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Age dependent dietary assessment model (AGE MODE)

Folate and vitamin A as examples

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Abstract

Age dependent dietary evaluation model (AGE MODE)
folate and vitamin A as examples

The ‘Age dependent dietary evaluation model’ (AGE MODE), described and demonstrated in this report, allows one to estimate usual intakes of micronutrients and to evaluate these intakes in relation to requirements.

A quantitative evaluation of micronutrient intakes is warranted for setting policy priorities and determining the need for political measures. Habitual micronutrient intakes are estimated using AGE MODE from short-term measurements, and the prevalence of inadequate intakes is obtained by relating habitual intakes to requirements. AGE MODE has several advantages above currently used methods. Most important is the feature of age dependency. Furthermore, the model is transparent, which provides insight into the data.

As case-study, AGE MODE is used to estimate the habitual intake of folate and vitamin A and to compare this to the dietary reference intakes.

Key words: model, dietary evaluation, habitual intake, requirements, micronutrients

Rapport in het kort

AGE MODE: een leeftijdsafhankelijk model voor toetsing van de inneming van voedingsstoffen
geïllustreerd voor foliumzuur en vitamine A

Dit rapport beschrijft de werking van het model AGE MODE. AGE MODE is een methode om de gebruikelijke inneming van microvoedingsstoffen, vitaminen en mineralen, te schatten en te toetsen aan de voedingsnorm.

AGE MODE is ontwikkeld door het RIVM. AGE MODE is een kwantitatieve methode om de voorziening van microvoedingsstoffen te beoordelen. Het kan gebruikt worden om prioriteiten te stellen in beleid dat gericht is op een adequate voedingsstoffenvoorziening voor de bevolking. Het model schat de gebruikelijke inneming van microvoedingsstoffen uit inneminggegevens afkomstig uit voedselconsumptiepeilingen en zet deze af tegen de behoefte aan dergelijke microvoedingsstoffen. Zo kan het percentage individuen voor wie de voorziening onder de voedingsnorm is, worden bepaald. AGE MODE heeft een aantal voordelen ten opzichte van bestaande methoden. Het is een leeftijdsafhankelijk model. Bovendien is het een transparant model, waardoor goed inzicht kan worden gekregen in de onderliggende gegevens.

Ter illustratie is AGE MODE gebruikt om een schatting te maken van de gebruikelijke inneming van foliumzuur en vitamine A en dit te vergeleken met de voedingsnormen.

Trefwoorden: model, voedselconsumptiebeoordeling, voedingsnormen, gebruikelijke inneming, micronutriënten.

Contents

Summary

The Dutch Ministry of Health, Welfare and Sports has expressed the need for a sound methodology to quantitatively evaluate the intake of micronutrients and other dietary components in relation to requirements. For this purpose an age dependent dietary evaluation model, called AGE MODE, has been developed at the RIVM.

General framework
The use of AGE MODE fits in a general framework for the evaluation of micronutrient intakes in relation to requirements, consisting of three parts:
1 Estimating the habitual intake distribution of the micronutrient
2 Describing the (distribution of) requirements for the micronutrient
3 Estimating the prevalence of inadequate intakes of the micronutrient by combining habitual intakes with requirements

The Dutch National Food Consumption Surveys provide intake data for two days. However, to correctly evaluate long-term intakes of micronutrients not the observed intakes but the mean intake over a longer period, the habitual intake, is needed. Therefore, the first part aims at eliminating the intra-individual (or day-to-day) variance from the dietary intake data and to only retain the inter-individual variance.
Information on the requirements, necessary for part 2, can be obtained from the Dietary Reference Intakes (DRIs), set by the National Health Council.
Two approaches exist to estimate the prevalence of inadequate intakes (part 3): the EAR cut-point approach and the probability approach. The probability approach is most appealing, as unbiased estimates can be obtained if the requirement distribution is specified. However, information on requirements is limited, so that many assumptions need to be made. This makes this approach not practicable. In contrast, the EAR cut-point approach is straightforward, although violation of implicit assumptions may cause bias. Still this approach is suggested as long as the DRIs do not provide adequate information.

Age dependent dietary evaluation model: AGE MODE
AGE MODE produces estimates for the prevalence of inadequate intakes of dietary components. The first part, estimating habitual intakes from short-term measurements, is statistically by far the most complex. Therefore, AGE MODE was developed with a main focus on this first part of the evaluation procedure.

The core of the procedure in AGE MODE consists of the description of the observed intakes by age using a fractional polynomial. From the intake data the model generates estimates for the habitual intake distribution, with mean habitual intakes and intake percentiles given for each year of age. Once the habitual intakes have been estimated, the EAR-cut-point approach

as well as the probability approach can be conducted within AGE MODE to estimate the prevalence of inadequate intakes.

Folate intake and vitamin A intake from the third Dutch National Food Consumption Survey (DNFCS-3) (1997/98) were used to illustrate AGE MODE. The results are satisfying, but some suggestions are made to further improve the model.

Comparison with other methods
The basic idea of AGE MODE, fitting an age dependent function, is based on ideas of Slob, implemented in 'STEM'. However, the applied methodology differs considerably. The strengths of AGE MODE are more flexible transformations (Box-Cox transformations in stead of log transformation), a fractional polynomial regression in stead of fixed functions and a back transformation step performed by Monte Carlo Simulations.

Another, nowadays frequently used method to estimate habitual intakes, is the Nusser method. The Nusser method estimates habitual intake distributions for specified gender and age groups. However, the feature of age dependency shows clear advantages above the creation of subgroups, as part of the variance in intakes can be explained by age. Also, when smaller subgroups are taken the reliability of the estimate may be poor due to the small numbers. Furthermore, the Nusser method is rather a 'black box'. This may bring about incorrect use. Furthermore, there is no insight into why problems arise and what can be done to solve them. Some features, that are present in the Nusser method, like the possibility to estimate the proportion of consumers and non-consumers for less frequently consumed dietary compounds, still need to be developed in AGE MODE.

Comparison of habitual folate intake distributions estimated with both AGE MODE and the Nusser method leads to the conclusion that the estimates produced by both methods are comparable but that AGE MODE has methodological advantages.

Assessing folate intake with AGE MODE
Folate intake data were obtained from the DNFCS-3 (1997/98) and habitual intake distributions were estimated. Mean habitual intakes range from 190 to 217 µg/day in adult males, and from 161 to 179 µg/day in adult females, the Estimated Average Requirement (EAR) being 200 µg/day. The EAR for folate was obtained from the DRIs set by the Health Council in 2003. Comparing the EAR with the findings of the study suggests that up to 80% of adolescent women has an inadequate folate intake from foods. For men the prevalence is about 20% lower, but still high.
Also requirement distributions were specified to be able to apply the probability approach, elucidating the complexity of doing so.

Assessing vitamin A intake with AGE MODE

Also vitamin A intakes, expressed in Retinol Activity Equivalents (RAEs), were calculated from the DNFCS-3 data. For this purpose RAEs were estimated for all products in the 2001 NEVO table. Habitual vitamin A intakes estimated with AGE MODE keep on increasing over the entire age range of 1 to 70, and range from 864 to 1174 RAE/day in adult males (EAR ~620 RAE/day), and from 684 to 834 RAE/day in adult females (EAR ~530 RAE/day). The requirements for vitamin A have been estimated with the Olson formula, using Dutch reference weights and growth factors. Especially in adolescents intake inadequacy seems to be high. It appears that up to 39% of adolescent women do not meet vitamin A dietary reference intakes. The health consequence of the potential inadequate supply to the population especially of folate, and to a lesser extent of vitamin A, needs to be assessed and trends in intake need to be closely monitored.

Conclusions and recommendations

In this report the newly developed age dependent dietary evaluation model (AGE MODE) is described and evaluated. Focus has so far been on micronutrients, but the model can also be applied to other dietary components. AGE MODE shows clear advantages above currently used methods to estimate habitual intakes like the Nusser method. The feature of age dependency is very important in this respect. Also, the model is transparent and clearly describes the data.

