



Applied nutritional investigation

The Maastricht FFQ: Development and validation of a comprehensive food frequency questionnaire for the Maastricht study



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ABSTRACT

Objective: The aim of this study was to develop and validate a comprehensive food frequency questionnaire (FFQ) for The Maastricht Study, a population-based prospective cohort study in Maastricht, The Netherlands.

Methods: Item selection for the FFQ was based on explained variation and contribution to intake of energy and 24 nutrients. For validation, the FFQ was completed by 135 participants (25–70 y of age) of the Nutrition Questionnaires plus study. Per person, on average 2.8 (range 1–5) telephone-based 24-h dietary recalls (24HRs), two 24-h urinary samples, and one blood sample were available. Validity of 54 nutrients and 22 food groups was assessed by ranking agreement, correlation coefficients, attenuation factors, and ultimately deattenuated correlation coefficients (validity coefficients).

Results: Median correlation coefficients for energy and macronutrients, micronutrients, and food groups were 0.45, 0.36, and 0.38, respectively. Median deattenuated correlation coefficients were 0.53 for energy and macronutrients, 0.45 for micronutrients, and 0.64 for food groups, being >0.50 for 18 of 22 macronutrients, 16 of 30 micronutrients and >0.50 for 17 of 22 food groups. The FFQ underestimated protein and potassium intake compared with 24-h urinary nitrogen and potassium excretion by –18% and –2%, respectively. Correlation coefficients ranged from 0.50 and 0.55 for (fatty) fish intake and plasma eicosapentaenoic acid and docosahexaenoic acid, and from 0.26 to 0.42 between fruit and vegetable intake and plasma carotenoids.

Conclusion: Overall, the validity of the 253-item Maastricht FFQ was satisfactory. The comprehensiveness of this FFQ make it well suited for use in The Maastricht Study and similar populations.

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Introduction

Diet plays a major role in the etiology of multiple chronic diseases such as diabetes [1,2], cardiovascular disease [3], and cancer [4,5]. Food frequency questionnaires (FFQs) are the most commonly

MvD, PD, NW, SM, and HB designed the Maastricht FFQ. PD, MvD, SE, MO, AG, JdV, HBM, and EF designed the validation study. AG, SM, and JdV acquired the data. SE analyzed the data. MvD, SE, and PD drafted the manuscript. All authors interpreted the data, critically reviewed the manuscript, and approved the final version. The authors have no conflicts of interest to declare.

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applied method to estimate habitual dietary intake in observational cohort studies. Despite some well-known methodological limitations [6,7], FFQs are suitable to rank individuals by their intake of foods, energy, and nutrients, and such ranking is of key importance to investigate associations between diet and chronic disease [8,9]. Newly developed FFQs need thorough validation in populations of interest to prevent that incorrectly estimated dietary intake will lead to incorrect estimation of the association between dietary factors and disease [10].

A comprehensive self-administered FFQ was specifically developed to assess dietary intake within the framework of The Maastricht Study in The Netherlands. This is an extensive phenotyping

study on the etiology of type 2 diabetes mellitus (T2DM), its classical complications, and its emerging comorbidities. Briefly, The Maastricht Study uses state-of-the-art imaging techniques and extensive biobanking to determine health status in a population-based cohort of eventually 10 000 individuals, enriched with T2DM individuals using stratified sampling. The Maastricht Study is one of the most comprehensive “deep-phenotyping” studies worldwide, combining individuals with and without T2DM from the general population. The assessment of dietary intake allows assessment of the relation among consumption of specific foods, nutrients, and bioactive compounds, and food groups and dietary patterns with different phenotypes of T2DM and its comorbidities in far more detail than in previous epidemiologic studies. Also, dietary assessment allows controlling for dietary intake when studying other risk factors in the pathogenesis of T2DM and its comorbidities. The present study reported on the development and validity of this new Maastricht FFQ. Validity was assessed against dietary intake from multiple 24-h dietary recalls (24HRs), 24-h nitrogen and potassium excretion in urine, plasma carotenoids, and fatty acids in cholesteryl esters.

Materials and methods

Study design and population

The validation study was embedded in the NQplus (Nutrition Questionnaires plus) study, an ongoing longitudinal study in the city of Wageningen and surroundings, The Netherlands [11,12]. Between 2011 and 2013, 2048 men and women 20 to 70 y of age were included. The NQplus study was approved by the Ethics Committee of Wageningen University and conducted according to the guidelines laid down in the Declaration of Helsinki. All participants provided written informed consent. Participants completed general and health questionnaires at baseline, year 1, and year 2. Moreover, a physical examination including blood and urine collection was performed at baseline, year 1, and year 2, and multiple 24HRs were administered throughout the 2-y study period (repeated sampling of blood and urine only in part of the population). For the present validation study, a random subsample of 150 participants with available data on nutrient intake according to 24HRs and biomarker assessment within 1 y before assessment of the Maastricht FFQ was invited to participate. Between June 2013 and December 2013, 135 (90%) of them, 25 to 69 y of age, accepted the invitation to complete a paper version of the Maastricht FFQ at home. Although we did not perform a formal power calculation, we used as a model other Dutch FFQs that were validated among populations varying from, for instance, 70 [13], 121 [14], to 383 [15] participants. Trained dietitians experienced in interviewing skills administered unannounced telephone-based 24HRs using a standardized five-step, multiple-pass method, which is a validated technique to increase accuracy [16,17]. For each participant, 24HR assessed within 1 y before assessment of the Maastricht FFQ were selected. Dates of 24HR assessment were randomly selected and scheduled evenly across the year and days of the week [12]. The mean \pm standard deviation (SD) number of days between subsequent 24HRs was 105 ± 54 d, and between the first and the last recall was 179 ± 82 d. The mean number of 24HRs filled out by the 135 participants was 2.8 (range 1–5), and 381 24HRs were used for statistical analysis. Average daily consumption of food items by the 24HRs was calculated by multiplying frequency and amount, whereas food items were transcribed into food codes using the Dutch Food Composition (NEVO) Table 2011 to calculate energy and nutrient intakes [18]. General and health questionnaires that were administered in 2012 (year 1 of NQplus study, which was 1 y before assessment of the Maastricht FFQ) were used to describe the current study population.

