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PhenolQuest: a new reference FFQ for a more precise and comparable assessment of (poly)phenol intake in Europe†

Dorian Teissandier,[a,b] Charlotte Gillet,[a] Soline Chaumont,[c] Sylvie Mercier,[a] Marie Lefebvre,[a] Wiame Lasri,[a] Aïcha Djama Guedi,[a] Marie Taillandier,[a] Nathalie Hanet,[c] Liliana Jimenez,[c] Laetitia Demaretz,[c] Christine Morand[a] and Claudine Manach *[a]

(Poly)phenols represent a large class of bioactive compounds present in our diet. An increasing number of epidemiological, clinical and pre-clinical studies are demonstrating the beneficial effects of (poly)phenols on various health parameters, parlicularly in relation to the prevention of cardiometabolic diseases. However, fully understanding their potential in preventive nutrition requires significant improvements in the assessment of individuals' exposure to a variety of (poly)phenols. One of the current limitations is the use of standard Food Frequency Questionnaires (FFQs) that are not specifically designed for that purpose and as a consequence lack precision and accuracy for the assessment of (poly)phenol intake. We developed the FFQ PhenolQuest, specially designed to assess with a high level of details the dietary intake of 120 (poly)phenols belonging to all main families, in populations following a European-style diet. It includes 188 foods with a number of additional variations (*n* = 75). Special effort was made to optimize the questionnaire's design and usability. In particular, the consumption frequency options were expanded compared to the standard FFQ and tailored to the different food groups. An application test conducted on a French population panel of 110 subjects demonstrated PhenolQuest's ability to capture the diversity of (poly)phenol source consumption patterns. PhenolQuest is shared in integrality for free use and further validation by the community. This article presents the challenges and strategies used for its development, as well as its scope of use.

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Introduction

(Poly)phenols are major bioactive compounds in the human diet. While some of them are widely distributed in foods, others are specific to certain botanical families. Dietary (poly) phenols encompass a wide variety of chemical structures, comprising over 800 compounds divided into several classes: flavonoids (subclasses: anthocyanins, flavan-3-ol monomers and proanthocyanidins, flavones, flavonols, flavanones, isoflavones, and dihydrochalcones), phenolic acids (subclasses: hydroxybenzoic acid monomers, ellagitannins and hydroxycinnamic acids), stilbenes, lignans and other minor classes. The chemical structures range from small polar phenolic acids to large polymers such as proanthocyanidins or ellagitannins. Considering that this diversity is likely to be associated with different bioavailability and bioactivities,[1] it is essential to distinguish the (poly)phenol subclasses and chemical structures when studying their intake and health effects.

Some (poly)phenols have been demonstrated to decrease cardiovascular disease risk. Recently the COSMOS study, a large randomized controlled clinical trial conducted on a cohort of 21 442 American adults free of cardiovascular disease at the baseline, demonstrated that a 4.6-year supplementation with a flavan-3-ol-rich cocoa extract resulted in a 27% reduction in cardiovascular mortality compared to the placebo. This significant effect on a hard clinical outcome was more pronounced among participants with high compliance to daily intake.[2] Other clinical trials have shown that (poly)

[a]Université Clermont Auvergne, INRAE, UNH, F-63000 Clermont-Ferrand, France. E-mail: claudine.manach@inrae.fr
[b]Emergency Department, CHU Clermont-Ferrand, Clermont-Ferrand, France
[c]Danone Global Research and Innovation Center, Saclay, France

† Electronic supplementary information (ESI) available: Supplementary figure 1: Full version of the FFQ PhenolQuest. Supplementary figure 2: Visualization of consumption profiles using a heatmap from hierarchical clustering analysis (HCA) of annual consumption data for 65 PhenolQuest foods/food groups in a French test population of 110 subjects. Supplementary table 1: PhenolQuest food list with serving sizes. Supplementary table 2: List of the 120 (poly)phenols targeted for the development of PhenolQuest. See DOI: **https://doi.org/10.1039/d4fo06326k**

phenols from berries, cocoa, tea, red wine and citrus fruits can improve endothelial function and reduce blood pressure.[3] Besides, (poly)phenols belonging to some families such as the anthocyanins, the proanthocyanidins or the ellagitannins may beneficially modify the composition and functionalities of the gut microbiota and improve intestinal permeability-associated biochemical and clinical markers.[4,5]

Documenting the health effects of (poly)phenols relies on an accurate assessment of the exposure of individuals to the diversity of dietary (poly)phenols, in clinical trials and epidemiological studies. Habitual dietary intake of (poly)phenols has been estimated in observational studies to compare the levels of intake across different populations or subgroups, to identify the main food sources contributing to this intake, and to search for associations with risk factors, disease incidence or mortality at a population scale.[6–8] With the rise of precision nutrition and deep-phenotyping approaches, (poly)phenol intake could increasingly be related to a wide range of health-related parameters and omics data, such as genomics and metabolomics. In particular, as the gut microbiota can metabolize (poly)phenols and (poly)phenols can modulate the gut microbiota,[5] studying the association between (poly)phenol intake and the gut microbiota composition, diversity and functionality in large populations will be of major interest.

Current methods for assessing (poly)phenol intake rely on dietary questionnaires that collect food intake data, which are then cross-referenced with food composition tables that inform about the amount of individual (poly)phenols in the consumed foods. A recent systematic review that examined the dietary assessment methods used to estimate (poly)phenol intake in observational studies showed that 73% of the 549 included studies used a food frequency questionnaire (FFQ), while only 9% used 24 h- or 48 h-recalls.[9] Although criticized for their lack of precision due to self-reporting limitations, FFQs remain very popular and are often the only tool that is affordable and practical for large cohort studies.[10] Moreover, FFQs have the advantage of reflecting habitual food intake over a long period, typically one year, and thus can capture the intake of (poly)phenol-rich foods that are consumed seasonally or infrequently. Another key observation of the systematic review by Xu *et al.*[9] was that the vast majority of studies used a general FFQ that was initially designed to assess food, energy and nutrient intake, while only 14 studies reported the administration of an FFQ specifically designed for (poly)phenols. Of these 14 studies, 9 focused on soy isoflavones, one on black tea, two on a few specific flavonols, flavones or flavanones, and two had a broader (poly)phenol coverage but were targeted to specific populations, *i.e.* pregnant Brazilian women and Australian population. Therefore, despite the large number of epidemiological studies conducted on (poly)phenols in Western populations, there is still no reference FFQ specifically designed to estimate their intake.

Conventional FFQs that were not specifically developed for (poly)phenols have various limitations when used to assess (poly)phenol intakes. They include many foods that do not contain (poly)phenols, which unnecessarily increases the responder's burden, and most importantly, a number of (poly)phenol-rich foods are either missing or insufficiently detailed. In addition, they often group several foods into a single item to reduce completion time, while many food groupings are inappropriate for (poly)phenols, as the grouped foods can differ significantly in their (poly)phenol profiles and contents. For example, this is the case when all berries or all fruit juices are grouped together. It also applies to red and white wines, frequently grouped into a single wine item, while only red wine contains anthocyanins and high levels of proanthocyanidins. Recently, Rodriguez-Mateos *et al.* developed a (poly)phenol-focused version of the EPIC-Norfolk FFQ for assessing (poly)phenol intake in the UK.[11] Their approach was to add missing (poly)phenol food sources and disaggregate the food groupings that are inappropriate for (poly)phenols.

Single or multiple 24 h recalls have also been used to assess (poly)phenol intake, offering greater diversity and granulometry in reported foods compared to FFQs. Converting food intake data into (poly)phenol intake is a complex process requiring careful matching of individual foods to entries in the food composition database. As an example, Knaze *et al.* inventoried more than 19 000 raw and prepared foods from the 24 h recalls completed by approximately 40 000 participants from 10 countries as part of the European Prospective Investigation into Cancer and Nutrition (EPIC) study and matched them to the Phenol-Explorer database.[12] Existing databases are incomplete, lacking data for many of the foods captured by 24 h recalls. As a result, considerable effort is needed to cross-reference foods with their closest equivalents, and apply some extrapolation rules.[12] Another limitation of 24 h recalls is that many (poly)phenol-rich foods are consumed episodically, making it difficult to capture their full diversity with one or a few recalls. While these instruments provide a snapshot of dietary intake, episodic or seasonal (poly)phenol sources may be overlooked. To accurately assess habitual (poly)phenol intake, multiple recalls or dietary records collected across the year are necessary, which increases both the burden and the cost for data analysis. Kent *et al.*[13] found that 6 to 10 days of weighted food records were required to estimate habitual intake of specific flavonoid subclasses in a population of Australian adults aged 60 years and over, with seasonal variations observed.