Nationally and internationally, a common sound dietary evaluation procedure should be established. If AGE MODE would be part of this (inter)nationally procedure, the method needs to be further developed. Most important is to study options to make the age dependent polynomial more flexible, so that it may even better describe the data by the use of co-variables; or to discern between consumers and nonconsumers.

With regard to the general framework for dietary evaluation use of the probability approach is called into question, as it appeared not possible to specify a requirement distribution without doing additional assumptions that may or may not be valid. Although application of the EAR cut-point approach involves implicit assumptions, it is much more practical, and therefore suggested for use, at least until the DRIs have been adapted to provide all the information necessary to specify requirement distributions.

1. Introduction

1.1 Background

The Dutch National Food Consumption Surveys (DNFCS)[1] provide two-day dietary intake data for a large population sample. It gives us insight into food consumption of the Dutch population and allows calculation of (micro)nutrient intakes. So far the intake of micronutrients was evaluated merely qualitatively by comparing mean intakes of specified gender and age groups with dietary reference intakes. In order to set policy priorities and to determine the need for political measures a quantitative evaluation of micronutrient intakes is warranted.

In a previous report, 'Method for micronutrient evaluation of the Dutch population: folate as an example'[2] a general approach has been proposed to evaluate micronutrient intake in the Dutch population in relation to dietary reference intakes (Waijers et al., 2004). An important step in the evaluation procedure is to estimate the habitual intake distribution from the two-day dietary data. Two methods developed for this purpose, STEM and the Nusser method, have been evaluated and compared. It was concluded that existing methods should be further examined and developed specific for assessing micronutrient intake in relation to requirements.

1.2 Objectives

A new model: AGE MODE
In accordance with the recommendations in the former report we have searched for the best way to obtain an adequate and reliable tool to assess the intake of micronutrients. An age dependent dietary evaluation model (AGE MODE) was developed. In this report AGE MODE is described and demonstrated, and its features and potential are discussed.

In order to evaluate whether the model and the general approach for dietary evaluation are supported, an expert meeting was organized. During this meeting on November 1st 2005 the new model was introduced to some experts in the area of micronutrient evaluation. In addition input was requested on several complex issues in the evaluation procedure. Appendix 1 contains a short report of the expert meeting. The conclusions from the expert meeting have been taken into account in the making of this report.

[1] In Dutch: 'Voedselconsumptiepeilingen' (VCP's)
[2] Report in Dutch; Dutch title: 'Methode voor schatting van de prevalentie van inadequate innemingen van micronutriënten. Toepassing: foliumzuur'

Applied for folate and vitamin A
The second objective in the report was to apply this new method for two micronutrients. In other words to evaluate the intake of folate and vitamin A in the Dutch population using this new model.

1.3 Outline

This report starts off with a recapitulation of the general framework to assess micronutrient intakes. This is followed by a detailed description of AGE MODE in Chapter 3. Important methodological issues are discussed. A comparison with other methods can be found in Chapter 4. In the next chapter, Chapter 5, AGE MODE is applied to estimate habitual folate intakes and to estimate the prevalence of inadequate intakes of the vitamin folate. In Chapter 6 the same is done for vitamin A. Final conclusions and recommendations can be found in the last chapter.

2. General framework for dietary evaluation

A general framework to assess micronutrient intake in relation to dietary reference intakes in the Dutch population has been proposed previously (Waijers et al., 2004). The evaluation procedure consists of three parts:

1 Estimating the habitual intake distribution of the micronutrient
2 Describing the (distribution of) requirements for the micronutrient
3 Estimating the prevalence of inadequate intakes of the micronutrient by combining habitual intakes with requirements.

2.1 Estimating the habitual intake distribution of the micronutrient

The DNFCs provide two-day dietary intake data, or observed intakes. Observed intakes can be used for example to evaluate short-term risks of exposure to a harmful dietary substance. The variance in intake comprises both the intra-individual (or day-to-day) variance and the inter-individual variance (Willett, 1998). However, to correctly evaluate long-term intakes of micronutrients not the observed intakes but the mean intake over a longer period, the habitual intake, is needed. The habitual intake distribution only contains the variation between individuals (inter-individual variation).

Therefore, the habitual intake distribution needs to be estimated from the observed intakes by eliminating the intra-individual variation. This is rather complex. Several statistical methods have been proposed (Hoffmann, 2002).
The method that is currently used most is the Nusser method, developed at Iowa State University (Nusser et al., 1996; Guenther et al., 1997). Software packages (SIDE and C-SIDE) are available to apply this method (Iowa State University, 1996a; Iowa State University, 1996b). It is a very flexible method, but may adhere strongly to the data. In addition the method requires subgroups (based on age) to be specified.
Another method that has been proposed to estimate habitual intakes from short-term measurements is the Statistical Exposure Model (STEM) (Slob, 1993a; Slob, 1993b). Although this model has also serious limitations (see paragraph 4.1), its basic idea, estimating a regression function of intakes on age, is very interesting. Not only are smaller numbers of observations sufficient to obtain estimates, it also provides new opportunities for application in micronutrient evaluation.
The new model AGE MODE which is described in this report is also based on the idea of estimating intakes with a regression function. In this model habitual intakes are estimated as a function of age.

2.2 Describing the (distribution of) requirements for the micronutrient

To be able to estimate the proportion of individuals for whom intake is inadequate not only the intake distribution, but also the (distribution of) requirements for the micronutrient in the population need to be known. Information on the requirements is obtained from the Dietary Reference Intakes (DRIs). In the Netherlands DRIs are established by the National Health Council. Recently the terminology and definitions used in the Netherlands have been adjusted and now correspond with the American DRIs.

Box 2.1: Dietary Reference Intakes: definitions[1]

The term 'Dietary Reference Intakes (DRI)' refers to a set of reference values for nutrients for use in dietary evaluation:

Estimated Average Requirement (EAR)	level of intake sufficient to meet the requirement for half of the healthy individuals in a particular life-stage and gender group
Recommended Dietary Allowance (RDA)	level of intake sufficient to meet the requirements for nearly all healthy individuals in a particular life-stage and gender group (EAR + 2*sd)
Adequate Intake (AI)	level of intake assumed to be sufficient for almost al individuals in a particular life-stage and gender group. Used when a RDA cannot be determined.
Tolerable Upper Intake Level (UL)	the highest average daily nutrient intake level likely to pose no risk of adverse health effects to almost all individuals in the general population.

[1] Terminology in Dutch:
Estimated Average Requirement (EAR) ~ 'gemiddelde behoefte'
Recommended Dietary Allowance (RDA) ~ 'Aanbevolen Dagelijkse Hoeveelheid' (ADH)
Adequate Intake (AI) ~ 'Adequate Inneming' (AI)

Each nutrient has a set of DRIs (Box 2.1). A nutrient has either an Estimated Average Requirement (EAR) and a Recommended Dietary Allowance (RDA) that is derived from the EAR by adding 2 times the SD, or an Adequate Intake (AI) (Institute of Medicine, 2000; Gezondheidsraad, 2003). The AI is the intake level that is assumed to be adequate for (almost) the entire population. It is used when the EAR cannot be determined. At population level the EAR is the reference value that should be used to obtain estimates of the prevalence of inadequate intakes (Institute of Medicine, 2000; Jahns et al., 2003). The EAR is based on specific criteria of adequacy, derived from published research results.

In general, for many nutrients, information on requirements is limited. Therefore, estimating nutrient requirements is a difficult task. If the EAR cut-point approach, described below, is used to estimate the prevalence of inadequate intakes, only the EAR is required. If, on the other hand, the probability approach is used, which is also discussed in the next paragraph, a distribution describing the requirements for the micronutrient in the population needs to be specified. For this purpose information on the variation in requirements and the shape of the distribution is needed. However, from the DRIs generally no information is available on the distribution of requirements in the population, only a coefficient of variation (CV) may be given.

2.3 Estimating the prevalence of inadequate intakes of the micronutrient

To obtain estimates for the prevalence of inadequate intakes for a certain micronutrient, i.e. estimates of the proportion of individuals for whom intake remains below the individual requirement, the habitual intake distribution needs to be related to the requirements. Two approaches exist: the EAR cut-point approach (Beaton, 1994) and the probability approach (National Research Council, 1986). Both approaches have been described in detail in a previous report (Waijers et al., 2004), but are summarized in Box 2.2.

