoodBall** used innovative approaches in several domains. Guidelines were implemented when searching and validating novel biomarkers. Innovative technologies were designed and validated to collect and analyze hundreds of small samples using by high performance liquid chromatography time of flight mass spectrometry (HPLC TOF-MS), for example. A new classification and scoring system for biomarker quality was set up as well as a food metabolome compound database of sharing data and resources.

miRDiet has advanced the knowledge of very specific potential biomarkers and their variation in context of obesity and weight loss/negative energy balance. Although only few miRNAs of interest have been identified, the experts consider the approach as discovery research. The results look promising and both experts agree that it is important that European Research Laboratories take part on such studies.

The experts evaluated **FoodBall** as an outstanding project with a very complete final report. The development of a dedicated web site, the database FoodComEx as well as the contribution to Exosome Explorer must make JPI HDHL proud of this JFA.

3.3.2 Conclusions

Identification of biomarkers for nutrition and health is of great importance and a lot of open questions still remain in this research field. This was already reflected during the call for proposals since 20 full proposals were submitted requesting almost 5 times more money than committed.

The two funded consortia worked of high quality trying to identify new biomarkers and answer some important questions in the field of nutrition and health. However, it has to be mentioned that the two consortia worked under different conditions (budget, number of partners, etc.). The high number of published papers as well as the development of online databases generated during the funding period clearly demonstrates the significance of the research field.

The aim of the call was to establish a limited number of ambitious, innovative, multi-national and multi-disciplinary collaborative research projects focusing on:

- Identification of New Biomarkers

- Validation of Biomarkers
- Investigation of intake/exposure and nutritional status of biomarkers
- Definition of more sensitive nutritional biomarker profiles

In general, both consortia worked on the basis of a multi-national and multi-disciplinary approach. The consortia consisted of 6 and 22 partners from 11 different countries. Regular meeting, telephone conferences and lab exchanges were established to support the collaboration of the research partners and to assure the optimal knowledge and result exchange. The consortia identified several new biomarkers and validated the biomarkers in blood, adipose tissue or urine, amongst others.

New innovative methods were implemented and harmonized for the generation of the results like lipidomics with very small biological samples or new HTG EdgeSeq next generation sequencing technology. By this, investigation of intake/exposure and nutritional status of the identified biomarkers were successfully performed. All actions and results of the consortia clearly demonstrate the success of the BioNH call. However, further work on defining more sensitive nutritional biomarker profiles needs to be done in the future since some of the results were only preliminary. The **FoodBall** consortium emphazised that there are still gaps between nutritional biomarkers and functional efficacy with respect to health outcomes. Following on this advancement will ensure future success within the European Nutrition community.

3.4 Annexes

3.4.1 Annex 1: List of BioNH partners

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

3.4.2 Annex 2: Used data sources

Call Text "Joint Action 2: Biomarkers for Nutrition and Health (BioNH)" published via https://www.healthydietforhealthylife.eu/index.php/call-activities/calls/98-calls-site-restyling/516-bionh-2014-site-restyling

BioNH proposals from FoodBall and miRDiet submitted in June 2014.

BioNH final report from FoodBall and miRDiet submitted on 01.10.2016 and 04.06.2018 (additional report submitted 22.03.2019), respectively.

Written feedback to final report from BioNH Scientific Advisory Board and Stakeholder Advisory Board members