An alternative method to dietary questionnaires is the use of biomarkers of food intake. Untargeted metabolomics has opened exciting perspectives for the identification of panels of novel biomarkers.[14,15] However, the vast majority of the newly discovered biomarkers still require further validation and many (poly)phenol-rich foods do not have good candidate biomarkers of intake identified so far.[16,17] Metabolites of (poly)phenols have themselves limited potential to represent reliable biomarkers for (poly)phenol intake, due to the high interindividual variation that occurs in their metabolism, in particular when the gut microbiota is involved.[18,19] A few candidate biomarkers have been proposed for specific families of flavonoids, but no reliable biomarker currently exists to cover the large diversity of dietary (poly)phenols.[20–26] Until a sufficient number of robust intake biomarkers for (poly)phenols or their dietary sources are discovered and validated, FFQs will remain a primary tool for assessing their dietary intake in observational studies, especially in large-scaled populations.

Our aim was to develop and make available to all researchers a semi-quantitative FFQ that is easy to use and specifically designed to assess, in a consistent way, the intake of a wide range of (poly)phenols of interest in populations following a European-style diet. The present article describes the development of the FFQ PhenolQuest, while its companion food composition database will be presented elsewhere.

Materials and methods

Strategy for PhenolQuest development

The workflow followed for the development of PhenolQuest is summarized in Fig. 1 and detailed in the following sections.

Coverage of the FFQ: targeted (poly)phenols

As a first step, a list of the most important (poly)phenols to be covered by the FFQ and the associated food composition database was drawn. According to the databases Phenol-Explorer (**https://phenol-explorer.eu/**) and PhytoHub (**https://www.phytohub.eu**), more than 800 (poly)phenols are present in the human diet. Some are widely distributed in commonly consumed foods, whereas others are only quantifiable in a few specific food items. (Poly)phenols were classified into 5 classes (flavonoids, phenolic acids, stilbenes, lignans, and other (poly)phenols) and 15 subclasses: anthocyanins, flavan-3-ol monomers, proanthocyanidins, flavonols, flavones, isoflavones, flavanones, dihydrochalcones, theaflavins and thearubigins, hydroxycinnamic acids, hydroxybenzoic acid monomers, ellagitannins, lignans, stilbenes, and other (poly)phenols (including tyrosols, alkylresorcinols, curcuminoids, xanthones, *etc.*) according to their chemical structures. Within each subclass of (poly)phenols we selected, based on expert agreement, the main representative compounds, *e.g.* the most commonly consumed ones, as well as some specific (poly)phenols widely studied for their beneficial bioactivities. We also retained some (poly)phenols of interest to study the diversity of (poly) phenol intake, even when present in a limited number of foods or in not widely consumed foods, such as spices.

Coverage of the FFQ: food and beverage list

In a second stage, the food items to be included in the FFQ for each targeted (poly)phenol were selected. First, foods and beverages already reported as major contributors to the intake of the considered (poly)phenols in studies measuring (poly) phenol intake in a Western population were compiled based on an extensive review of the literature, as illustrated by the following major references.[6,12,27–35] Then, those with contents >3 mg per 100 g fresh weight for the targeted (poly)phenols according to Phenol-Explorer,[36] eBASIS,[37] USDA databases[38–40] or the literature were added, as well as those providing at least 3 mg (poly)phenols per serving.[35,36,38] Particular attention was given to the highest contributors to (poly)phenol intake, such as coffee, tea, or apples, to distinguish some food variations, which could reflect some modes of consumption likely to affect the (poly)phenol supply, for example the strength of tea or the consumption of apple with or without peel. Other types of food variations are related to the type of production (freshly squeezed orange juice *vs.* industrial orange juice from concentrate), type of preparation (tea bags *vs.* loose tea leaves) or the food or beverage composition (*e.g.* for smoothies or herbal teas). The food and beverage list was refined after the development of the companion food composition database. Some of the foods initially selected were not retained in the final version of PhenolQuest, due to the absence of data of sufficient quality for their (poly)phenol content, or because their contribution was ultimately considered to be negligible for the vast majority of individuals in Europe[41] and their removal allowed the reduction of the length of the questionnaire. Examples are pineapple and fortified wines. Noteworthily, tomato and tomato products (sauce, ketchup, *etc.*) were not included, since they are on the one hand relatively low sources of (poly)phenols, and on the other hand represent widely consumed foods or ingredients with potentially high intake levels, but whose contribution is difficult to assess due to their presence in a large diversity of recipes and industrialized foods. It was considered that even small errors in the estimation of their (poly)phenol contents could lead to substantial overestimations of (poly)phenol intake. Excluding them may slightly underestimate the total amount of (poly) phenols consumed, but ensures a better accuracy in the stratification of the individuals according to their (poly)phenol intake. In a few cases, *e.g.* some herbal teas and supplements, it was decided to include them in the FFQ despite the paucity of data on their (poly)phenol composition. Tracking a high level of regular consumption of these (poly)phenol sources was considered important for data treatment, as it may indicate a substantial underestimation of (poly)phenol intake for the individual.

To confirm the food choices made for PhenolQuest, its food list was also compared to other FFQs used to assess (poly)phenol intake according to Del Bo' *et al.*,[6] and for which the full version was available. These included the EPIC-Norfolk FFQ,[42] a FFQ developed for adults living in Sicilia,[43] the FFQ developed by Kent *et al.*[44] for flavonoids in Australia, as well as questionnaires focusing on isoflavones,[45] tea[46] and cocoa.[47] This did not lead to the addition of new food items.

Portion sizes. A reference portion size was provided for each food item, along with an explanation clarifying how respondents who usually consume a different portion size for a given food should accordingly adjust their declaration of frequency of consumption of this food. Although some data exist on recommended food portions or on the usual consumption per day (which integrates the frequency of consumption and the consumed portion) in different European population studies (EFSA Comprehensive European food consumption database[41]), we could not find reference data for the usual portion sizes consumed in Europe. Therefore, several sources of information were used to define the PhenolQuest reference portion