With the probability approach an accurate estimate of the number of individuals with an inadequate intake can be obtained, assuming that the specified requirement distribution reflects the true distribution of requirements in the population. A cut-point approach does not require specifying a requirement distribution. The EAR is sufficient to obtain prevalence estimates. This approach is therefore more straightforward. However, for this approach assumptions are made, violation of which may result in biased prevalence estimates (Waijers et al., 2004).

In accordance with the recommendations in the previous report the National Health Council has declared to favor the probability approach. However, as little is actually known on the true distribution of requirements in the population, in order to specify a requirement

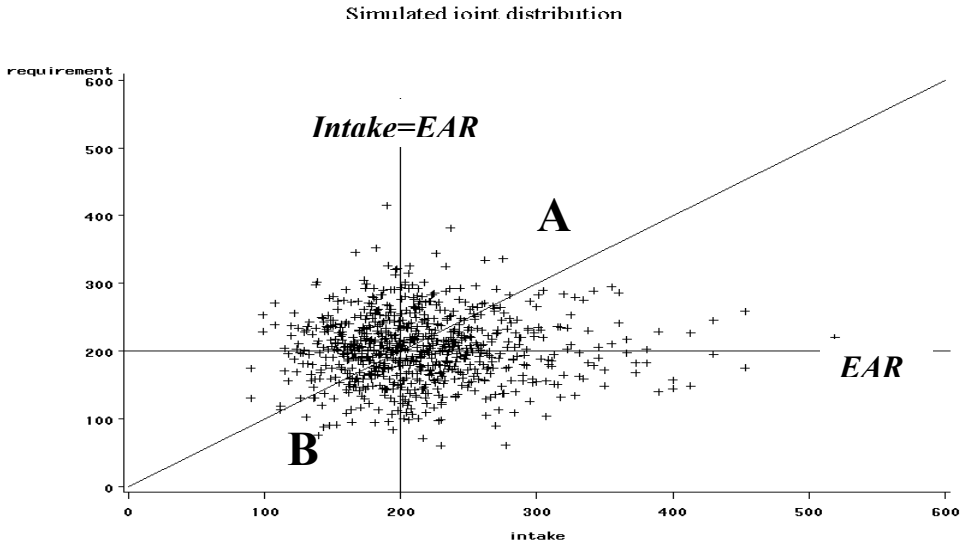
distribution many additional assumptions need to be made. The DRIs do not provide enough information to specify requirement distributions.
Initially, from the expert meeting, it was suggested that in order to let the final prevalence estimates be generally accepted, these additional assumptions should be decided on by the members of the Steering Committee on Nutrition of the National Health Council (see Appendix 1). If consensus was achieved, the requirement distributions could then be specified (as a function of age). However, at the moment this idea appeared to be not practicable.

Specification of a requirement distribution is extremely complex and choices made may be called into question. Although, the EAR cut point approach involved assumptions that are not tested nor made visible, we suggest for practical reasons to use the EAR cut-point approach until the DRIs have been adapted to provide all the information necessary to specify requirement distributions.
It should be noticed that this is a general issue that needs attention, irrespective of the methodology used to estimate habitual intakes.

Box 2.2: Two approaches to estimate the proportion of individuals with inadequate intakes.

The EAR cut-point approach
Counting the number of individuals with a habitual intake below the EAR
→the number of individuals to the left of the vertical line indicating the EAR

The probability approach
Calculating a risk curve from the specified requirement distribution and calculating and summing the risks of inadequacy for all individuals in the population from the habitual intake distribution and the risk curve.
→the number of individuals above the diagonal line



3. Age dependent dietary evaluation model (AGE MODE)

In line with the conclusions from the previous report (Waijers et al., 2004) it has been endeavored to develop a new model, in which intakes are considered age dependently, to evaluate micronutrient intakes. This was implemented in S-PLUS (Anonymous, 2005), a sophisticated software package for statistical analysis and data-visualization. Computational and programming efforts have resulted in a new model called 'AGE MODE': Age dependent dietary evaluation model. Although the focus has so far been on micronutrients, it is a general methodology that can be applied to all types of dietary compounds.

3.1 AGE MODE: model description

AGE MODE was developed with a main focus on the first part of the evaluation procedure, estimating habitual intakes. This part is statistically by far the most complex. However, also the third part can be performed in AGE MODE.

AGE MODE contains several steps. The core of the procedure consists of the description of the observed intakes by a fractional polynomial as a function of age, which is fitted to the data by linear regression. From the intake data the model generates estimates for the habitual micronutrient intake distribution, with mean habitual micronutrient intake and intake percentiles given for each year of age. Once the habitual intakes have been estimated it is (technically) rather straightforward to estimate the prevalence of inadequate intakes. The consecutive steps in AGE MODE are described below. A more detailed description, containing the formulas, can be found in Appendix 2.

Step 1: Transformation to normally distributed data
Intake data are generally skewed, whereas the linear regression requires normally distributed data. Therefore the data need to be transformed. For this purpose a Box-Cox transformation is applied. The Box-Cox method searches for the best transformation to obtain normally distributed data, reflected by the transformation parameter lambda.

Step 2: Fitting a fractional polynomial to the transformed data
Since there are no physical relations which describe the relation between intakes and age, fractional polynomials are chosen to describe the observed intakes as a function of age. After the Box-Cox transformation automatically the best fitting fractional polynomial is found and the regression parameters are estimated.

Step 3: Estimating the inter- and intra-individual variance
The obtained regression model is refit by a mixed-effect model. This method allows to

estimate the inter-individual variance (the variance between individuals) and the intra-individual variance (the variance within the individual or day-to-day variance).

Step 4: Identification of possible outliers

Outliers can seriously influence the estimates and therefore deserve special attention. In AGE MODE outliers are identified (on the transformed scale) by a statistical test proposed by Grubbs and Beck (Grubbs and Beck, 1972), which is based on the fact that the residuals of the mixed-effect model are normally distributed with zero mean and estimated (known) variance. This test calculates cut offs beyond which occurrence of an observation is very unlikely. Observations beyond these cut offs are considered outliers and are removed.

Step 5: Check of λ

Finally a check of normality is carried out with some graphs and a normality test, which always rejects the null-hypothesis, given the large amount of data. Therefore the Box-Cox transformation is carried out again, because the residuals should be at least symmetrically distributed. The estimated Box-Cox parameter, reported as 'λ-check' should be near to one, which means that no additional transformation is needed.

Iterations of steps 1 to 5

Outliers can influence the Box-Cox estimate, the powers of the fractional polynomial and the estimates of the mixed-effect model. Therefore, if outliers have been removed, steps 1 to 5 need to be repeated until no outliers are detected anymore. Two or three iterations seem to be sufficient in practice.

Step 6: Back transformation to the original scale by Monte Carlo simulations

The habitual intake distribution reflects the variation in mean individual micronutrient intakes for individuals of a particular age. To obtain the habitual micronutrient intake distributions on the original scale the function obtained in step 1-5 needs to be back transformed. Direct back transformation of the characteristics of the distributions on the transformed scale by applying the inverse function of the forward transformation is not possible, because the intra-individual variation needs to be left out. To avoid complex calculations the back transformation step is performed by Monte Carlo simulations. For each year of age *n* individuals are simulated according to the linear mixed effect model and with the inter-individual variance. For each individual *k* days are simulated, normally distributed with mean zero and the variance equal to the intra-individual variance. All *k* x *n* intakes on the transformed scale are back transformed to the original scale. Next the *k* intakes per individual are averaged to obtain the individual habitual intake. Consequently the habitual intake distribution of each year of age is obtained. A fast back transformation with $n = k = 1{,}000$ takes only two minutes. To obtain smooth curves *n* and *k* should be at least 10,000 each, which takes about two hours. These back calculations can easily be carried out in batch mode.

This part of AGE MODE is a substantially different from the Nusser method, since it uses the fractional polynomial as a model description for the data. Therefore, the intra-individual variation is integrated out by generating a long sequence of observations for each individual under the assumption that the inter-individual variation does not change over age. If this is the case the model should be extended, which is possible since a mixed effect model is used.