The Maastricht FFQ

The Maastricht FFQ was designed with the aim of obtaining comprehensive and standardized data on habitual food, energy, and nutrient intake in general population individuals. It was developed with FFQTOOL [19], an online tool that generates tailor-made FFQs. First, an inventory of nutrients and foods of interest was made among members of the multidisciplinary research group collaborating in The Maastricht Study, which is concerned with a broad range of nutrition-related research questions and hypotheses [20]. Furthermore, both absolute intake and variance in intake of each concerned nutrient should be cumulatively covered for $\geq 80\%$ and preferably 90% by the selected food items, based on data from the Dutch Food Composition (NEVO) Table and the Dutch National Food Consumption Survey (DNFCS). The resulting list of energy and 24 nutrients and food constituents for which the FFQ specifically was developed included energy, total protein, vegetable protein, animal protein, total fat, saturated fatty acids (SFAs), monounsaturated fatty acids

(MUFAs), polyunsaturated fatty acids (PUFAs), carbohydrates, polysaccharides, mono- and disaccharides, dietary fiber, cholesterol, alcohol, calcium, phosphorus, iron, sodium, potassium, magnesium, vitamin B₁, vitamin B₁₂, vitamin C, vitamin D, and folate equivalents. In addition to these 24 specific nutrients, we also reported results for 30 other relevant nutrients with available data in the Dutch Food Composition table to increase transparency and completeness of study findings and to facilitate interpretation of these specific nutrient–disease relationships as well (Appendix 1). In general, good coverage of the nutrients of secondary interest may be expected based on the wide range of food products selected to cover the nutrients of primary interest.

The Maastricht FFQ consists of 253 food items with questions on frequency and consumed amounts, with a 1-y reference period. Frequency questions used an answer model with 11 options, from not used to 7 d/wk. Each of the frequency questions was combined with an amount (quantity) question, using an answer model with fourteen standard household servings, from <1 d to >12 d. Average daily consumption of food items were calculated similarly as for the 24HRs, thus by multiplying frequency and amount and by transcribing food items into food codes using the Dutch Food Composition (NEVO) Table 2011 to calculate energy and nutrient intakes [18]. None of the 135 participants were excluded for reasons of extremely low energy intake (<2092 kJ/d [<500 kcal/d] in women and <3347 kJ/d [<800 kcal/d] in men) or extremely high energy intake ($>14\,644$ kJ/d [>3500 kcal/d] in women and $>16\,736$ kJ/d [>4000 kcal/d] in men) [21]. Macronutrients were calculated both as absolute amounts and as energy densities to adjust for energy.

Comparison of the FFQ with the database from the Dutch National Food Consumption Survey 2007–2010, using the Dutch Food Composition (NEVO) Table 2011 [18], indicated that the Maastricht FFQ covered $\geq 96\%$ of the absolute intake of energy and 39 nutrients, 75% to 100% of the covered variance in intake of energy and macronutrients, and 71% to 97% of the covered variance in intake of micronutrients, as assessed by two non-consecutive 24HRs in the National Food Consumption Survey [22].

Urine and blood collection and analyses

Procedures for 24-h urine (ambulatory) and blood sampling (at study center) have been previously described [15]. Aliquots of 24-h urine were stored at -20°C until analysis. Total 24-h nitrogen excretion was determined by the Kjeldahl technique (FOSS Kjeltec 2300 analyzer). Urinary protein was calculated with the following formula: $6.25 \times (\text{urinary N}/0.81)$ [23], accounting for $\sim 19\%$ fecal and skin losses. Urinary potassium concentration measurements were performed with an ion-selective electrode on a Roche 917 analyzer (Roche, Indianapolis, IN, USA); a urinary excretion of 81% was assumed [24]. Duplicate urinary samples were available for all 135 participants to assess urinary concentrations of nitrogen and potassium.

Trained research assistants took blood samples from an antecubital vein after a 10-h overnight fast. Blood was immediately centrifuged and plasma stored at -80°C until analysis. Carotenoids were determined using high-performance liquid chromatography and ultraviolet–visible spectroscopy detection [25]. Fatty acids from plasma cholesteryl esters were quantified by gas liquid chromatography using the solid-phase extraction method to separate the cholesteryl esters with acidified methanol. Peak retention times and area percentages of total fatty acids were determined using known cholesteryl ester standards and analyzed with the Agilent Technologies ChemStation software (Agilent, Amstelveen, The Netherlands) [26]. Plasma carotenoids and plasma fatty acids were available for 132 and 134 participants, respectively.

Descriptives

Height was measured to the nearest 0.1 cm without shoes with a stadiometer (SECA). Body weight was measured without shoes and sweaters and with empty pockets to the nearest 0.1 kg on a digital scale. These measures were obtained by trained research assistants at the study center [12]. Questionnaires were used to assess self-reported smoking status, educational attainment (low: no, lower or lower vocational education; intermediate: intermediate vocational; high: higher vocational or university), disease history, and whether participants followed a diet regimen.