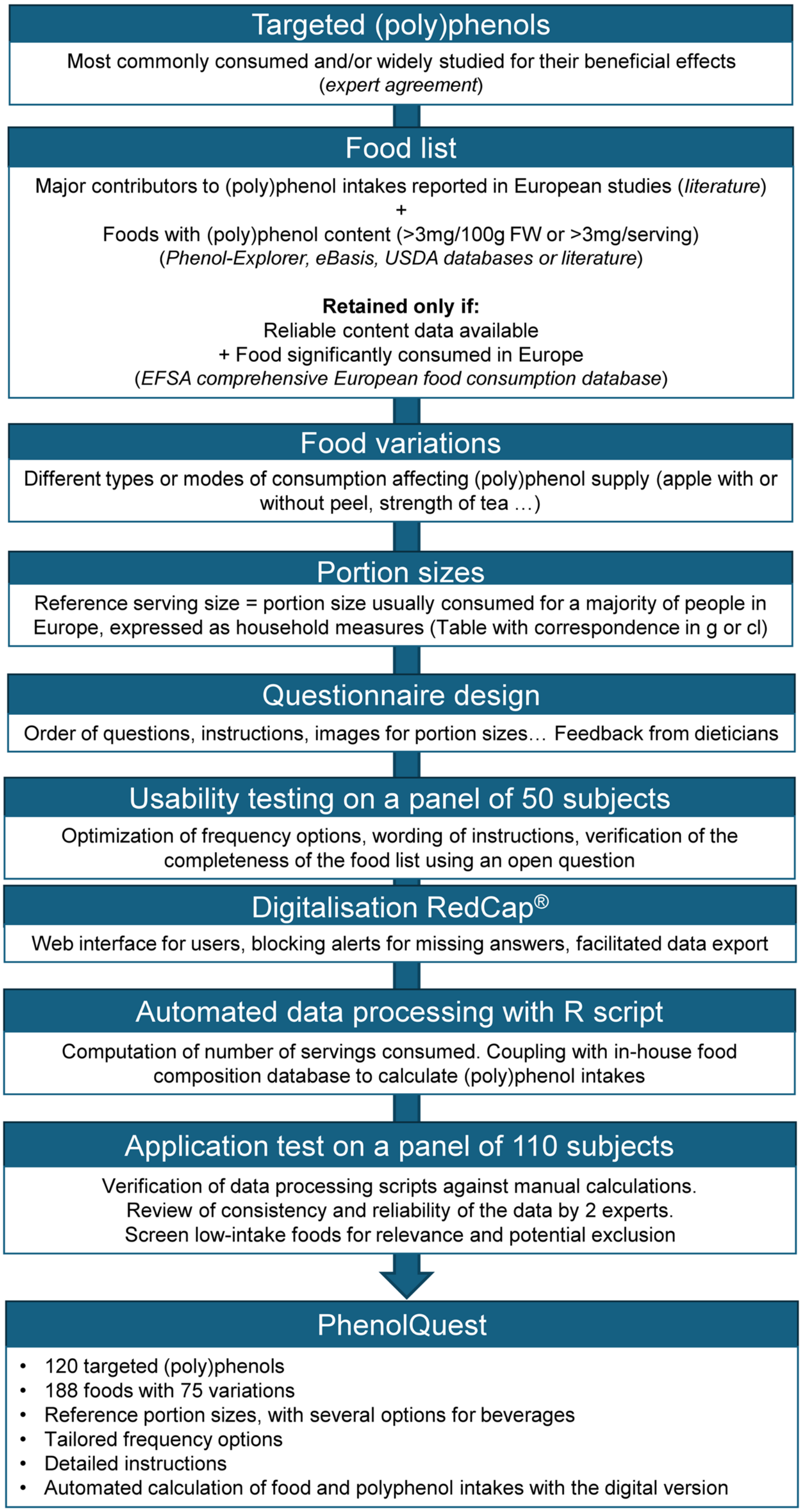

Fig. 1 Workflow of PhenolQuest development.

sizes, including a validated manual of portion photographs developed for the large intervention study SU.VI.MAX study,[48] the widely used EPIC FFQ[42] and the portion size of marketed products. In PhenolQuest, the reference portion sizes were chosen to reflect as closely as possible the usual portion for a majority of respondents in Europe, and to avoid as far as possible the requirement for respondents to calculate portion adjustments. When variations in habitual portion sizes are frequent, such as for coffee, several portion sizes were proposed. Reference portion sizes are given as household measures (*e.g.* glass, cup, spoon, *etc.*) and standard food portions (*e.g.* one apple) adapted for every item. All reference portion sizes used for PhenolQuest are given in ESI Table 1.†

Structure of the FFQ. The questionnaire was designed according to the layout and format of classic FFQs for covering the dietary habits during the previous year. Recommendations from Cade *et al.*[49] and common practices[50] for the development of FFQs were taken into account. For example, the order of the questions was chosen to allow learning on slightly less important items, before introducing the most important food groups. Then, as (poly)phenols are present in a wide variety of foods, the challenge was to cover a maximum of significant sources, while coping with the respondent fatigue associated with filling in a long questionnaire. One of the strategies was to avoid any kind of hesitancy by offering clear options for every possible situation. The choices of intake frequency options were adapted for the different types of food, depending on their usual level of intake or how their consumption varies with the seasons. Several propositions were tested by a first panel of 50 French volunteers in the context of a citizen science activity, as described below.

We identified a risk of overestimation of fruit intake due to the high number of individual items in this food group and the fact that they represent socially well-perceived food. There is a widely described bias of over-reporting for healthy foods, and FFQs generally yielded higher estimates for fruits and vegetables than weighted food records.[51] Furthermore, values for median frequency of total fruit and vegetable intake, determined by summing across all fruits and vegetables included in the respective questionnaires, were shown to increase proportionally to the number of questions asked.[51] A cross-check question was added in PhenolQuest on the total number of fruit servings per day: "Over the past year, and for each of the seasons mentioned, how many servings of frozen, fresh, or cooked fruits (excluding canned fruits, compotes, fruit purees and jams) have you consumed on average per day?" with a distinction between spring/summer and autumn/winter. This makes it possible to compare the sum of the intake declared for individual fruits to the daily total intake of fruits or vegetables declared in the summary cross-check question, leaving the possibility for researchers to decide regarding an adjustment.

Optimization through a citizen science activity. PhenolQuest was translated in French and tested on a panel of 50 French adult volunteers recruited during INRAE open-days and by word of mouth in a context of participatory research. PhenolQuest was self-administered to the volunteers, with a feed-back questionnaire with open questions to complete under anonymous conditions. The readability and clarity of questions, the layout, and frequency options were optimized through an iterative process, incorporating the feedback from volunteers on the time and difficulty they experienced while completing the different parts of the questionnaire. In particular, respondents were asked whether they had experienced difficulties in understanding any instructions (and if so, which ones), selecting a frequency option for certain items (and which ones), or estimating the portion size for some foods (and which ones). In addition, volunteers could indicate a list of plant foods that they regularly consume and that were absent in PhenolQuest. The relevance of adding these additional food items was examined with regard to the significance of their (poly)phenol content and the availability of composition data, as assessed with a specific literature search. No additional food was finally added at this stage. The intermediate versions of PhenolQuest were reviewed by 3 trained dieticians along the process. All improvements made with this application test in the French population were implemented in the English version of PhenolQuest.

Digitalisation of PhenolQuest. The RedCap platform[52,53] was used to transpose PhenolQuest into a digital form. RedCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing (i) an intuitive interface for validated data capture; (ii) audit trails for tracking data manipulation and export procedures; (iii) automated export procedures for seamless data downloads to common statistical packages; and (iv) procedures for data integration and interoperability with external sources. Access to the questionnaire is granted *via* a unique internet link specific to the study. The user-friendly web interface generated with RedCap for PhenolQuest facilitated the implementation of blocking alerts for the lack of answer on mandatory questions, thereby minimizing the risk of missing data. The system is hosted by INRAE and data can be extracted for statistical analysis upon request to a data manager.

PhenolQuest data are processed using an R script (version 4.4.1) that calculates the frequencies of intake for all food items and their variations, integrates the portion size, and links each food item and associated variables to the companion food composition database. A template for the analysis is available at **https://doi.org/10.5281/zenodo.14515133**, with an example of a dataset for selected food items. The companion table of composition was specially compiled by INRAE from a critical assessment and selection of data from eBASIS, PhenolExplorer, the USDA databases, as well as an extensive literature survey. This table provides content data in mg per 100 g FW for the targeted polyphenols in their native form, without hydrolysis into aglycones. The description of the development of the companion database is beyond the scope of this article and will be presented elsewhere. The whole data processing workflow calculated for each individual is as follows: (i) the number of servings of each food item consumed per day, (ii) the quantity in grams consumed per day, based on reference serving sizes and (iii) the daily intake of each (poly)phenol, using the food composition database. The daily intake of (poly)phenols from different families or subclasses as well as the total (poly)phenol daily intake are obtained by summing the daily intake of the individual (poly)phenols of the considered category. The relative contribution of the different foods to the intake of each (poly)phenol, family of (poly)phenols or the total (poly)phenol is also calculated.

Application in a French test population. The electronic version of PhenolQuest was administered to another panel of 110 volunteers, in the context of a new participatory action research, to determine whether any adjustments were needed before its use in research projects. The subjects were recruited through flyers, website, communication in citizen-science events, word of mouth, and mailing in the ReseautAGE network, a local multi-actor community led by INRAE, developing participatory action research for personalized nutrition and healthy aging. The data collected were manually reviewed to verify all functionalities of the digital version of PhenolQuest, and to track any abnormal completion of the questionnaire that might be repeated by several respondents due to an unsufficiently clear formulation. As no recurrent mistakes were observed, no corrections were deemed necessary. The calculations performed by the data processing scripts were also carefully verified through comparison with manual calculations. Descriptive statistics such as boxplots for the consumption of individual food, food groups, (poly)phenols, families of (poly) phenols, total (poly)phenols, as well as the relative contribution of the different (poly)phenols and foods to the total intake (data not shown) were reviewed by two experts to check the consistency and reliability of the data obtained.

Results

PhenolQuest is an FFQ designed to capture the habitual intake, using the previous year as the reference period, of all major food sources of 120 individual (poly)phenols representing all (poly)phenol families. When combined with a food composition database covering the same foods, it allows stratifying subjects according to their total (poly)phenol intake, the consumption of specific (poly)phenol families or compounds, the overall (poly)phenol consumer profile, or any score calculated from these data. The English version of PhenolQuest is provided in integrality in the ESI (ESI Fig. 1†), as well as on the Zenodo platform (**https://doi.org/10.5281/zenodo.15214458**) for free use in populations with a European-style diet. The French version is available upon request.

Coverage of the FFQ

The list of the 120 individual (poly)phenols considered for the development of the FFQ and its associated database is detailed in ESI Table 2.† The represented families are anthocyanins (n = 21), flavan-3-ol monomers (n = 6), proanthocyanidins (n = 6 categories according to their degree of polymerization, as proposed in the USDA database[39]), flavonols (n = 18), isoflavones (n = 8), flavanones (n = 5), flavones (n = 4), theaflavins and thearubigins (n = 4), dihydrochalcones (n = 2), hydroxycinnamic acids (n = 15), hydroxybenzoic acid monomers (n = 4), ellagitannins (n = 6), lignans (n = 8), stilbenes (n = 2), and other (poly)phenols (n = 11).