Step 7: Additional steps in dietary evaluation
Estimating habitual intake distributions generally is only a first step in dietary evaluation. Additional steps in dietary evaluation can also be accomplished in AGE MODE. Population intakes are for example evaluated through comparison with Dietary Reference Intakes, including Tolerable Upper Intake Levels. If information on required levels of intake is provided, it is straightforward to estimate the fraction of the population with a habitual intake above or below the requirements. Most straightforward is the use of a cut-off value, but also a probabilistic approach can be executed in AGE MODE applying Monte Carlo Simulations if a requirement distribution has been specified. Both methods can easily be performed in AGE MODE since all simulated intakes per year of age are saved in the model.

3.2 AGE MODE exemplified by folate

3.2.1 Estimated habitual folate intakes

We used folate intake from the third Dutch National Food Consumption Survey (1997/98) (DNFCS-3) to illustrate AGE MODE. To gain insight into the consequences of analytical choices for the final estimates several analyses have been performed.

The consecutive steps in AGE MODE are illustrated with folate intakes from males and females, aged 1 to 70. Model estimates are presented in Table 3.1a and 3.1b. Shown are numbers of observations and individuals, estimates for the transformation parameter lambda, the function for the fitted polynomial (on the transformed scale), and the number of identified outliers according to the criteria of Grubbs and Beck (Grubbs and Beck, 1972). The ‘λ-check’ indicates the additional transformation required (on the transformed scale) to obtain normally distributed data and should be close to 1 (no further transformation required). The results are satisfying.

All identified outliers were removed and analyses were repeated until no additional outliers were observed. It can be seen that removal of outliers affects the function of the polynomial on the transformed scale. For males not just the coefficients in the regression equation change from the first to the second iteration, but the polynomial takes a different function. To what extent this affects final habitual intakes will be visualized later on.

Figure 3.1 to 3.3 are illustrations of the consecutive steps (for males only). These figures mainly serve to illustrate how AGE MODE works. Figure 3.1 shows the result of the

Table 3.1: Steps 1 to 3 of estimating the habitual intake as a function of age in AGE MODE: transformation, fitted polynomial on transformed scale, and the number of outliers removed for 3 series of input data.

a) Males from 1 to 70 years

			step
Round 1	Number of observations	5432	
	Number of individuals	2716	
	Box-Cox transformation, lambda	0.122	1
	Fitted fractional polynomial	$y \sim 7.7-1.4*age^{-1} -2.6* age^{-1}* \log(age)$	2-3
	Number of outliers	11	4
	'λ-check'	1.096	5
Round 2	Number of observations	5410	
	Number of individuals	2705	
	Box-Cox transformation, lambda	0.188	1
	Fitted fractional polynomial	$y \sim 6.4+0.8*age^{0.5} -0.06*age$	2-3
	Number of outliers	1	4
	'λ-check'	1.021	5
Round 3	Number of observations	5408	
	Number of individuals	2704	
	Box-Cox transformation, lambda	0.194	1
	Fitted fractional polynomial	$y \sim 6.5+0.8*age^{0.5}-0.06*age$	2-3
	Number of outliers	0	4
	'λ-check'	1.013	5

b) Females from 1 to 70 years

			step
Round 1	Number of observations	6056	
	Number of individuals	3028	
	Box-Cox transformation, lambda	0.281	1
	Fitted fractional polynomial	$y \sim 11.7-2.7*age^{-1} -3.4*age^{-1}*\log(age)$	2-3
	Number of outliers	13	4
	'λ-check'	0.844	5
Round 2	Number of observations	6030	
	Number of individuals	3015	
	Box-Cox transformation, lambda	0.219	1
	Fitted fractional polynomial	$y \sim 0.59-2.0*age^{-1} -2.4*age^{-1}* \log(age)$	2-3
	Number of outliers	1	4
	'λ-check'	0.941	5
Round 3	Number of observations	6028	
	Number of individuals	3014	
	Box-Cox transformation, lambda	0.184	1
	Fitted fractional polynomial	$y \sim 8.6 -1.6*age^{-1}-2.2*age^{-1}* \log(age)$	2-3
	Number of outliers	0	4
	'λ-check'	0.985	5

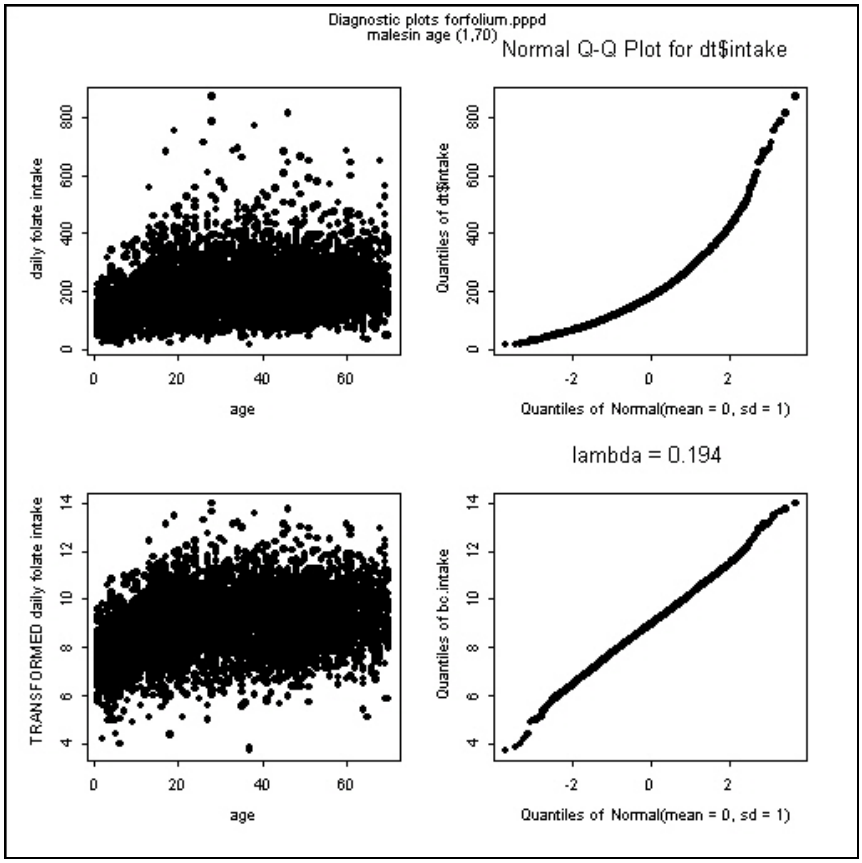


Figure 3.1: Box-Cox transformation: Observed intakes before transformation (upper figures) and after transformation (lower figures) for males (1-70 years), 3rd iteration.

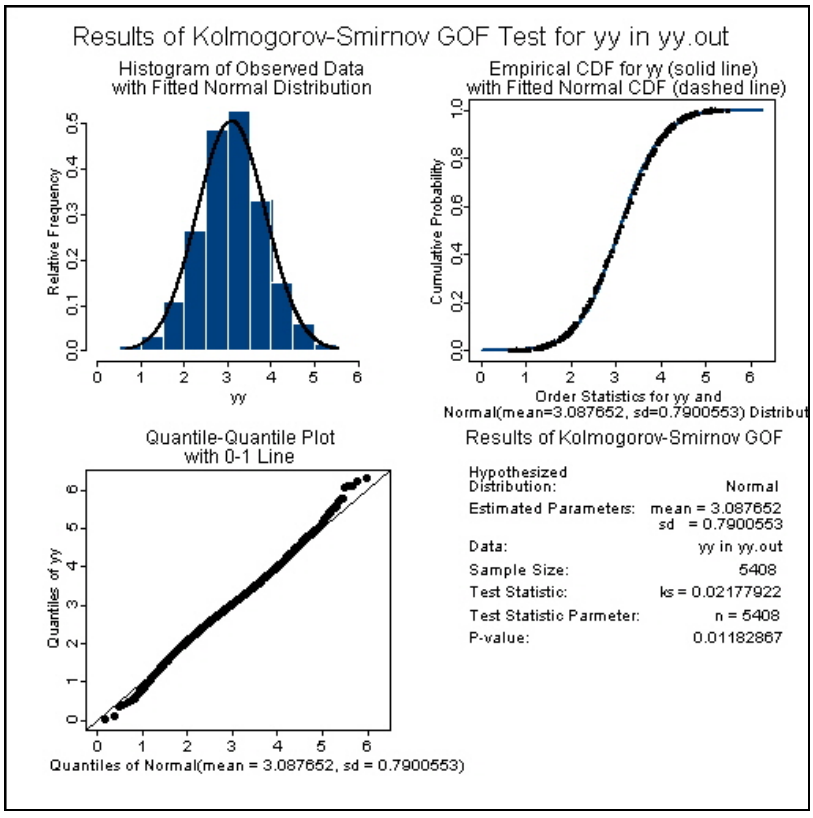


Figure 3.2: Normality test of the transformed intakes for males (1-70 years), 3rd iteration.