Statistical analysis

Several indicators of validity were assessed using energy, nutrients, and food groups. To adjust for energy intake, macronutrients and alcohol also were expressed as energy percent. To assess the capability of the FFQ to correctly rank an individual's level of intake, absolute intake of energy, nutrients, and food groups was divided into quintiles, and the proportion of agreement between the Maastricht FFQ and reference methods was assessed for sum of exact and adjacent quintiles and extreme quintiles. Next, correlation coefficients of the Maastricht FFQ with reference methods were assessed by linear mixed models with a random intercept for participants, taking multiple measurements of the reference method per person into account. To operationalize the potential degree of underestimation of diet–disease associations, we calculated attenuation factors as the slope in the linear regression of reference methods on the reported intake according to the Maastricht FFQ. An attenuation factor close to 1 indicated minimal attenuation,

whereas an attenuation factor close to 0 indicated maximum attenuation [27]. Finally, the validity coefficient or deattenuated correlation coefficient was estimated as the correlation coefficient between the Maastricht FFQ and the reference instrument divided by the square root of the intraclass correlation coefficient of replicates of the reference method [28]. For concentration biomarkers, exact or adjacent versus extreme quintiles in addition to Pearson correlations are reported. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Results are reported as estimates with 95% confidence intervals (CIs).

Results

Population characteristics

Mean (standard deviation) age of the 135 participants was 56.7 (9.3) y, and 52% were women (Table 1). Mean body mass index (BMI) was 25.9 (4.5) kg/m², and 52% of participants were classified as being overweight (BMI ≥25 kg/m²) or obese (BMI ≥30 kg/m²). Of the sample, 8% were current smokers and 44% were former smokers. Ten percent followed a diet regimen. The majority of participants had a high level of education (61%), and 15% had a disease history of cardiovascular disease, diabetes, or cancer. Men were older, attained a higher level of education, were more often current or ex-smokers, and had a higher prevalence of chronic diseases than women.

Energy and nutrient intake as estimated by the Maastricht FFQ compared with 24HRs

Mean absolute energy intake as estimated by the Maastricht FFQ was similar to energy intake assessed by 24HRs (+2% difference). For 39 of 54 nutrients, mean absolute intake estimated by

the FFQ was within 10% of the intake as estimated by 24HR. For animal protein, saturated fat, trans-fatty acids (TFAs), α-linolenic acid (ALA), water, retinol equivalents (REs), vitamin B₆, vitamin B₁₂, and vitamin D, measured mean intake was almost identical by both methods (<2.5% difference). The Maastricht FFQ gave slightly higher intake estimates (2.5–5%) for the macronutrients protein (total, vegetable), fat (total fats, PUFAs, linoleic acid [LA], fat-energy%) and the micronutrients zinc, selenium, β-carotene, vitamin B₁, and folate. Higher estimates of intake (5–10%) were found for protein-energy%, MUFAs, cholesterol, and total carbohydrates (g and energy%), and the micronutrients sodium, potassium, iron (total, hemoglobin, non-hemoglobin), calcium, magnesium, phosphorus, and vitamin B₂, whereas 10% to 20% overestimations by the Maastricht FFQ were seen for docosahexaenoic acid (DHA), monodisaccharides, dietary fiber, copper, β-cryptoxanthin, nicotinic acid, vitamin C, and vitamin E, and >20% for lutein, zeaxanthin, and lycopene. In contrast, absolute intake estimated by the Maastricht FFQ was slightly (2.5–5%) lower for polysaccharides and retinol activity equivalents (RAEs) and lower (5–10%) for eicosapentaenoic acid (EPA), retinol, and folate equivalents. Underestimations >10% were found only for alcohol (g and energy%), iodine, and α-carotene (Table 2, Appendix 1).

The allocation of participants to the same and adjacent quintiles, based on the Maastricht FFQ and the 24HRs, was >70% for energy and the majority of nutrients, with scores ≥80% for alcohol and copper. Proportions of 60% to 70% were found for fat (all except SFAs and DHA, which were >70%), iron (total, hemoglobin, non-hemoglobin), selenium, REs, β-carotene, zeaxanthin, lycopene, vitamin B₁, vitamin B₆, nicotinic acid, vitamin D, and vitamin E. The level of agreement was 50% to 60% only for sodium, RAEs, α-carotene, and lutein. Distribution in extreme quintiles (quintile 5 for the Maastricht FFQ and quintile 1 for 24HRs, or vice versa) was <5% for energy and all nutrients except TFAs, sodium, RAEs, β-carotene, lycopene, and vitamin E (5–7%), and 11% for lutein. The best scoring nutrients (<1% extreme quintiles) were protein-energy%, carbohydrate (total and energy%), fiber, alcohol (g and energy%), calcium, and vitamin C (Table 2, Appendix 1).

The correlation between the FFQ and 24HRs, as assessed by mixed models, was 0.49 for energy, and for most nutrients ranged from 0.30 (MUFAs) to 0.88 (alcohol). Lower correlations were found for PUFAs (0.28), ALA (0.21), LA (0.28), DHA (0.29), TFAs (0.13), fat energy% (0.29), sodium (0.07), iodine (0.05), retinol (0.13), REs (0.24), RAEs (0.17), carotenoids (except β-cryptoxanthin; 0.13–0.18), vitamin B₁ (0.24), nicotinic acid (0.27), vitamin D (0.24), and vitamin E (0.17). Median correlation coefficients were 0.45 for energy and macronutrients and 0.36 for micronutrients (Table 2, Appendix 1). When considering only energy and those 24 nutrients for which the FFQ was specifically designed, the median correlation coefficient for energy and macronutrients was 0.49 and 0.40 for micronutrients, respectively (Table 2).