The final food list of PhenolQuest comprises 188 food items (with 75 variations for 17 of them) and 16 types of supplements, as summarized on Fig. 2 and detailed in ESI Table 1,† which also provides the reference portion sizes. Foods were classified into 12 food groups: (1) vegetables, potatoes and legumes, (2) fresh, frozen or cooked fruits, (3) processed fruits, including canned fruit, compotes, purees, jams and dried fruits, (4) nuts, (5) cocoa products, (6) non-alcoholic cold beverages, including fruit juices, smoothies, iced tea and iced coffee, (7) non-alcoholic hot beverages, including coffee, black tea, green tea, herbal teas, (8) alcoholic beverages, (9) cereal products, (10) cooking ingredients (oils, herbs, spices and condiments), (11) soy-based foods, and (12) (poly)phenol-rich supplements.

In PhenolQuest, special attention was given to the major contributors to (poly)phenol intake described in the literature, namely fruits in all their forms, coffee, tea and chocolate.

Fruits provide a large variety of (poly)phenols from diverse families and each fruit is characterized by a distinctive profile of (poly)phenols. A portion of fruit generally provides 100–200 mg of (poly)phenols, with some berries containing much higher levels. PhenolQuest includes a particularly wide range of fresh, frozen or cooked fruits, with 21 items covering pome fruits, citrus fruits, stone fruits, tropical fruits, grapes and berries. An additional question gives the possibility to the respondents to indicate other fruits that they consume more than twice a week. Furthermore, the respondent is asked to indicate his/her habitual daily intake of fruits, both in spring/summer and in autumn/winter. This cross-check question was introduced for a comparison with the sum of the declared intake for all individual fruits, and to allow a potential correction of overreporting if relevant. For some fruits a further level of details is introduced to minimize uncertainties linked to known factors of variation in (poly)phenol contents. A question for apple and peach allows specifying whether they are usually consumed with or without the peel, as high concentrations of (poly)phenols have been measured in the peel of these fruits. Furthermore, as (poly)phenol contents vary widely depending on the apple cultivar, PhenolQuest makes a distinction between some heritage varieties such as Canada or Reinette, which are richer in (poly)phenols, and other classic table apples such as Gala, Pink lady® or Golden, considering that the average content between these two types of apples can vary by a factor of 2 to 4. White and red grapes are also distinguished.

In Europe, fruits are widely consumed in the form of processed products, while the (poly)phenol supply can vary significantly depending on the form in which the fruit is consumed. PhenolQuest includes all major types of processed foods made from fruits: fruit juices (n = 14), smoothies (n = 8), canned fruits (n = 5), fruit compotes (n = 12), fruit purees (n = 8), jams (n = 11) as well as dried fruits (n = 6). Within fruit juices, a distinction was made between industrial/clear and artisan/cloudy apple juices, as well as between orange juice from concentrate and freshly squeezed or store-bought 100% pure juice. For the whole category of fruits and processed fruits, the only food groupings in PhenolQuest are those of clementine with mandarin, peach with nectarine and bilberry with blueberry. Those fruits have similar (poly)phenol con-

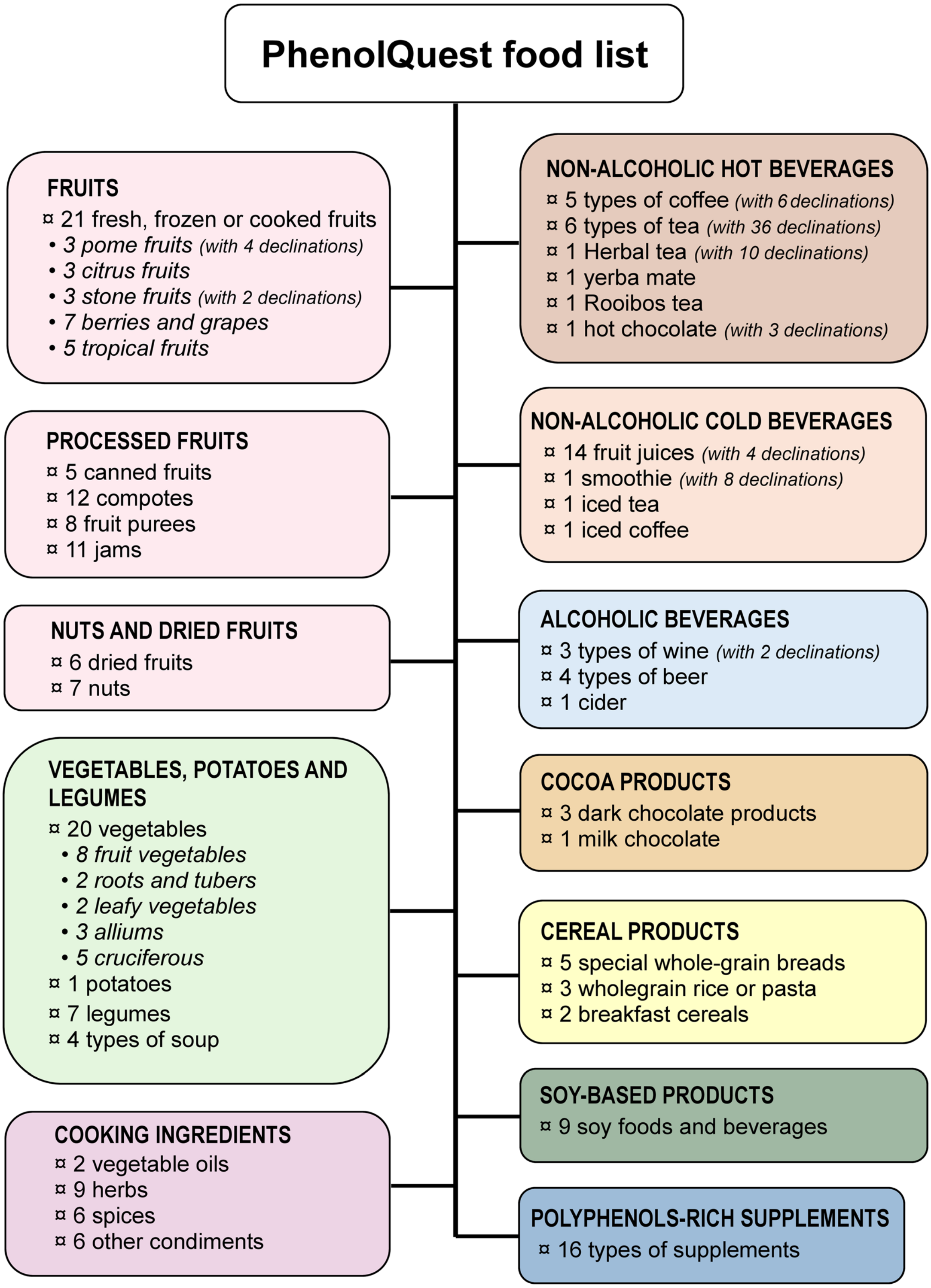

Fig. 2 Simplified PhenolQuest food list organized by food groups.

tents and it would be too difficult for the respondents to distinguish them in terms of the level of intake. The group of nuts, which has been overlooked so far in terms of (poly)phenol intake, is represented with 7 items, considered alone or mixed.

The non-alcoholic beverages such as tea and coffee represent other major sources of (poly)phenols that are consumed on a daily basis by a lot of people in Europe. It is thus particularly important to carefully capture their intake. Regarding coffee, several modes of preparation are commonly used across Europe, which may affect the final (poly)phenol composition of the beverage. The major categories that could be distinguished in PhenolQuest after consideration of the composition data available in databases and literature, are expresso, decaffeinated expresso, long coffee, decaffeinated long coffee, latte/cappuccino/coffee with milk and iced coffee. For long coffee, respondents are invited to indicate whether they like their coffee weak, medium or strong, as varying amounts of water can be used for the same dose of coffee powder. The size of a cup of coffee can also vary greatly from one person to another and sometimes from one drinking moment to another for the same person. Four cup sizes are proposed (expresso, standard cup, large cup/mug, and bowl), with the possibility to combine different cup sizes over one day (Fig. 3).

7.1. During the past year, have you consumed coffee (or similar beverages like cappuccino, latte, etc) at least once a month?