transformation. Age dependent plots and QQ-plots, that give insight into the extent to which the data are normally distributed, are displayed. The more the transformed observations lie along the straight diagonal line, the more the obtained distribution acquires normality. Another QQ-plot, that of the regression residuals, is portrayed in Figure 3.2. The large numbers make the Kolmogorov Smirnov-test (to test whether the data are normally distributed) significant, but the QQ-plot shows satisfactory results. This can also be concluded from the 'λ-check', being near 1. The grafted polynomial that is fit through the transformed intakes is shown in Figure 3.3. In the left pane of this figure outliers are depicted. It can be seen that outliers are mainly at the higher site.

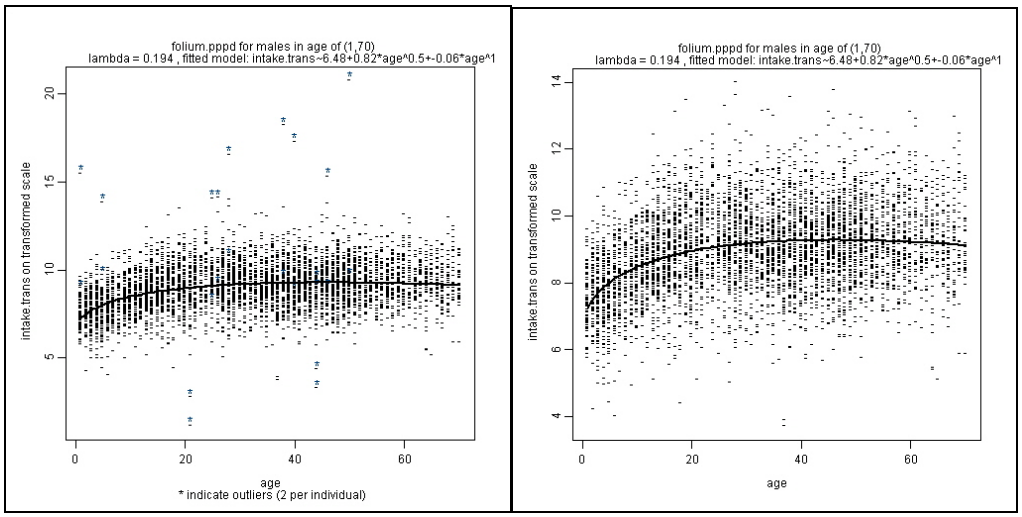


Figure 3.3: Grafted polynomial through the transformed intakes for males (1-70 years), 3rd iteration. In the left pane outliers are indicated, being removed in the right pane.

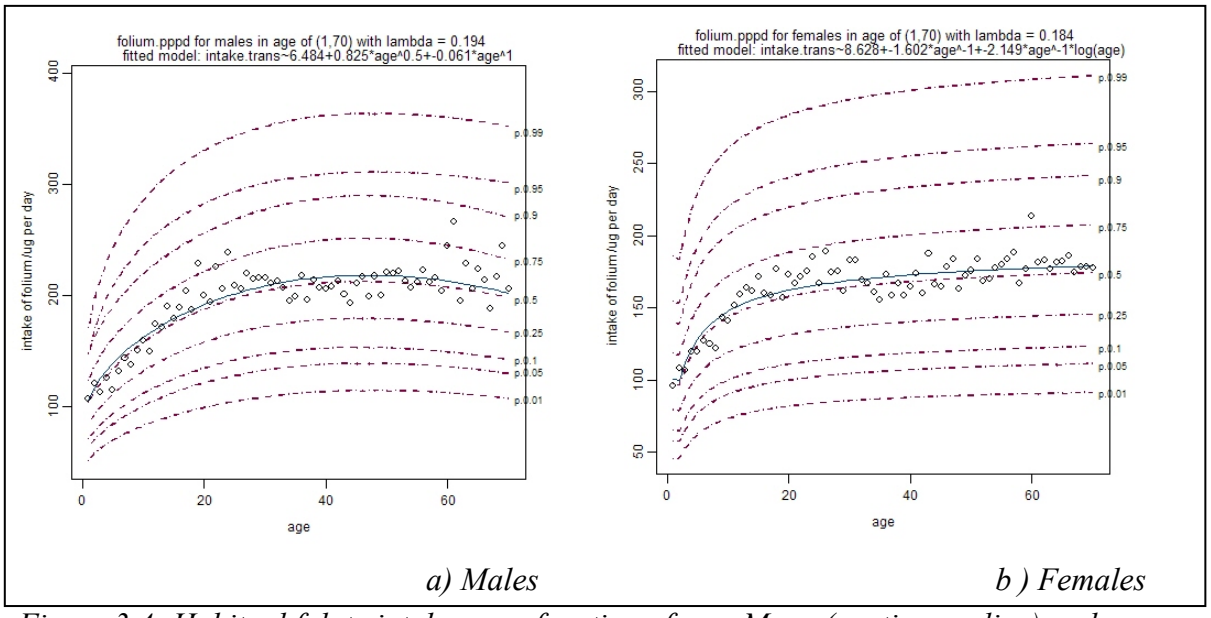


Figure 3.4: Habitual folate intakes as a function of age. Mean (continuous line) and percentiles of the habitual intake distribution. The dots represent the mean observed folate intakes for each age year.

Finally, in Figure 3.4 resulting habitual intakes are presented for males and females. The dots represent the mean observed folate intakes for all individuals, except the removed outliers, in a certain age year. The estimated mean habitual intakes seem to adequately describe the intakes.

Some examples of resulting habitual intake distributions are depicted in Figure 3.5. Several issues, like the age range that is departed from, and (removal of) outliers may affect the habitual intake estimates. These aspects are more closely examined in the next paragraphs.

3.2.2 Estimating the prevalence of inadequate folate intakes

In the next step intakes are related to requirements, which is statistically rather straightforward and can also be accomplished in AGE MODE. For a detailed description of folate requirements we refer to second paragraph of the next chapter. Figure 3.6 represents the age dependent estimates for the prevalence of inadequate folate intakes. These prevalences have been calculated as the number of individuals (per age) with a habitual folate intake below the EAR (EAR cut-point approach).

The sharp angle at the age of 16 can be explained by the fact that the requirements at that age reach the maximum of 200 μg/day, while intake still rises (thus prevalence of inadequate intakes decreases). This can be seen from Figure 3.7. Before this age the requirement increases stronger than intake increases. AGE MODE thus also gives insight into the requirements.

3.3 The effect of age ranges and subgroups on the estimation of habitual intakes

With AGE MODE habitual intakes are estimated as a function of age. It is obvious that the age range that serves as input determines the form of the polynomial that is fit through the data. In theory all age ranges can be used as input for the model. For example, if intake data are limited to children from 1 to 12 years, the polynomial may take a linear form, as for children intake will increase with age. And if data are limited to 19-to-30-year old men, no polynomial is fit (the slope being zero), meaning that age does not influence the level of intake within this age range. Using the age range of 1 to 70 years as input will, on the other hand, results in the shown polynomials.