3.4.3 Annex 3: Overview on general indicators

	miRDiet	**FoodBall**
4.1.1 Alignment of national funding		
- Number of countries/partners participating in the call	13 countries and 16 funding organizations	
- total committed budget	5.74 Mio €	
4.1.2 Involvement of national scientific communities		
- Number of submitted pre/full-proposals per country/funding organisation	20 full-proposals	
- Number of accepted proposals per country/ funding organization	2 consortia	
- Committed budget per country	5.74 Mio € in total	
- Budget requested /allocated per country	27.3 Mio € in total	
- % of the total budget spent	88.7% (5.1 Mio € spent in total)	
-Committed budget per consortium	**miRDiet**: 0.7 Mio€	**FoodBall**:4.38 Mio €
- Number and type (Research/SME/Large industry) of organisations/teams in the funded consortia	6 partners (1 partner from large industry, rest research institutes and academia)	22 partners (all from research institutes and academia)
4.1.3 Success of implementing collaboration		
- Interdisciplinary collaboration		
Number of disciplines per consortium	**miRDiet:** 3	**FoodBall:** 9
list of disciplines	nutrition, "omics" techniques, clinical interventions	nutrition, metabolomics, epidemiology, clinical science, analytical chemistry, molecular biology, food sciences, bioinformatics, statistics
- Success of transnational collaboration		
Number of new collaborations with academia	**miRDiet**: 0	**FoodBall**: 1 (COST Action "POSITIVe")
Number of collaboration with other JPI funded projects	**miRDiet**:2 (ENPADASI and DEDIPAC)	**FoodBall**: 1 (ENPADASI)
- Number of project coordinators/partner per country	**miRDiet**: See Fig 3 and 4	**FoodBall**: See Fig. 5 and 6
- Intensity of Collaboration		

Number of Meetings	**miRDiet**: 3 physical meetings + 8 TC	**FoodBall**: 7 physical meetings
Number of mobility/lab visits within a consortium	**miRDiet**: 0	**FoodBall**: 4 lab visits
4.1.4 Success of scientific collaboration		
- Number of new publications related to the project	**miRDiet**: no (2 in preparation)	**FoodBall**: 56 published paper (13 submitted or in preparation)
- Number of presentations related to the project	**miRDiet**: 7 conferences	**FoodBall**: 67 oral presentations and 33 poster presentations
- New funding obtained	**miRDiet**: 1	**FoodBall**: 0
4.1.5 Involvement in other JPI HDHL activities	**miRDiet**: ENPADASI and DEDIPAC	**FoodBall**: ENPADASI
4.1.6 Capacity Building		
- Training activities	**miRDiet**: 2 Bachelor degrees	**FoodBall**: 10 different training activities
- New jobs/positions generated in the project	**miRDiet**: 9 positions (1 research engineer, 2 assistant engineers, 1 biostatician, 1 medical research assistant, 1 technichian, 1 PhD student, 2 research associates (Master degree)	**FoodBall**: 29 positions (11 Post-docs, 12 PhD students, 3 graduate students, 2 programmer analysts, 1 clinical research associate)
- Use of existing tools and/or development of new capacities or resources (e.g. a transnational database, biobanks, animal models, cohorts)	**miRDiet**: data storage FORCE database	**FoodBall**: databases FooDB, FoodComEx, PhytoHub
4.1.7 Data and Knowledge Sharing		
- Use of existing data: Has existing data been used / pooled for the project?	**miRDiet**: 0	**FoodBall**: 8 different cohort studies
- Has the consortium used samples from existing cohorts and / or other epidemiological studies?	**miRDiet**: 0	**FoodBall**: 7 study centres
- To perform the project, have you used samples (omics-based) from bio-bank or/and other disease register sample collections?	**miRDiet**: no	**FoodBall**: no
- FAIR-Data principles: Has the data generated in the project made available by following the FAIR principles?	**miRDiet**: yes	**FoodBall**: 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)	**miRDiet**: standardization of sampling and process protocol	**FoodBall**: databases FooDB, FoodComEx, PhytoHub
- Activities towards innovation	**miRDiet**: no	**FoodBall**: no
New industry collaboration	**miRDiet**: no	**FoodBall**: no
Development of new methods/research tool/products	**miRDiet**: no	**FoodBall:** 3 databases and a public web portal
Patents: number and geographical scope	**miRDiet**: no	**FoodBall**: no
- Contribution to public health	**miRDiet**: no	**FoodBall**: yes

Target groups	**miRDiet:** scientists and health professionals	**FoodBall:** health professionals and citizens
Interaction with End-Users (e.g. consumers, patients in intervention studies)	**miRDiet**: no	**FoodBall**: no
- New strategies/applications to reduce incidence of diet related chronic diseases)	**miRDiet**: no	**FoodBall**: no