☐ No *(Please proceed directly to question 7.2)*
☐ Yes *(Please describe your consumption by completing the table below)*

***Note**: Please pay attention when recording your consumption, particularly if you used different types of containers (cup, bowl, etc.). Refer to the table of correspondences provided below to calculate the correct number of servings.*

BEVERAGE *(Serving size)*	CONSUMPTION OVER THE LAST 12 MONTHS									
	Never	1 to 3 times a month	Once a week	2 to 3 times a week	4 to 6 times a week	Once a day	Twice a day	3 times a day	4 times a day	5 times or more a day
COFFEE (capsule, filter, percolator, instant, ...)										
Espresso *(1 espresso cup, 7cl)*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Decaffeinated espresso *(1 espresso cup, 7cl)*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Regular Long Coffee	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

When you consumed a long coffee, what was your typical serving size?

☐ Standard cup *(10cl)*
☐ Large cup or mug *(25cl)*
☐ Bowl *(30cl)*
☐ Varies (e.g., a bowl at breakfast, a cup at lunch)

If you have ticked "Varies", please estimate the number of servings that you consumed on a typical day, using the explanations below.

☐ 2,5 ☐ 3 ☐ 3,5 ☐ 4
☐ 4,5 ☐ 5 ☐ 5,5 ☐ 6
☐ 6,5 ☐ 7 ☐ 7,5 ☐ 8 and more

Correspondence :

A standard cup *(10cl)* = ***1 serving***
A bowl (30cl) = ***3 servings***

A large Cup or A mug (25cl) = ***2,5 servings***

Example: 1 bowl of coffee in the morning, 1 large cup at noon, and 1 standard cup in the afternoon= 3 + 2,5 + 1 = 6,5 servings per day

How did you drink your long coffee? ☐ Light ☐ Medium ☐ Strong ☐ Don't know

Fig. 3 Screenshot of PhenolQuest showing the questions on coffee consumption frequency, portion size and strength.

For tea, PhenolQuest collects data on green tea and black tea separately, with precision regarding the type of black tea (Darjeeling, Earl grey, English breakfast, Oolong, or others), the mode of preparation which includes the use of tea bags, capsules or loose-leaf tea, the strength of the infusion, and the habitual addition of mint in green tea. Homemade iced tea consumption data are also collected as it may represent an important source of (poly)phenols for some European people during summer. Eleven types of herbal teas and Yerba mate have also been introduced in PhenolQuest to complete the list of (poly)phenol-rich non-alcoholic beverages that are likely to provide high amounts of (poly)phenols when consumed on a regular basis.

Cocoa is another important source of (poly)phenols, especially of the well-studied flavan-3-ols. Three types of food products made with dark chocolate (bar/confectionary chocolates, mousse, and cake) are covered in PhenolQuest. A clear distinction is made with milk chocolate products, which usually contain around 20% cocoa. Hot chocolate drinks are also included in the category of non-alcoholic beverages, with details regarding the type of cocoa powder used, as the (poly)phenol content can vary significantly between breakfast commercial preparations and pure cocoa powder.

Red wine can be an important source of (poly)phenols. In PhenolQuest its consumption is distinguished from that of rosé and white wines, which provide much less (poly)phenols, especially anthocyanins or proanthocyanidins. A question is proposed to declare a preference for tannic wines, as they contain more proanthocyanidins. However, it was impossible to obtain more details regarding the type of red wine consumed, given the large number of wine types available across Europe and the possible diversity of wines consumed by each red wine enthusiast. Different types of beers are detailed (Blond, Amber/Dark, IPA, and wheat/white beers) to consider their diverse (poly)phenol compositions. Cider is also included as its level of consumption is significant in certain areas in Europe, especially in UK, Spain and the French region Brittany.

Vegetables generally represent minor contributors to (poly)phenol intake in Europe. However, although many vegetables are low in (poly)phenols, some are quite rich, and a selection of 20 of them has been retained in PhenolQuest. Vegetable soups and gazpacho are included, although recipes may differ from country to country and the associated food composition database may have to be adapted accordingly. Potatoes are considered, except when consumed as French fries or crisps, as their industrial processing eliminates (poly)phenols. It is worth noting that PhenolQuest contains a selection of legumes, *e.g.* kidney/black beans, pinto beans, broad beans, white beans and 3 types of lentils. This is quite new for the assessment of (poly)phenol intake, but justified by their potential to provide proanthocyanidins in particular, and by the current trend to recommend their consumption as alternative sources of proteins in the context of the dietary transition towards a more plant-based diet. PhenolQuest has a specific section for soy-based foods, rather than having them with other legumes. Soy-based foods represent almost exclusive sources of the phytoestrogenic isoflavones and deserve special attention in this regard. Although they were not widely consumed by European populations until recently, with the exception of vegetarians and vegans, the current transition towards more plant-based diets should also significantly increase their level of intake. Nine soy-based foods or beverages with the highest isoflavone contents are covered in PhenolQuest.

PhenolQuest has a section on cereal products, which includes several sources of (poly)phenols that can be consumed frequently, typically on a daily basis. This includes some types of bread, *e.g.* whole wheat bread, rye bread, multi-grain bread, sesame seed or flaxseed bread, as well as muesli and oat flakes/bran, whole wheat pasta, brown rice and red/black rice.

A number of selected culinary ingredients are included in PhenolQuest, in particular extra virgin olive oil, which provides specific (poly)phenols and is consumed in very large quantities in Mediterranean countries, a selection of 9 herbs and 6 spices, as well as green and black olives, green pesto, lime and lemon juice or capers.

Finally, a list of 16 types of (poly)phenol-rich supplements widely available on the market has been added, even though the (poly)phenol intake from these sources will not be calculated. Indeed, the (poly)phenol dose may vary largely even for closely related supplements and maintaining an up-to-date composition database for all available supplements would require considerable efforts. However, it has been considered that high consumers of such supplements should be identified as respondents for whom (poly)phenol intake is underestimated.

Questionnaire design and usability

Respondents are asked to indicate how often, on average, they consumed a specified quantity of each food item over the previous year. To ensure a satisfactory level of precision in assessing food consumption, it is essential to provide clear and comprehensive guidance to participants when completing the FFQ. Significant effort has been invested in improving the quality of visuals and explanations provided to participants. For instance, an "Instructions" section is included at the beginning of the questionnaire, explaining how participants can adjust their usual portion size, if necessary, relative to the proposed reference portion (ESI Fig. 1†). Moreover, assistance is provided throughout the questionnaire, with tailored instructions based on food groups. Testing the design and instructions with a panel of 50 French adults was crucial in identifying and addressing potential misunderstandings, particularly around portion sizes and frequency estimation. This process improved the clarity of the instructions and portion images, reduced the risk of systematic errors and made the questionnaire more intuitive for diverse respondents.

PhenolQuest offers a wide range of consumption frequency options tailored to each type of food, with a much higher level of details than what is typically provided in classic FFQs. Different frequency categories are proposed, to better align with the consumption patterns of each food or drink, making it easier for respondents to complete the questionnaire. For example, the consumption of red fruits like strawberries or cherries may vary markedly between seasons, making it challenging for respondents to estimate their average consumption over one year when they primarily consume these fruits fresh during the few months of their local production period. After testing different approaches with the panel of 50 French adult volunteers, the selected method for collecting fruit intake data involved first asking the number of months during which the person consumed a given fruit (from 0 to 12) and then the frequency of consumption during those months of consumption, with six possible options: "once a month", "2–4 times a month", "2–3 times a week", "4–6 times a week", "once a day" or "2–3 times a day" (ESI Fig. 1†). This presentation was applied to fruits, vegetables, and non-alcoholic cold beverages, which are the food groups most affected by seasonality. For processed fruits, dried fruits and nuts, cocoa products, cereal products, vegetable oils and soy products, only the question on frequency was asked, with "never or less than once a month" as an additional proposition. It was considered that those consumptions were less likely to vary along the year. For coffee, black tea, green tea and other non-alcoholic hot beverages, the number of possible frequencies of consumption was expanded after the test on the French panel, to better reflect the diversity of habits, and provide greater precision for these rich sources of (poly)phenols: "never", "1–3 times a month", "once a week", "2–3 times a week", "4–6 times a week", "once a day", "twice a day", "3 times a day", "4 times a day" or "5 times a day or more". Additionally, respondents could select different portion sizes that corresponded to one or multiple servings of the reference portion size. By combining frequency and portion size options, the range of possible consumption levels is significantly expanded. Finally, for the most important contributors to (poly)phenol intake, fruits and non-alcoholic hot beverages, the number of possible values for annual consumption in servings is much greater than those in general FFQs such as the EPIC Norfolk FFQ. As illustrated in Fig. 4, PhenolQuest allows for 67 and 59 possible values of servings per year for coffee and individual fruits like orange, respectively, compared to only 9 possible values in the EPIC Norfolk FFQ. By increasing and tailoring the frequency options to the specific characteristics of different food groups, PhenolQuest enables more accurate data collection and better captures the variability of dietary habits.