Attenuation factors were between 0.40 and 0.70 for energy and 34 of 54 nutrients. Attenuation factors <0.40 were found for MUFA, PUFA, ALA, LA, TFAs, fat-energy%, sodium, iodine, REs, RAEs, lutein, zeaxanthin, lycopene, vitamin B₁, nicotinic acid, and vitamin E (Table 2, Appendix 1), indicating substantial attenuation of risk estimates for these specific nutrient–disease associations.

Adjustment of correlation coefficients for within-subject variation of the repeated 24HRs resulted in increased deattenuated correlation coefficients (= validity coefficients) for all nutrients except water, sodium, potassium, calcium, magnesium, phosphorus, zinc, copper, selenium, iodine, retinol, lutein, zeaxanthin, lycopene and nicotinic acid, where de-attenuated correlations were similar to the original correlations. The deattenuated correlation was 0.58 for energy and >0.60 for the nutrients animal protein, carbohydrate

Table 1
Characteristics of participants in the Maastricht FFQ validation study*

	All (N = 135)	Men (n = 65)	Women (n = 70)
Age, y	56.7 ± 9.3	59.3 ± 8.1	54.4 ± 9.8
BMI, kg/m ²	25.9 ± 4.5	25.6 ± 3.5	26.1 ± 5.2
BMI categories (%) [†]			
Normal weight (<25 kg/m ²)	70 (57)	30 (49)	40 (66)
Overweight (25–29.9 kg/m ²)	44 (36)	27 (44)	17 (28)
Obese (≥30 kg/m ²)	20 (16)	7 (11)	13 (21)
Waist, cm	91.9 ± 12.7	95.4 ± 11.5	88.7 ± 12.9
Waist/hip ratio	0.89 ± 0.09	0.93 ± 0.08	0.84 ± 0.07
Smoking status (%) [‡]			
Never	58 (48)	24 (39)	34 (56)
Former	54 (44)	30 (49)	24 (39)
Current	10 (8)	7 (11)	3 (5)
Educational attainment (%) [§]			
Low	7 (5)	3 (5)	4 (6)
Medium	46 (34)	19 (29)	27 (39)
High	82 (61)	43 (66)	39 (56)
Disease history (%)			
None	110 (84)	50 (82)	60 (88)
Myocardial infarction	3 (2)	2 (3)	0 (0)
Stroke	3 (2)	1 (2)	1 (1)
Diabetes	5 (4)	4 (7)	1 (1)
Cancer	10 (8)	4 (7)	6 (9)
Diet regimen (%) [¶]			
Yes, always	8 (6)	4 (6)	4 (6)
Sometimes	5 (4)	1 (2)	4 (6)
No	120 (90)	59 (92)	61 (88)

BMI, body mass index; FFQ, food frequency questionnaire

*Values are mean ± SD or N (%).

[†]One missing.

[‡]Thirteen missing.

[§]Educational attainment (low: no, lower or lower vocational education; intermediate: intermediate vocational; high: higher vocational or university).

^{||}Four missing.

[¶]Two missing.

Table 2
Absolute intake of energy and nutrients for which the Maastricht FFQ was developed, 24-h dietary recalls, and indicators of validity (N = 135)