We examined the effect of using different age ranges by estimating the habitual folate intake, taking various age ranges as input. First however the (observed) intakes need to be inspected to get acquainted with the data and to detect irregularities. This should in fact be done before any analysis, but is often omitted. An advantage of AGE MODE is that automatically mean observed intakes according to age are calculated and presented, as in Figure 3.8. We have

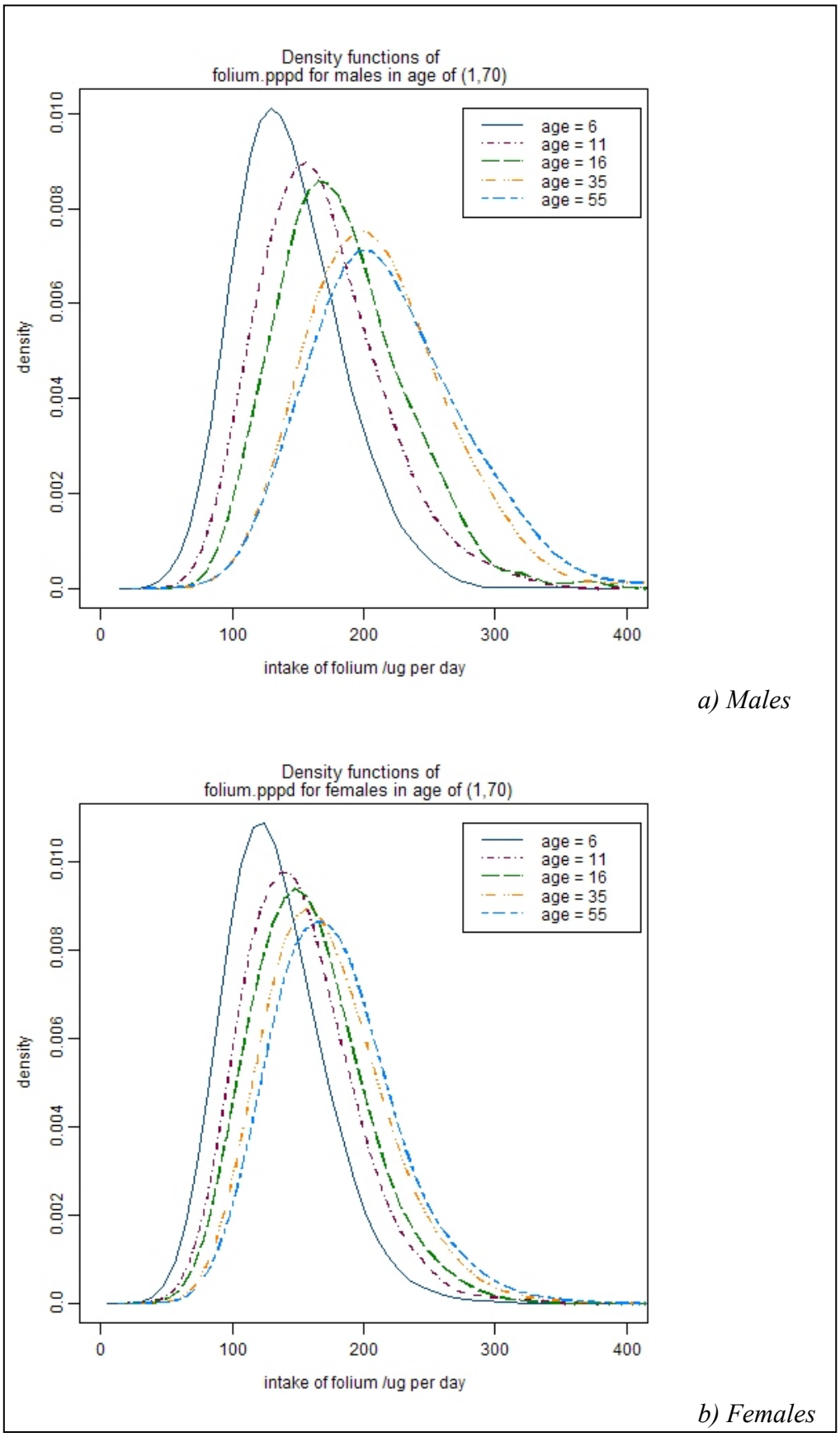


Figure 3.5: Examples of resulting habitual intake distributions of folate for males (a) and females (b) of several ages.

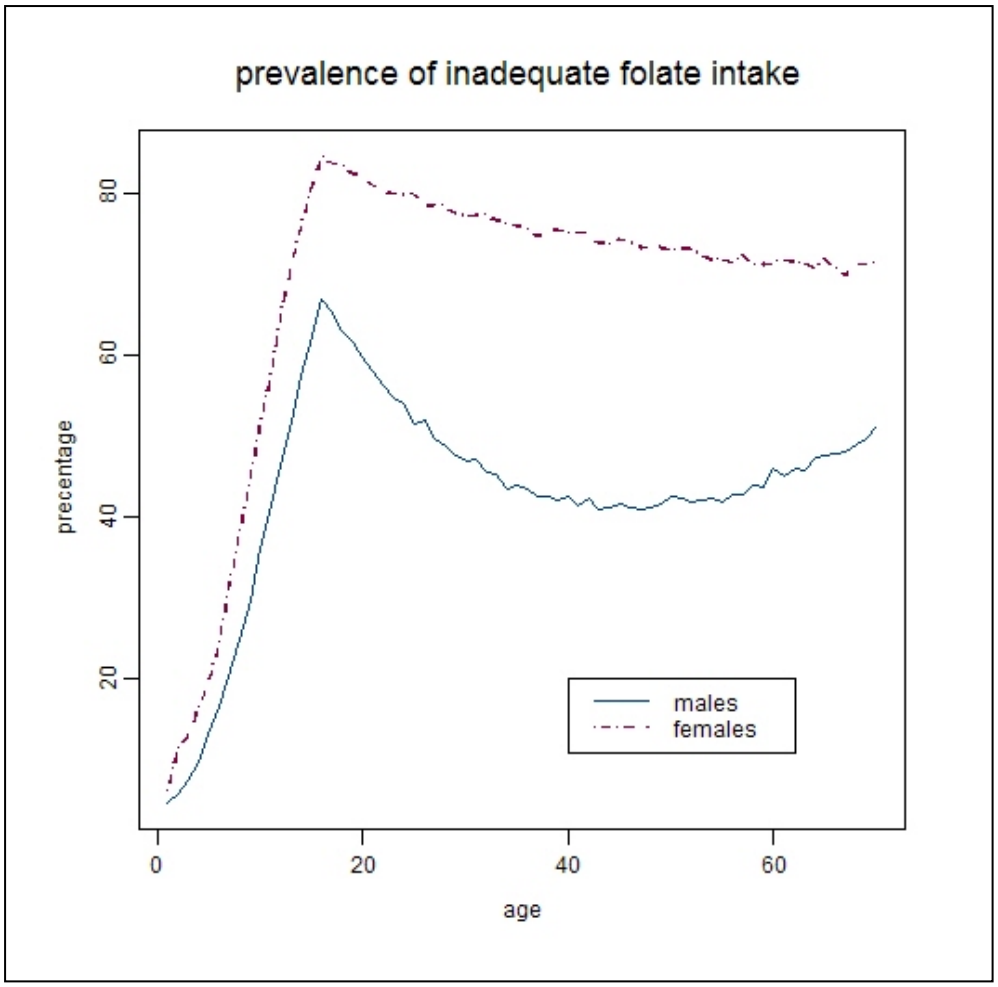


Figure 3.6: Estimated prevalences of inadequate folate intakes as a function of age for males and females.