Application test on a panel of volunteers. A total of 110 French adults completed the questionnaire in digital form, comprising 73 women, 35 men and two respondents who did not disclose their gender. The age distribution was as follows: 15 respondents were 18–25 years old, 18 were 26–35, 4 were 36–45, 10 were 46–55, 23 were 56–65, 38 were 66–75, 1 was 76–85 and one respondent did not report the age.

The optimized digital version on RedCap reduced the completion time. The median completion time was 35 minutes with the initial paper version tested by the first 50 participants, and 28 minutes (range 14–45 min), in the test with 110 participants. Participants aged over 66 years took significantly longer to respond compared to the rest of the population, particularly when compared to younger participants (15–35 years), as confirmed by a Kruskal–Wallis test (p value < 0.01), followed by a *post hoc* analysis (Dunn test). The median response time was 31.5 min for participants over 66 years, compared with 20 min for participants under 35 years.

The percentage of consumers for the different foods ranged from 0.9% (tempeh) to 98.2% (apple). The (poly)phenol-containing foods with the highest percentage of consumers (>95%) in this population were apple, potato, lettuce, grean beans, lentils, strawberry, clementine, cherry tomato and peach. Only 10 food items of PhenolQuest were consumed by less than 10% of the 110 participants. Among them were five soy-based foods: tempeh, soy cheese, edamame, soy-based steak and tofu. These foods were nonetheless kept in the PhenolQuest food list because, on the one hand, the consumption of soy-based products is increasing, particularly among younger populations, and on the other hand, their intake can significantly contribute to isoflavone supply for individuals who consume them. Pomegranate juice was consumed by only 5.5% of the test population, but it represents a potentially significant source of specific ellagitanins of interest for health, the punicalagins and punicalins. It may also be consumed in larger quantities in pomegranate-producing countries like Spain. Homemade iced tea and iced coffee, consumed by 9.1% and 3.6% of the participants, respectively, were also retained as they provide significant amounts of flavan-3-ols and hydroxycinnamic acids, particularly for regular consumers, given the potentially high consumption quantities.

This application test also provided valuable insights into PhenolQuest's ability to capture the levels of intake of (poly)phenol dietary sources and the diversity of consumption patterns within a population. It should be noted that calculating and comparing (poly)phenol intake are beyond the scope of this article. Fig. 5 illustrates in boxplots the distribution of the consumption levels of the PhenolQuest foods, grouped into 35 food subgroups. Coffee, teas and special breads were the most consumed (poly)phenol sources, followed by pome and stone fruits and olive oil. Skewed distributions were evident in many food groups, with some individuals reporting little or no consumption while others consume these foods frequently, including several outliers with very high consumption. For example, black tea had a high mean consumption but a median of 0 serving. These findings highlight the importance of including foods with low median consumption in PhenolQuest, as they may be key sources of (poly)phenols for certain individuals. A visualization of consumption profiles using a heatmap from hierarchical clustering analysis of the consumption data revealed a cluster of 10 subjects with low consumption levels of all (poly)phenol sources and another cluster of 23 subjects with high consumption levels of almost all (poly)phenol sources, while a wide diversity of consumption profiles was observed among the remaining 77 subjects, without any clear separation into distinct clusters (ESI Fig. 2†).

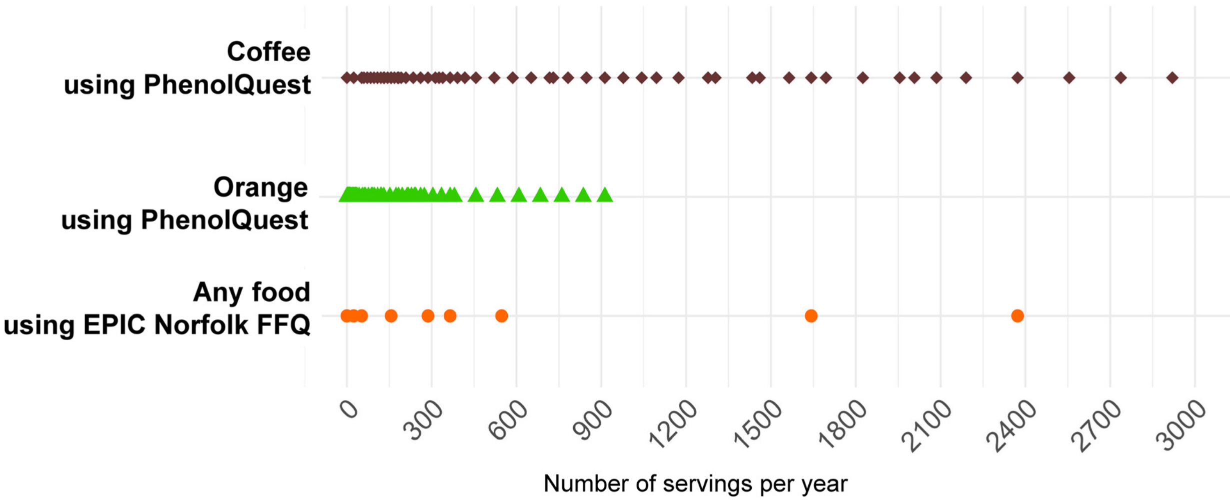

Fig. 4 Comparison of frequency options in PhenolQuest and EPIC Norfolk FFQ. Each point represents a possible option for reporting consumption frequency. The diamonds are for coffee in PhenolQuest, triangles for the example of orange in PhenolQuest, and dots are for any type of food in the EPIC Norfolk FFQ. Five additional options (3285, 3650, 4380, 5018.7, and 6022.5 serving per year) not represented in the figure also exist for coffee consumption in PhenolQuest.

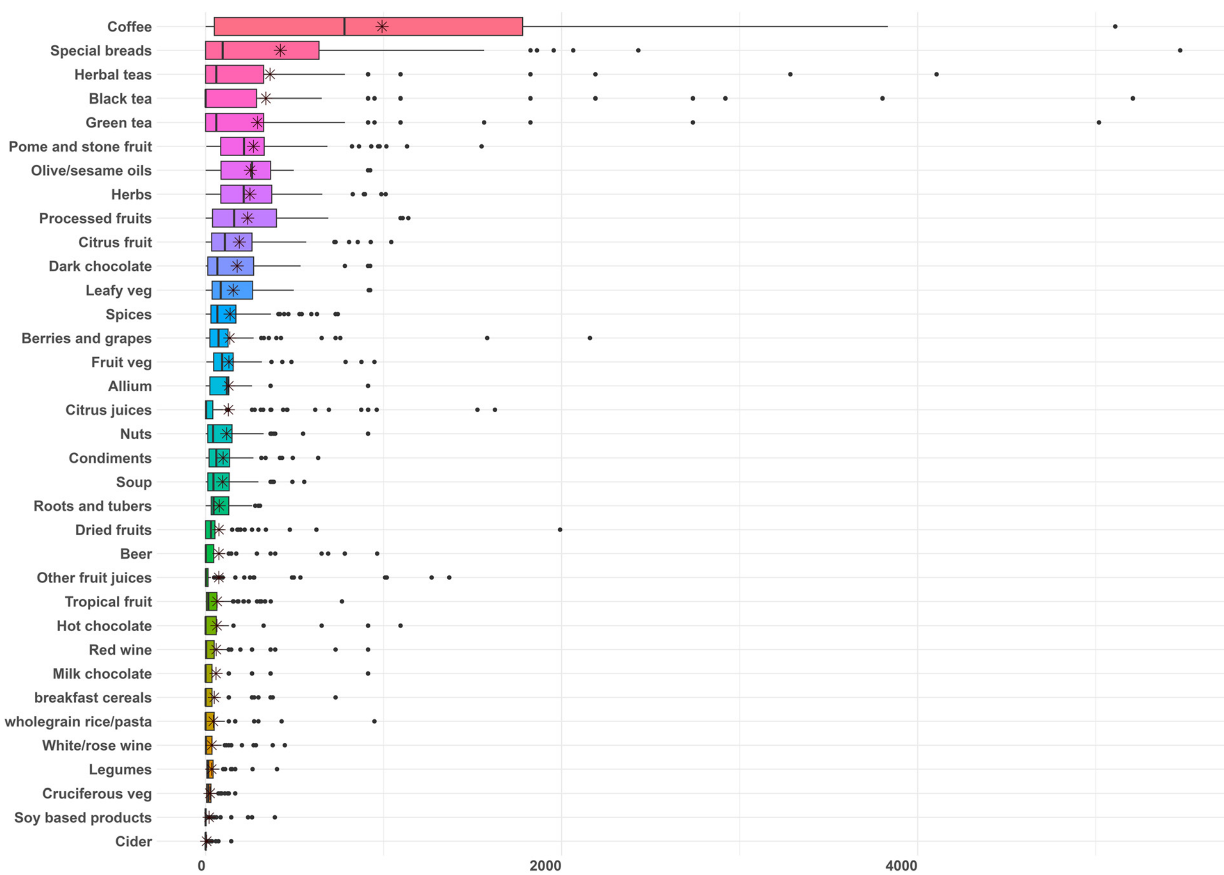

Fig. 5 Boxplots illustrating the distribution of the consumption levels of 35 food groups in a French test population. Data are numbers of servings per year measured for 110 French adults using PhenolQuest. The average number of servings for each food group is represented by a star.