	Absolute intake		Indicators of validity			
	FFQ Mean (SE)	24-h recalls mean (SE)	Exact + adjacent or extreme level of agreement*	Correlation coefficient (95% CI)	Attenuation factor (95% CI)	Deattenuated correlation coefficient (95% CI)
Energy, kcal	2160 (49)	2116 (39)	71.9/3	0.49 (0.41–0.71)	0.44 (0.33–0.56)	0.58 (0.41–0.70)
Protein, total, g	83.1 (1.8)	80.7 (1.6)	77.1/2.2	0.48 (0.40–0.71)	0.51 (0.38–0.64)	0.57 (0.39–0.70)
Vegetable	35.3 (1.0)	33.8 (0.9)	73.3/1.5	0.51 (0.43–0.75)	0.50 (0.37–0.62)	0.59 (0.42–0.70)
Animal	47.9 (1.3)	46.9 (1.4)	76.3/1.5	0.52 (0.48–0.79)	0.63 (0.50–0.77)	0.65 (0.47–0.77)
Protein, energy%	16.5 (0.3)	15.7 (0.2)	78.5/0.7	0.42 (0.34–0.70)	0.48 (0.35–0.61)	0.53 (0.34–0.67)
Fat, total, g	83.5 (2.4)	80.7 (2)	69.6/3	0.38 (0.29–0.66)	0.40 (0.27–0.52)	0.49 (0.29–0.64)
SFA	29.6 (1.0)	29.6 (0.8)	76.3/2.2	0.41 (0.33–0.70)	0.44 (0.31–0.56)	0.53 (0.33–0.67)
MUFA	29.3 (0.9)	27.5 (0.8)	68.1/2.2	0.30 (0.19–0.61)	0.36 (0.22–0.50)	0.41 (0.20–0.58)
PUFA	17.2 (0.6)	16.4 (0.5)	62.2/2.2	0.28 (0.16–0.56)	0.32 (0.18–0.46)	0.37 (0.16–0.54)
Fat, energy%	34.5 (0.5)	33.1 (0.4)	65.9/3.7	0.29 (0.17–0.58)	0.36 (0.21–0.51)	0.39 (0.18–0.56)
Cholesterol, mg	210 (7)	198 (9)	70.4/1.5	0.32 (0.26–0.67)	0.59 (0.39–0.80)	0.46 (0.24–0.63)
Carbohydrates, g	239.22 (6.19)	226.5 (5.15)	70.36/0.74	0.56 (0.50–0.78)	0.49 (0.38–0.61)	0.65 (0.49–0.76)
Polysaccharides	120 (3)	124 (3)	78.6/2.2	0.58 (0.53–0.79)	0.58 (0.45–0.72)	0.67 (0.52–0.77)
Mono- or disaccharides	117 (4)	103 (3)	74.1/4.4	0.47 (0.39–0.71)	0.42 (0.31–0.53)	0.56 (0.38–0.69)
Carbohydrate, energy%	46.4 (0.5)	43.7 (0.6)	75.5/0.7	0.50 (0.45–0.77)	0.63 (0.47–0.78)	0.62 (0.44–0.74)
Dietary fiber, g	27.4 (0.7)	24 (0.6)	73.3/0.7	0.55 (0.51–0.80)	0.51 (0.39–0.62)	0.68 (0.50–0.78)
Water, g	2539 (55)	2593 (52)	70.4/2.2	0.50 (0.36–0.63)	0.50 (0.35–0.64)	0.51 (0.35–0.62)
Alcohol, g	11.7 (1)	14.9 (1.4)	84.4/0.7	0.78 (0.70–0.83)	1.41 (1.17–1.65)	0.88 (0.78–0.93)
Alcohol, energy%	3.77 (0.33)	4.70 (0.42)	85.9/0.7	0.88 (0.83–0.91)	1.49 (1.28–1.70)	0.99 (0.94–1.02)
Sodium, mg	2804 (80)	2554 (73)	57/7.4	0.07 (–0.10 to 0.24)	0.10 (–0.06 to 0.26)	0.07 (–0.10 to 0.24)
Potassium, mg	3803 (88)	3516 (71)	76.3/1.5	0.56 (0.43–0.67)	0.48 (0.37–0.59)	0.56 (0.42–0.67)
Total iron, mg	12.2 (0.3)	11.4 (0.3)	69.6/2.2	0.39 (0.29–0.64)	0.41 (0.27–0.55)	0.47 (0.28–0.62)
Calcium, mg	1109 (32)	1028 (27)	78.5/0	0.63 (0.52–0.73)	0.55 (0.45–0.66)	0.64 (0.51–0.73)
Magnesium, mg	391 (9)	370 (8)	75.6/3	0.53 (0.39–0.64)	0.52 (0.39–0.64)	0.53 (0.38–0.64)
Phosphorus, mg	1575 (35)	1495 (30)	76.3/1.5	0.54 (0.41–0.66)	0.51 (0.39–0.63)	0.55 (0.40–0.65)
Vitamin B ₁ , mg	1.07 (0.03)	1.02 (0.03)	67.4/3	0.24 (0.10–0.55)	0.36 (0.18–0.55)	0.33 (0.11–0.52)
Vitamin B ₁₂ , µg	4.53 (0.16)	4.47 (0.22)	72.6/2.2	0.41 (0.26–0.54)	0.71 (0.53–0.90)	0.62 (0.40–0.77)
Folate equivalents, µg	277 (7)	297 (10)	70.4/1.5	0.37 (0.35–0.84)	0.59 (0.38–0.80)	0.61 (0.38–0.77)
Vitamin C, mg	125 (5)	108 (5)	72.6/0.7	0.42 (0.38–0.77)	0.52 (0.38–0.67)	0.59 (0.38–0.73)
Vitamin D, µg	3.39 (0.14)	3.36 (0.17)	65.2/4.4	0.24 (0.12–0.61)	0.41 (0.22–0.60)	0.37 (0.13–0.56)

CI, confidence interval; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SE, standard error; SFA, saturated fatty acid

*Proportion of participants assigned to the same plus adjacent quintiles/extreme quintiles.

(total, polysaccharides, energy%), dietary fiber, alcohol (g and energy%), calcium, β -cryptoxanthin, vitamin B₂, vitamin B₁₂, folate, and folate equivalents. Validity coefficients between 0.50 and 0.60 were found for protein (total, vegetable, energy%), fat (saturated, EPA, DHA), mono- and disaccharides, water, potassium, hemoglobin iron, magnesium, phosphorus, and vitamin C. Deattenuated

correlations between 0.40 and 0.50 were found for fat (total fat, MUFAs), cholesterol, iron (total, non-hemoglobin), zinc, copper, and vitamin B₆. Values <0.40 were found for PUFAs (0.32), ALA (0.26), LA (0.37), TFAs (0.20), fat-energy% (0.39), sodium (0.07), selenium (0.34), iodine (0.06), retinol (0.13), REs (0.33), RAEs (0.31), carotenoids (0.08–0.37, except β -cryptoxanthin [0.74]),

vitamin B₁ (0.33), nicotinic acid (0.28), vitamin D (0.37, and vitamin E (0.26). Median deattenuated correlation coefficients were 0.53 for energy and macronutrients and 0.45 for micronutrients. Eighteen of 22 macronutrients and 16 of 30 micronutrients had a deattenuated correlation coefficient >0.40 (Table 2, appendix 1). When considering only energy and those 24 nutrients for which the FFQ was specifically designed, the median deattenuated correlation coefficients for energy and macronutrients was 0.58, and 0.55 for micronutrients, respectively. Moreover, 10 of 14 macronutrients and 6 of 9 micronutrients for which the FFQ was specifically designed had deattenuated correlation coefficients >0.50 (Table 2).

Intake of food groups as estimated by the Maastricht FFQ compared with 24HRs

Mean absolute intake of the food groups grains, bread and breads, meat, soy and vegetarian products, fats, oils, sauces, and alcoholic or non-alcoholic beverages, estimates by both methods were <10% apart. For potatoes, vegetables, fruits, savory sandwich fillings, milk and milk products, egg' and sugar, honey, jams, candy, the Maastricht FFQ showed 10% to 35% higher intake than the 24HRs, whereas for cake and cookies, cheese, fish, composite dishes, and soups, the Maastricht FFQ showed 10% to 40% lower intake than the 24HRs. For legumes and nuts, seeds, and snacks, intake estimated by the Maastricht FFQ was almost double the intake based on 24HRs (Table 3).