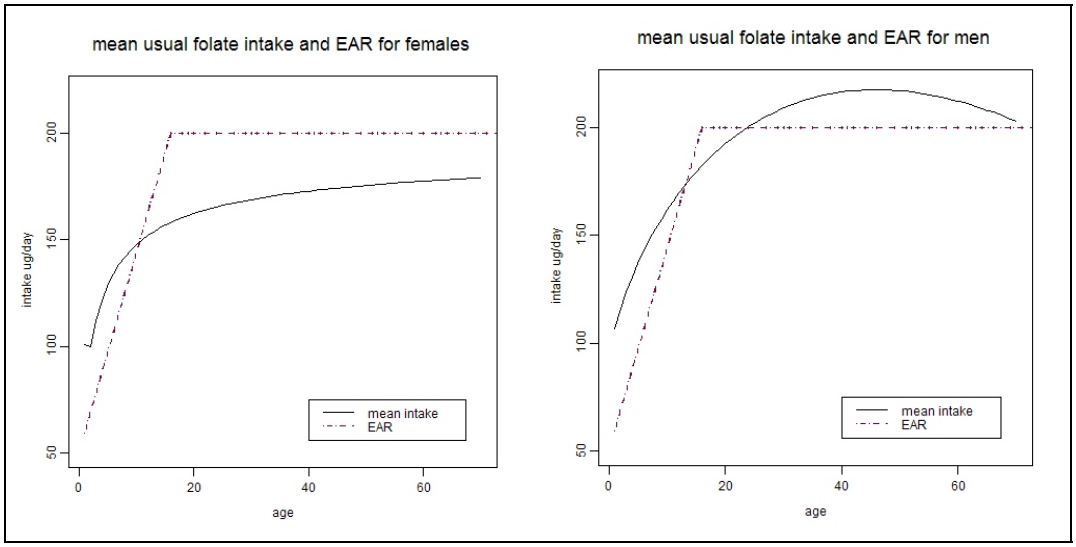


Figure 3.7: Course of the mean habitual intake and the Estimated Average Requirement in males and females as a function of age.

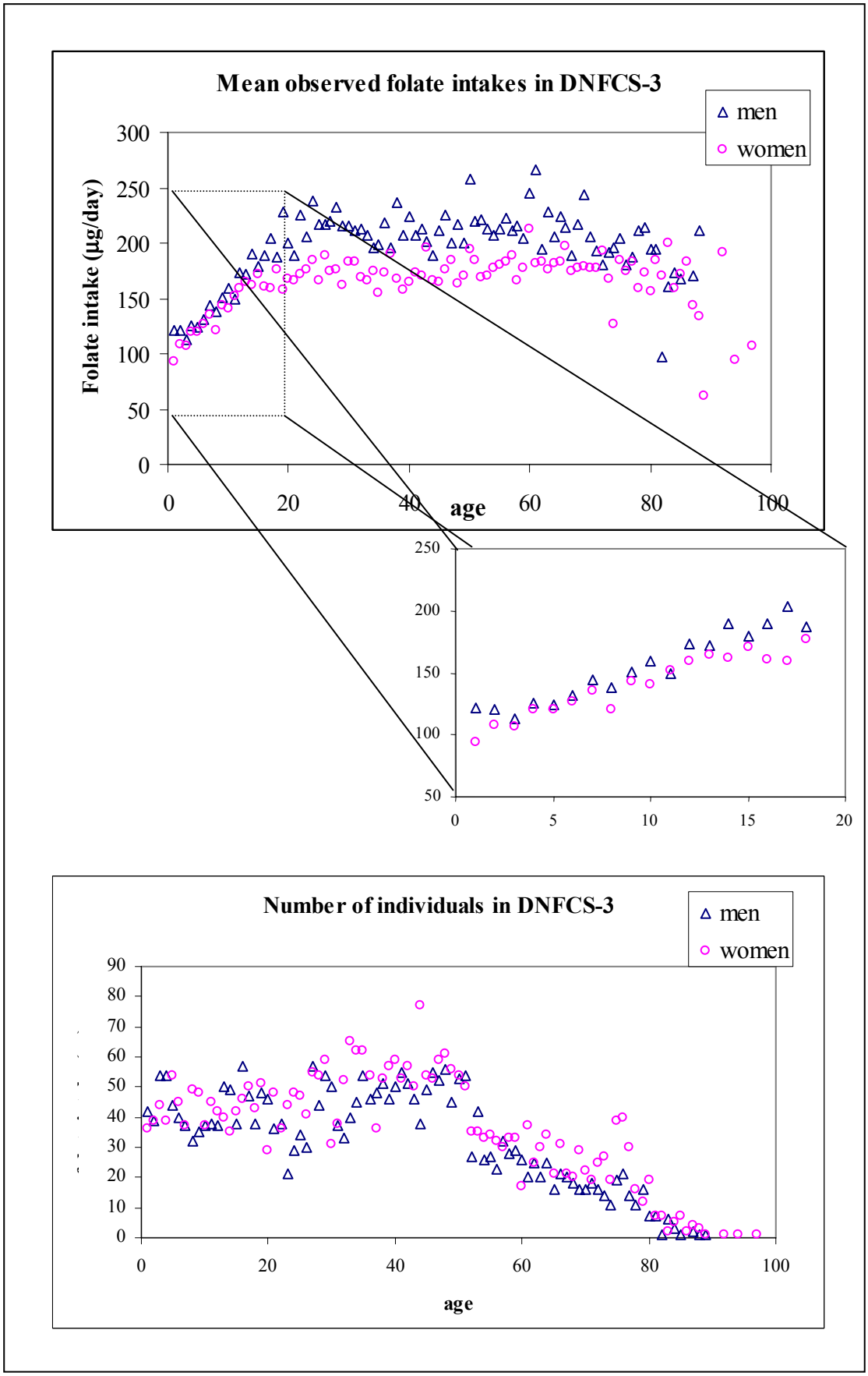


Figure 3.8: Mean folate intakes and numbers of men and women for each year of age.

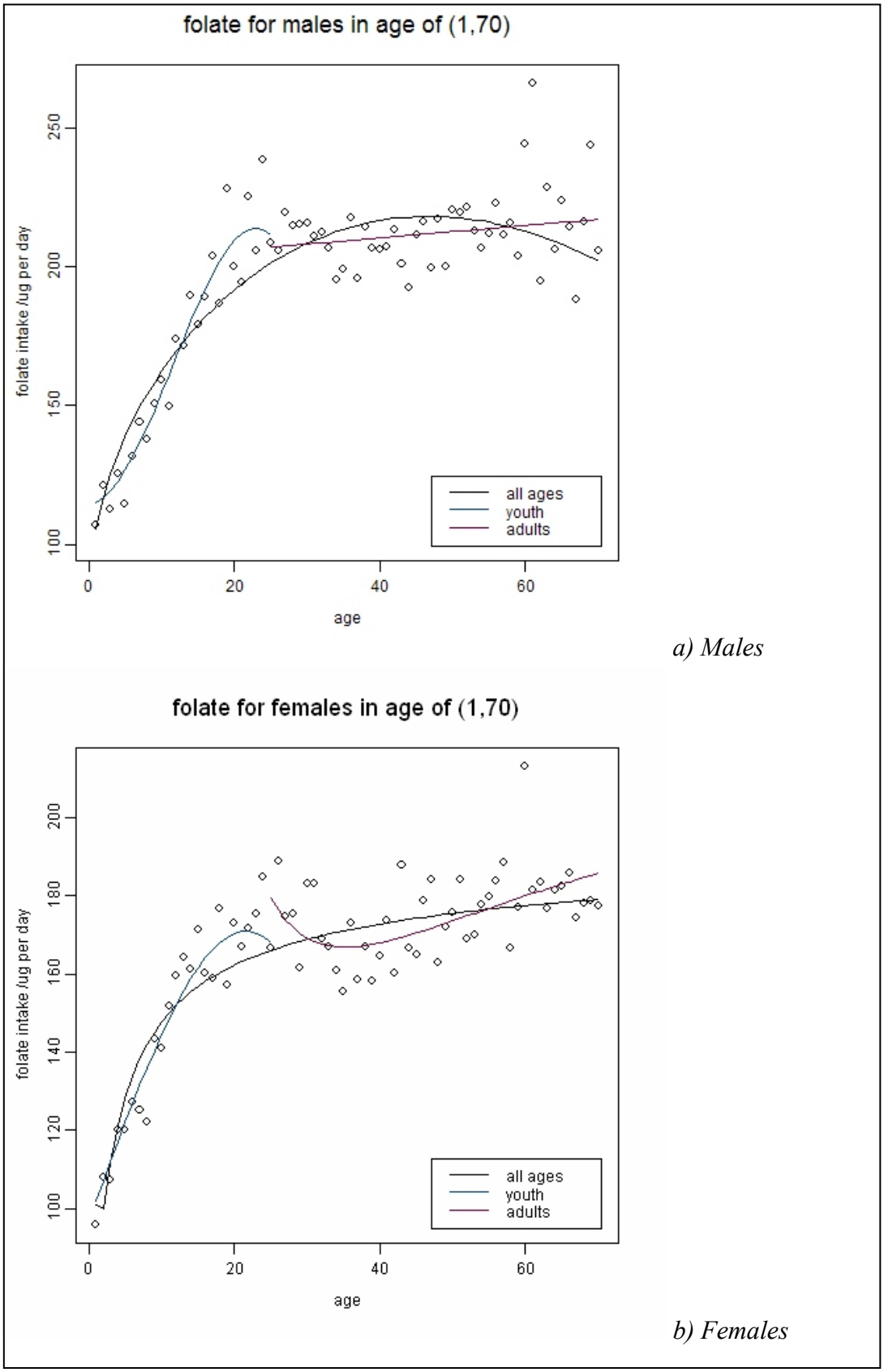


Figure 3.9: Mean habitual folate intakes in males (a) and females (b); input age ranges 1 to 25, 25 to 70, and 1 to 70 years.