Discussion

PhenolQuest is the first FFQ specifically designed for the assessment of (poly)phenol intake that is made publicly available for use in populations with a European-based diet. The main motivation for this work was the observation that most epidemiological studies conducted so far on (poly)phenols have used general FFQs that were not specifically designed for this purpose, likely resulting in imprecise (poly)phenol intake data and reducing the ability to detect true association between (poly)phenol intake and health outcomes.[9] PhenolQuest's main strengths are its carefully selected list of foods and its optimized design and usability.

Establishing the food list of an FFQ focused on (poly) phenol intake is challenging because of the ubiquitous distribution of (poly)phenols in plant-based foods and their occurrence at significant levels in a large number of foods that are consumed only occasionally. A compromise has to be found between, on the one hand, the number of foods selected and level of details for each of them, and on the other hand the length of the questionnaire in order to remain within a reasonable completion time. The possibility to group several foods into a single item is limited in the case of (poly)phenols, as their content can vary significantly even for foods derived from closely related botanical families. PhenolQuest details many (poly)phenol-rich foods that are absent or grouped together in a single item in a conventional FFQ, such as the widely used EPIC Norfolk FFQ. As an example, considering individual fruit juices in PhenolQuest represents an important addition. A glass of fruit juice can provide 50–200 mg of (poly)phenols of various families, with marked differences between the types of juices.[36] Depending on the dietary habits of individuals, fruit juices may thus account for a significant part of the total (poly)phenol intake. Processed fruits are another important addition, as well as nuts, herbal teas and legumes. PhenolQuest will offer the possibility to evaluate the importance of these additional food items as (poly)phenol sources. Furthermore, the greater level of details for the most contributing sources of (poly)phenols that are fruits, processed fruits, teas, coffee and cocoa products, will increase the accuracy of (poly)phenol intake assessment.

PhenolQuest has been built for a selection of 120 compounds that are considered the most relevant for assessing (poly)phenol intake and studying their associated health benefits. Should new (poly)phenols be included, it may be necessary to add the corresponding food items to the questionnaire. The selection of PhenolQuest food items was primarily based on their richness in these (poly)phenols, the quantity provided by one portion, and their level of consumption in the European population. Nearly all fruits are included in PhenolQuest. This comprises all those consumed in quantities over 3 g day^{-1} on average by the adult population, according to the most recent consumption surveys from 22 European countries available in the EFSA comprehensive European food consumption database.[41] Only a few fruits were eventually not retained, since data on their (poly)phenol content were lacking or not robust enough, even after a dedicated literature search. This was the case of pineapple and melon. Similarly, certain variations of specific foods (*e.g.* different varieties of apples, white *vs.* green tea, Arabica and Robusta coffee) were not individualized in PhenolQuest although initially considered, because the (poly)phenol content values for these different variations were not sufficiently described or because, given the variability of the data available, the median values were not significantly different for these variations. The food list may evolve in future versions of PhenolQuest if the selection criteria are met, in particular the availability of high-quality composition data indicating substantial polyphenol content. Food processing can have a marked impact on the (poly)phenol composition of foods but is difficult to integrate in an FFQ. On the one hand, the content data or retention factors for processed foods are still scarce, and on the other hand, going into details about the types of processing or the brand consumed would make the questionnaire excessively long and complex. As an example, although the (poly)phenol content may significantly vary in coffee according to the degree of roasting of the beans, it is impossible for the respondents to assess and report whether they drink lightly or heavily roasted coffee. PhenolQuest does not include mixed dishes and recipes, as it would considerably increase the length of the questionnaire. The estimation of the intake of foods consumed as part of complex dishes relies on the respondent's ability to estimate the proportion of each food in the dish. This is one of the inherent limitations associated with self-reporting instruments.

People can also consume high amounts of (poly)phenols with supplements. However, their (poly)phenol composition cannot be precisely recorded due to the high diversity of supplements on the market and significant differences between brands. PhenolQuest gives the possibility to detect subjects with a high and regular consumption of the most common (poly)phenol supplements, which allows the investigator to flag a probable underestimation of their total (poly)phenol intake.

PhenolQuest therefore incorporates state-of-the-art knowledge about dietary sources of (poly)phenols in a European-style diet. However, data remain incomplete for several sources, such as tropical fruits, herbal teas, spices, legumes, cereal products or supplements, and our work highlights the crucial need for large-scale campaigns to analyse (poly) phenols in a wide variety of foods consumed worldwide. Additionally, information is sparse for certain types of (poly) phenols, especially ellagitanins, proanthocyanidins and other non-extractable (poly)phenols that are bound to the food matrix. Future iterations of PhenolQuest may include new items, depending upon the consolidation of data regarding their (poly)phenol composition.

The food intake data obtained for each respondent using the semi-quantitative FFQ must be cross-referenced with a (poly)phenol-specific table of food composition. Theoretically, any food composition table may be used to provide the (poly) phenol content data. However, using the food composition database specifically designed for PhenolQuest offers significant advantages. This database, which will be available for collaborative projects and reported elsewhere, perfectly matches the PhenolQuest list of food items. Our PhenolQuest food composition database integrates an expert-based selection of the relevant data from Phenol-Explorer, eBasis and the USDA databases, supplemented by extensive additional data from the literature, making it the most comprehensive database for the food list of PhenolQuest. Using another database to treat data from PhenolQuest would require approximations by assigning the closest food item and assuming its (poly)phenol content is similar to that of the intended food.

The median filling time of the digital version of PhenolQuest was 28 minutes in our application test on a French population. Given the efforts made to optimize the food list and enhance the questionnaire's design and usability, this time appears necessary to ensure a reliable assessment of (poly)phenol intake. A further reduction in the number of food items would likely result in a significant loss of accuracy, unless a preliminary application in a representative subgroup of the target population shows that certain foods are not significantly consumed.

The electronic version has several advantages. Administration and data treatment are facilitated. Optional questions can be displayed only when appropriate, depending on the subject's initial responses, and blocking alerts can be made when an answer is missing. The filling time has been shown to be reduced by 20% on average, which decreases respondent fatigue, and likely enhances the quality of the data collected at the end of the questionnaire. Another major advantage is that no retranscription or coding is needed. Furthermore, programs can rapidly generate result outputs.

Scope of use and limitations

PhenolQuest is mostly designed for research purposes and targets populations with a European-style diet. Its long length may hamper its use in many contexts of real life. In particular, self-administration is not possible in populations with limited literacy or illectronism, and support will be required to assist people in such cases. Educational levels were not collected in our application test, which prevents us from assessing the potential influence of literacy on the ability to complete the questionnaire accurately. This will need to be evaluated in future studies. It is also well known that FFQs are country and culture-specific. If in its current form, PhenolQuest is specifically designed for populations with a European-style diet, it can be relatively easily tailored to other Western populations by adjusting the food list, frequency options, and portion sizes. However, adapting PhenolQuest for use in regions such as South America, Africa or Asia would require significantly more effort. The adaptation should follow the same principles but would rely heavily on the expertise of local scientists and nutritionists to identify all (poly)phenol-rich foods unique to these regions and to ensure that the questionnaire accurately reflects the diversity of local dietary habits.

It is important to acknowledge that PhenolQuest has limitations when it comes to estimating absolute (poly)phenol intake. In addition to the well-known challenges associated with self-reporting methods, total (poly)phenol intake may be underestimated due to the absence of certain (poly)phenol-containing foods, for which reliable content data are not yet available. The primary objective of developing PhenolQuest was rather to enhance the reliability of ranking or stratifying individuals based on their (poly)phenol intake, which is often the main objective in epidemiological studies. PhenolQuest can also be highly valuable for comparing the most contributing food profiles of individuals within a population, as similar intake levels may result from significantly different dietary patterns.