The exact and adjacent level of agreement of the distribution in quintiles between the FFQ and the 24HRs was ≥70% for most food groups, except for cake and cookies (62%); nuts, seeds, and snacks (53%); cheese (68%); eggs (65%); fats, oils, and sauces (63%); legumes (58%); and composite dishes (55%). The correlations between the FFQ and 24HRs for food groups generally ranged from 0.30 for cake and cookies and soups to 0.69 for milk and milk products. Lower correlations were found for grains (0.23); nuts, seeds, and snacks (0.07); legumes (0.17); fats, oils, and sauces (0.23); and composite dishes (−0.03; Table 3).

Attenuation factors were generally between 0.40 and 0.70, except for nuts, seeds, and snacks (0.07); fish (1.21); fats, oils, and sauces (0.37); and composite dishes (−0.16), indicating substantial attenuation of risk estimates for these specific food group–disease associations. Deattenuated correlations (validity coefficients) were considerably higher than direct correlations for the large majority of food groups, resulting in deattenuated correlations >0.60 for all food groups except grains (0.50); savory sandwich fillings (0.59); nuts, seeds, snacks (0.17); composite dishes (−0.12); and soups (0.59). The median deattenuated correlation coefficient of food groups was 0.64 of which 17 of 22 food groups had values >0.50 (Table 3).

Validity of intake of protein, potassium, fish, fruits, and vegetables based on biomarkers

FFQ-estimated protein intake was on average 18% lower than based on 24-h urinary nitrogen excretion. For potassium, FFQ-estimated intake was almost identical (−2%) to 24-h urine excretion. For protein and potassium, 67% and 60% of the participants, respectively, were allocated to the same or adjacent quintiles, and for both nutrients, ≤3% of participants were allocated to extreme quintiles. Correlations of protein and potassium intake with 24-h urinary excretion were 0.35 and 0.38, attenuation factors 0.51 and 0.46, and deattenuated correlations 0.40 and 0.60, respectively (Table 4).

For intake of fish and fatty fish, 66% and 67% of the participants, respectively, were allocated to the same or adjacent quintile when based on the FFQ or on plasma concentrations of EPA + DHA, and

≤5% were allocated to extreme quintiles. Pearson correlations for fish and fatty fish were 0.55 and 0.50, respectively (Table 4).

For fruits and vegetables, >60% of the participants were allocated to the same or adjacent quintiles when based on the FFQ or on plasma concentrations of carotenoids, and again ≤5% were allocated to extreme quintiles. Correlations were between 0.26 and 0.42; highest correlations were seen for total fruits and vegetables with sum of carotenoids (0.42); for fruit with sum of carotenoids (0.39) and with β- cryptoxanthin (0.39); and for vegetables with the sum of lutein and zeaxanthin (0.36) (Table 4).

Discussion

This study described the validation of the Maastricht FFQ, a comprehensive 253-item FFQ for The Maastricht Study, which was developed based on explained variation and contribution to intake of energy and 24 nutrients. Results showed that protein and potassium intakes as measured by the Maastricht FFQ were comparable with 24-h urinary excretion of nitrogen and potassium, both in terms of absolute intake (underestimation by the FFQ: 18% and 2%, respectively), deattenuated correlations (0.40 and 0.60, respectively), and allocation to exact/adjacent quintiles (both ≥60%) and extreme quintiles (both ≤3%). When compared with 24HR, the Maastricht FFQ gave similar intake (<10% difference) for energy and 39 of 54 nutrients. For food groups, there was a slight overestimation (10–35% for most food groups). For energy and the majority of nutrients and food groups, >70% of participants were allocated to the correct or adjacent quintiles based on the FFQ and 24HR and <5% to extreme quintiles. Correlation between intake measured by the FFQ and by 24HR was 0.49 for energy and ranged between 0.30 and 0.88 for most nutrients and foods. Attenuation factors (reflecting underestimation of the diet–disease association by the FFQ) were between 0.40 and 0.60 for energy and most nutrients, and between 0.40 and 0.70 for most food groups. Adjustment of correlation coefficients for within-subject variation of the repeated 24HRs resulted in deattenuated correlation coefficients (validity coefficients) of 0.58 for energy, >0.40 for most nutrients, and >0.50 for most food groups.

An extensive review of international FFQs and design characteristics was previously published by Molag et al. [29]. FFQs are mainly used in large-scale cohort studies to study associations between dietary intake and chronic disease-related outcomes. Results of the current study indicate that the Maastricht FFQ can be used for studying associations both at nutrient and food levels. A general trend in nutritional epidemiology is to perform dietary pattern analyses in relation to chronic diseases, rather than focusing on specific nutrients [30]. With 253 food items included, the Maastricht FFQ is currently one of the most comprehensive FFQ in The Netherlands. Some earlier Dutch FFQs include the 104-item FFQ used in the Leiden Longevity Study [31], the NLCS' (Netherlands Cohort Study) 150-item FFQ [32], the 160-item FFQ-NL1.0 [15], and the 178-item FFQ of the EPIC (European Prospective Investigation into Cancer and Nutrition) study [14]. The large number of food items present in the Maastricht FFQ will facilitate the study of dietary patterns and specific food groups in relation to disease etiology and prognosis.