Foods without (poly)phenols, particularly foods of animal origin, are intentionally not included in PhenolQuest. As a result, PhenolQuest cannot be used to assess energy and macro- or micronutrient intake. Adjusting (poly)phenol intake by energy intake, or calculating the (poly)phenol-to-energy ratio of a diet will thus require the use of complementary instruments such as general FFQs, 24 h recalls or dietary records designed for that purpose.

Insights from the application test on 110 subjects

The application test conducted on 110 French subjects validated the entire process of data collection and demonstrated that PhenolQuest is an effective tool to capture the diversity of (poly)phenol sources in a French population. The cross-check question for fruits showed that 6 subjects (only 5.4% of the panel) had clearly misunderstood the questions and were excluded. For the remaining 104 subjects, the sum of the declared intake for all individual fruits and the total daily fruit intake declared in the summary cross-check question showed a moderate-to-strong correlation (Spearman correlation r = 0.69). The differences between the two measures (the sum of individual fruit intake minus summary cross-check question data) indicate a discrepancy of less than one serving on average (mean: −0.48; median: −0.54). Only 10.6% of the subjects (n = 11) reported a total fruit intake from the sum of the individual fruits that exceeded by at least one daily serving, the estimate provided by the cross-check question, suggesting that the extended list of individual fruits did not lead to a substantial overestimation bias.

Besides, our preliminary findings showed that PhenolQuest could better assess the intake of foods previously underrepresented, such as herbal teas, herbs or processed fruits, thereby improving our understanding of their contribution to (poly)phenol exposure and health effects. Although our panel may not fully represent all culinary cultures in Europe, PhenolQuest seems sufficiently detailed to capture the diversity of the individual dietary patterns contributing to (poly)phenol intake across European countries.

Validation of the FFQ

Newly developed FFQs are typically validated against a gold standard method, which can consist of dietary questionnaires, weighted food records, or biomarker measurements.[10,49,54] However, no reliable gold standard method could be identified for meaningful validation of PhenolQuest. As mentioned in the introduction, it is clear that general FFQs not specifically tailored to (poly)phenols, as well as 24 h recalls or food records, have important limitations and are not appropriate to serve as reference methods for the assessment of (poly)phenol intake. An alternative approach could be the use of biomarkers. Xu *et al.*'s systematic review reported that only 8% of studies assessing (poly)phenol intake in epidemiology used FFQs validated by biomarkers and these were limited to a few specific (poly)phenol families such as isoflavones or lignans[9] that represent modest contributors to (poly)phenol intake in the European population. Some attempts were made to validate dietary questionnaires by comparison with a global measurement of urinary excretion of (poly)phenols with the Folin–Ciocalteu assay.[55] However, this assay actually measures total reducing capacity, and its results may be influenced by non-phenolic compounds such as ascorbic acid or some amino acids.[56] A few studies have attempted to validate total flavonoid or (poly)phenol intake using a range of (poly)phenol derived metabolites quantified in biofluids, although these metabolites were not fully recognized or validated as biomarkers of (poly)phenol intake.[11] Actually, identifying a reliable combination of (poly)phenol metabolites as robust quantitative biomarkers and developing a standardized quantification protocol remains a significant challenge. Obstacles in that direction include the high inter-individual variation that exists for (poly)phenol biotransformations, resulting in variable circulating concentrations or urinary excretions of their metabolites for a similar intake.[18,19,57] Additionally, there is a lack of commercially available and affordable standards for many (poly)phenol metabolites. It will also take considerable time before the robustness and dose–response relationships between (poly)phenol biomarkers and intake data are thoroughly studied across different populations and settings. In FFQ validation studies, correlations between FFQ data and other dietary assessment tools or biomarkers typically range from 0.3 to 0.7, or even less for (poly)phenols, while there is no consensus threshold to consider that the FFQ is truly validated.[9,50] As a result, all authors conclude that, despite moderate correlations, their FFQ is sufficiently validated for use. Without a gold-standard method to determine the true intake value, such validations offer limited insight. This was recently illustrated with the validation of the KP-FFQ designed for the intake of (poly)phenols in the UK, with an important effort invested to compare data from KP-FFQ to those calculated from a 7-day food diary and to the concentrations of 110 (poly)phenol metabolites in plasma and urine.[11] The study concluded that agreement between assessment tools and urinary biomarkers was low to moderate depending on the (poly)phenol subclasses, while no significant correlations were found with plasma metabolites.

Rather than investing time and effort into reaching a similar conclusion, we made the choice to present in this paper comprehensive details on the development and limitations of PhenolQuest. Our goal is to encourage the widespread use, validation and possible refinement of PhenolQuest by the research community. To support a collaborative validation process and its follow-up by users, PhenolQuest has been deposited on Zenodo (**https://doi.org/10.5281/zenodo.15214458**), which allows version tracking as the questionnaire evolves over time. Additional testing of its measurement properties and feedback from users will be used to validate its scope of use and its reproducibility, as well as to confirm its broader utility in identifying meaningful association between (poly)phenol intake and health outcomes. Future validation efforts could in particular explore comparisons of intake rankings of key foods assessed with PhenolQuest or food records tailored for this purpose and collected across different seasons to evaluate repeatability and seasonal effects on intake assessment. While not without limitations, there is no doubt that PhenolQuest substantially enhances the precision of (poly)phenol intake assessment compared to the currently available tools. By reducing the risk of attenuation due to imprecision, it increases the likelihood of detecting true association between (poly)phenol intake and health outcomes.

Our vision is that future advancement in the field will likely come from a combined use of dietary questionnaires and biomarkers. Biomarkers, in addition to being challenging to identify and validate, have intrinsic limitations. For instance, circulating or excreted metabolites used to reflect (poly)phenol intake cannot capture certain types of (poly)phenols, such as proanthocyanidins, which are neither absorbed nor metabolized. Yet, these non-absorbed (poly)phenols may play an important role in health through their effects on the gut microbiota or local actions within the intestine with possible repercussions at the systemic level.[5] Dietary questionnaires are thus more suitable than biomarkers for assessing exposure to non-absorbed (poly)phenols and investigating their health benefits. Considering the complementary strengths and limitations of both questionnaire and biomarker approaches for assessing (poly)phenol intake, their strategic combination and continued refinement will be essential for achieving more accurate assessments than currently possible.

Conclusion

PhenolQuest is a freely accessible tool specifically designed to compare (poly)phenol intake in European populations. Built on expert knowledge of (poly)phenol diversity, metabolism, and food content, it provides comprehensive coverage of (poly)phenol-rich foods with a high level of precision, making it a state-of-the-art tool for research. Compared to existing methods, PhenolQuest offers significant advantages, particularly when used with its associated food composition database, enabling a more reliable ranking of individuals by (poly)phenol consumption and facilitating meaningful comparisons in epidemiological and clinical studies. Scores of diversity for (poly)phenol intake and contributing sources can also be applied on the collected data. PhenolQuest will evolve over time, based on its application in diverse European populations, further validation efforts, and advances in characterizing the polyphenol content of specific food sources. All future versions will remain accessible and transparently version-tracked through the same (https://doi.org/10.5281/zenodo.15214458), and we encourage the research community to use, evaluate, and contribute to its refinement. This timely tool is essential for advancing our understanding of the health benefits of (poly)phenols, and for contributing to the development of dietary recommendations for these bioactive compounds.

Author contributions

Conceptualization: CMo and CMa. Investigation; DT, CG, SC, SM, WL, CMo, and CMa. Formal analysis: DT, SM, and MT. Software: ML and ADG. Writing – original draft: DT and CMa. Writing – review & editing: DT, SC, NH, LJ, LD, CMo, and CMa. Funding acquisition: LJ and CMa. Project supervision: CMa.

Data availability

No primary research results have been generated. The article describes the development of PhenolQuest, a new food frequency questionnaire (FFQ) designed to assess (poly)phenol intake in Europe. The FFQ is provided in its entirety in the ESI† and is accessible on zenodo at https://doi.org/10.5281/zenodo.15214458 with version tracking. Additionally, the list of (poly)phenols targeted for the conception of the FFQ, the associated food and beverage sources included in PhenolQuest and their portion sizes are shared in the ESI.† An example R script developed to process the questionnaire data and calculate intake frequencies for all food items and their declinations is available at https://doi.org/10.5281/zenodo.14515133, alongside a sample dataset for selected food items.

Conflicts of interest

LD, SC and LJ are full-time employees of Danone Research & Innovation. The authors declare that a part of the funding for this study was received by INRAE as part of a research collaboration with Danone. This funding supported the conduct of the study but had no influence on the design, data interpretation, or conclusions drawn.

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