In population studies, a field of interest will also be the description of dietary intake of the concerned population, both in terms of absolute energy and nutrient intake and in terms of food patterns. FFQs are usually considered less suitable for assessing absolute levels of intake. Nevertheless, results of the current study suggest that the Maastricht FFQ performs well in this respect, with only 2% overestimation of energy and <5% overestimation for the majority of nutrients. For food groups, there was more variability in

Table 3
Absolute intake of food groups according to both the Maastricht FFQ and 24-h dietary recalls and indicators of validity (N = 135)

	Absolute intake (g/d)		Exact + adjacent or extreme level of agreement*	Indicators of validity		
	FFQ Mean (SE)	24HRs Mean (SE)		Correlation coefficient (95% CI)	Attenuation factor (95% CI)	Deattenuated correlation coefficient (95% CI)
Potatoes	95 (5)	72 (6)	71.9/2.2	0.37 (0.35–0.84)	0.63 (0.44–0.81)	0.61 (0.38–0.77)
Vegetables	170 (8)	141 (8)	70/5.2	0.46 (0.32–0.59)	0.55 (0.42–0.69)	0.75 (0.55–0.88)
Fruit	243 (13)	196 (13)	80.8/1.5	0.63 (0.66–0.93)	0.63 (0.50–0.76)	0.81 (0.66–0.90)
Grains	50 (3)	53 (5)	70.4/4.4	0.23 (0.14–0.83)	0.66 (0.34–0.98)	0.50 (0.22–0.71)
Bread and breads	131 (6)	137 (5)	83/3.7	0.49 (0.46–0.80)	0.49 (0.36–0.62)	0.64 (0.46–0.77)
Cake and cookies	30 (2)	39 (3)	62.2/4.4	0.30 (0.29–0.93)	0.61 (0.39–0.83)	0.63 (0.36–0.81)
Savory sandwich fillings	3.8 (0.6)	3 (0.5)	87.4/0	0.40 (0.37–0.79)	0.43 (0.30–0.57)	0.59 (0.38–0.74)
Nuts, seeds, snacks	42 (3)	23 (2)	52.6/5.2	0.07 (–0.21 to 0.54)	0.07 (–0.04 to 0.18)	0.17 (–0.12 to 0.43)
Legumes	13 (1)	7 (2)	58.5/0.7	0.17 (0.01–0.33)	0.49 (0.21–0.77)	NA
Milk and milk products	372 (20)	309 (16)	83/0.7	0.69 (0.58–0.76)	0.53 (0.43–0.63)	0.90 (0.77–0.97)
Cheese	28 (2)	33 (29)	68.1/5.2	0.39 (0.24–0.52)	0.51 (0.36–0.66)	0.65 (0.42–0.81)
Eggs	15 (1)	12 (2)	65.2/0	0.32 (0.31–0.91)	0.58 (0.38–0.78)	0.63 (0.37–0.80)
Meat	89 (5)	83 (5)	71.1/2.2	0.41 (0.26–0.55)	0.56 (0.41–0.72)	0.78 (0.56–0.93)
Fish	19 (1)	24 (4)	74.8/1.5	0.36 (0.20–0.50)	1.21 (0.84–1.59)	0.80 (0.56–0.96)
Soy, vegetarian products	16 (4)	15 (4)	73.3/0	0.65 (0.54–0.74)	0.53 (0.42–0.64)	0.82 (0.68–0.90)
Sugar, honey, jams, candy	30 (2)	27 (2)	71.9/1.5	0.43 (0.28–0.56)	0.43 (0.32–0.54)	0.79 (0.57–0.93)
Fats, oils, sauces	39 (2)	42 (2)	63/3	0.23 (0.21–1.28)	0.37 (0.20–0.54)	0.77 (0.48–0.96)
Composite dishes	26 (2)	40 (6)	54.8/3	–0.03 (–0.80 to 0.58)	–0.16 (–0.76 to 0.44)	–0.12 (–0.42 to 0.21)
Soups	48 (6)	66 (8)	70.4/2.2	0.30 (0.27–0.89)	0.56 (0.34–0.78)	0.59 (0.33–0.78)
(Non)-alcoholic beverages	1543 (43)	1716 (46)	71.9/1.5	0.49 (0.44–0.76)	0.57 (0.41–0.73)	0.61 (0.43–0.74)

FFQ, food frequency questionnaire; NA, not applicable

*Proportion of participants assigned to the same plus adjacent quintiles/extreme quintiles.

estimated absolute intake (mostly 10–30% over- or underestimation). It is noteworthy that the relative difference in intake estimated by the FFQ and 24HRs was larger for foods eaten less regularly or in smaller amounts, such as legumes and nuts, seeds, and snacks. For instance, the absolute intake of legumes as estimated by the Maastricht- FFQ was 13 g/d compared with 7 g/d by 24HR, an absolute difference of 6 g/d, which gives a relative difference of >40%. Another potential cause of the discrepancy between the two assessment methods could be the relatively low number of 24HRs per participant.

Because measurement errors in FFQs and dietary recalls are partly correlated, it is recommended that objective biological markers of dietary intake be used for validation purposes [10,33]. In this respect, both recovery and concentration biomarkers were used. Recovery biomarkers are specific biologic products that are directly related to intake and not subject to homeostasis or substantial interindividual differences in metabolism [33]. Thus far, only few recovery biomarkers are known, except for urinary nitrogen and potassium, which are considered the best biomarkers for protein and potassium intake. Correlation coefficients and deattenuated correlation coefficients of protein intake and urinary nitrogen in the Maastricht FFQ were

comparable to five US validation studies [34], and the same applied to potassium intake and potassium excretion [35]. Previously reported attenuation factors for FFQs were on average 0.17 for protein and 0.25 to 0.30 for potassium [34,35]. The present study showed attenuation factors of 0.51 for protein and 0.46 for potassium, indicating substantially less attenuation of relative risks.

In contrast to recovery biomarkers, concentration biomarkers are affected by metabolism (e.g., absorption, nutrient–nutrient interactions or nutrient–gene interactions) or lifestyle factors (e.g., smoking, physical activity, BMI) [33]. Nevertheless, concentration biomarkers are correlated to dietary intake and often are used to assess diet–disease associations. Plasma carotenoids are considered concentration biomarkers of the consumption of fruits and vegetables during the previous weeks or months [33,36]. Correlation coefficients between fruit and vegetable intake and plasma carotenoids in the present study were similar or slightly higher than for the Dutch EPIC FFQ [36] and the FFQ-NL1.0 [15]. In an Australian cohort, correlation coefficients between fruits and vegetable intakes with plasma carotenoids varied from 0.26 to 0.52 [37], which is comparable with results of the present study.

Table 4
Validity of protein, potassium, fish, fruit, and vegetable intake estimated by the Maastricht FFQ compared with biomarkers

	Absolute intake (g/d) or urinary or plasma status		Indicators of validity			
	FFQ	Urine/blood	Exact + adjacent or extreme level of agreement	Correlation coefficient (95% CI)	Attenuation factor (95% CI)	Deattenuated correlation coefficient (95% CI)
For recovery biomarkers in urine						
Protein (g/d)	83.1 (1.7)	100.7 (2)*	66.7/2.3	0.33 (0.21–0.58)	0.51 (0.29–0.72)	0.40 (0.20–0.56)
Potassium (mg/d)	3803 (88)	3880 (78)	59.9/3	0.38 (0.36–0.81)	0.46 (0.29–0.63)	0.60 (0.37–0.76)
For biomarkers in blood						
Fish, EPA + DHA (mg)	19.1 (1.4)	NA	65.7/5.2	0.55 (0.47–0.64)		
Fatty fish, EPA + DHA (mg)	9.4 (1.1)	NA	67.2/4.5	0.50 (0.40–0.58)		
F&V, sum carotenoids (µg)	414 (17)	NA	68.2/3	0.42 (0.31–0.51)		
Fruit, sum carotenoids (µg)	243 (13)	NA	62.9/4.6	0.39 (0.29–0.49)		
Vegetable, sum carotenoids (µg)	170 (8)	NA	61.4/3.8	0.26 (0.15–0.37)		
F&V, α-carotene (µg)	414 (17)	NA	65.9/3.8	0.34 (0.22–0.44)		
F&V, β-carotene (µg)	414 (17)	NA	65.9/3	0.31 (0.20–0.42)		
Fruit, β-cryptoxanthin (µg)	243 (13)	NA	64.4/1.5	0.39 (0.28–0.49)		
Vegetable, lutein + zeaxanthin (µg)	170 (8)	NA	67.4/3.0	0.36 (0.25–0.46)		

CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; F&V, fruits and vegetables; NA, not applicable. Attenuation factor (95% CI) estimated as the slope in the linear regression of the biomarker on the reported intake. Correlations shown for plasma biomarkers are Pearson correlation coefficients

*Calculated from 24-h urinary nitrogen excretion.

EPA and DHA are frequently used as concentration biomarkers to evaluate fish intake [38]. In the present study, correlation coefficients were 0.55 for intake of fish and 0.50 for fatty fish. This compares favorably with reported correlations between fatty fish intake and plasma concentrations of EPA (0.17) and DHA (0.29) in the EPIC study [38] and correlations with total plasma ω-3 fatty acids of 0.17 for total fish intake and 0.19 (women) and 0.23 (men) for fatty fish intake [39]. Correlations of the Maastricht FFQ are slightly higher than for the FFQ-NL1.0 for fish (0.43) and similar for fatty fish (0.47) [15].

The Maastricht FFQ was developed using the Dutch FFQTOOL by selecting food items with the largest contributions to both absolute intake and explained variance in intake of energy and 24 nutrients based on the Dutch National Food Consumption Survey 2007–2010. We validated the Maastricht FFQ within the NQplus study population [15]. Population characteristics in The Maastricht Study [40] were generally comparable with the NQplus population with respect to age, BMI, smoking status, and educational attainment. A limitation of the current validation study was the well-known issue of correlated errors between dietary intake assessed by FFQ and 24HR. For this reason, we included biomarkers in blood and urine, which are uncorrelated to FFQ errors.

The 253-item Maastricht FFQ is currently being used for dietary assessment in The Maastricht Study. So far, ~7500 FFQs have been completed within this cohort. In addition, the Maastricht-FFQ is being applied in several smaller ongoing cohort studies. Our current experience with this FFQ within The Maastricht Study shows excellent response rate (~95%). The median time needed to complete the FFQ is 1 h and the large majority of completed FFQs (~70%) had no missing items; of the FFQs with missing items, ~33% had 1 to 2 missing items, 33% had 3 to 10 missing items, and ~33% had >10 missing items). All participants with one or more

missing items were contacted via phone by a trained dietitian to complete these items. Of note, although many studies tend to use questionnaires filled out online, we opted for the use of a paper version to facilitate maximal flexibility with respect to turning pages and checking answering options; an online version is available on request.

Conclusion

Overall, the validity of the 253-item Maastricht FFQ was satisfactory. Results for protein and potassium (mean absolute intake, allocation to same/adjacent or extreme quintiles, and correlations) are comparable with 24-h urine excretion of nitrogen and potassium. When compared with 24HRs as reference method, the Maastricht FFQ provides a small (<5%) overestimation of the absolute intake of energy and most nutrients. Deattenuated correlations were >0.40 for energy and most nutrients and >0.50 for the majority of food groups. For energy and most nutrients and foods, >70% of participants are allocated to the correct of adjacent quintiles and <5% to extreme quintiles. These features, and the comprehensiveness and completeness of this FFQ, make it well suited for use in The Maastricht Study and similar populations.

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