also depicted the numbers of observations for each age, as the reliability of the mean depends on the number of individuals on which it is based.

The important question is now how robust the estimates from the model are for different age ranges. To gain more insight into this matter sensitivity analyses were conducted. Results are shown for males and females from 1 to 25 and 25 to 70 vs. 1 to 70 years (Figure 3.9). In the extremities of the (smaller) age ranges and in the points of inflection, resulting mean habitual intakes differ. However, these differences are very small, especially when the variation in intake is beard in mind (Figure 3.8). And these differences fall within the uncertainty of the measurement. Therefore the best option seems to use the greatest possible age range to make best use of the data.

In this example of folate, intakes for men and women are approximately equal until the age of 13, as can be seen from Figure 3.8. Beyond this age intakes for men are higher and keep increasing until age of 24, whereas for women the level of intake stabilizes around the age of 18. It seems therefore that for these data males and females can be considered together till the age of 13, but should be considered separately beyond this age.

Considering these findings and the general fit of the polynomial through the data (mean observed intakes) it appears important to study how the second step in AGE MODE can be further improved. This could be obtained by increasing the order of the polynomial, or using B-spline methods or joint points when fitting the polynomial. However, one should be cautious to prevent ‘overfitting’.

3.4 Outliers closer examined

AGE MODE provides the possibility to remove outliers, based on the statistical test proposed by Grubbs and Beck (Grubbs and Beck, 1972). The problem of outliers is complicated (Bakker and Slob, 2005). The central question is whether or not outlying observations should be removed. On the one hand they can disturb calculations, but on the other hand they can contain true information. Statistical outliers should be more closely examined for possible explanations before deciding whether or not they are removed. The members of the expert meeting on AGE MODE in November 2005 (Appendix 1) felt that it would be incorrect to remove outliers if these intakes do really occur (and can be explained). However, although explainable, statistical outliers may severely disturb the data and analysis.
If a logical explanation for the outlier exists a possibility would be to remove not only the outlier, but all data associated with the same explanation. In fact a subpopulation is discerned in this way. For example, liver consumption often causes extreme intakes for folate. In that case knowledge of true occurrence and frequency of (liver) consumption is of interest.

Table 3.2: Consumption data for low outliers identified applying the test of Grubbs and Beck (Grubbs and Beck, 1972) in men (a) en women (b).

a) Men

AGE	TOTAL FOLATE (µg)	TOTAL ENERGY (kJ)	PRODUCT	FOLATE CONTENT (µg/100g)	CONSUMED QUANTITY (g)	FOLATE from PRODUCT (µg)
21	3	389	Water	0	470	0
			Broth	1.36	200	2.73
21	9	2857	Semi-skimmed milk	5.16	120	6.19
			Sugar	0	15	0
			Lemon syrup	0	1175	0
			Water	0	470	0
			Coffee	0	124	0
			Tea	0	290	0
			Broth	1.36	200	2.73
44	12	521	Semi-skimmed milk	5.16	240	12
			Coffee	0	720	0
			Tea	0	480	0
44	23	4302	Meat snack (frikadel)	1	139	1
			Sugar	0	24	0
			Mayonnaise	2	25	1
			Coffee	0	1440	0
			French Fries	14	150	21

b) Women

AGE	TOTAL FOLATE (µg)	TOTAL ENERGY (kJ)	PRODUCT	FOLATE CONTENT (µg/100g)	CONSUMED QUANTITY (g)	FOLATE from PRODUCT (µg)
1	1.05	1766	Meat snack (frikadel)	1	77	0.77
			Chocolate	7	4	0.28
			Lemon syrup	0	90	0
			Water	0	510	0
8	3.02	1201	Dutch rusk (beschuit)	7	20	1.4
			Full fat milk	4.04	40	1.62
			Sugar	0	32	0
			Lemon syrup	0	23	0
			Water	0	77	0
			Tea	0	360	0
20	0	1143	Apple Juice	0	810	0
34	0	0	Water	0	128	0
46	0.7	759	Dutch rusk (beschuit)	7	10	0.7
			Sugar	0	26	0
			Margarine	0	5	0
			Tea	0	250	0
49	0	914	Apple juice	0	648	0
			Tea	0	90	0
50	5.9	367	Semi-skimmed milk	5	32	1.6
			Smoke-dried beef	12	10	1.2
			Water	0	370	0
			Coffee	0	370	0
			Tea	0	370	0
			Cracker	31	10	3.1

Table 3.3: Selection of products (with high folate content) for high outliers identified applying the test of Grubbs and Beck (Grubbs and Beck, 1972) in men (a) and women (b).

a) Men

AGE	TOTAL FOLATE (µg)	TOTAL ENERGY (kJ)	PRODUCT	FOLATE CONTENT (µg/100g)	CONSUMED QUANTITY (g)	FOLATE from PRODUCT (µg)
1	1275	3686	Beef liver	1205	100	1205
5	834	6431	Beef liver	1205	60	723
25	881	28793	Liver sausage	207	120	248
28	1663	12944	Pork liver	540	295	1593
			Strawberries	65	238	155
			Beer	5	2000	100
			Orange juice	20	800	160
38	2430	12793	Chicken liver	1385	140	1939
40	1969	13144	Beef liver	1205	150	1808
46	1226	7846	Beef liver cooked	1057	100	1057
50	4150	11543	Chicken liver	1385	280	3878
			Liver sausage	207	40	83

b) Women

AGE	TOTAL FOLATE (µg)	TOTAL ENERGY (kJ)	PRODUCT	FOLATE CONTENT (µg/100g)	CONSUMED QUANTITY (g)	FOLATE from PRODUCT (µg)
7	807	4624	Beef liver	1205	60	723
34	1749	9661	Chicken liver	1385	94	1302
37	2318	9220	Beef liver	1205	177	2133
42	1140	4057	Beef liver cooked	1057	100	1057
43	847	7619	Pork liver cooked	120	540	648
50	2512	9285	Chicken liver	1385	168	2327
			Liver sausage	207	40	83
66	941	10143	Broad beans	150	564	846

We will now closer examine the outlying observations for the folate data. Both high and low folate intakes were identified as outliers. We inspected the consumption causing the 'extreme' folate intakes. The results are presented in Table 3.2 (low intakes) and 3.3 (high intakes).

Table 3.2 shows all products consumed during the day of the observed low (outlying) folate intake. The low folate intakes (4 males, 7 females) clearly resulted from extremely low consumption in general. All men and women with the low intakes had reported that their consumption was 'considerably lower than normal' due to illness, and one men (the one that had consumed the French fries) due to other reasons. As these are unusual observations, not representative for normal intakes, it seems allowed to remove these observations. It should then be considered to remove all observations for individuals who reported lower intake than normal due to illness, though.

For the 'high outliers' only relevant products causing the high folate intake are shown (Table 3.3). It can be seen that the high folate intakes are mainly due to liver consumption. For one woman consumption of a very high quantity (564 g) of broad beans[1] resulted in the high folate intake. For a male participant consumption of liver sausage in combination with

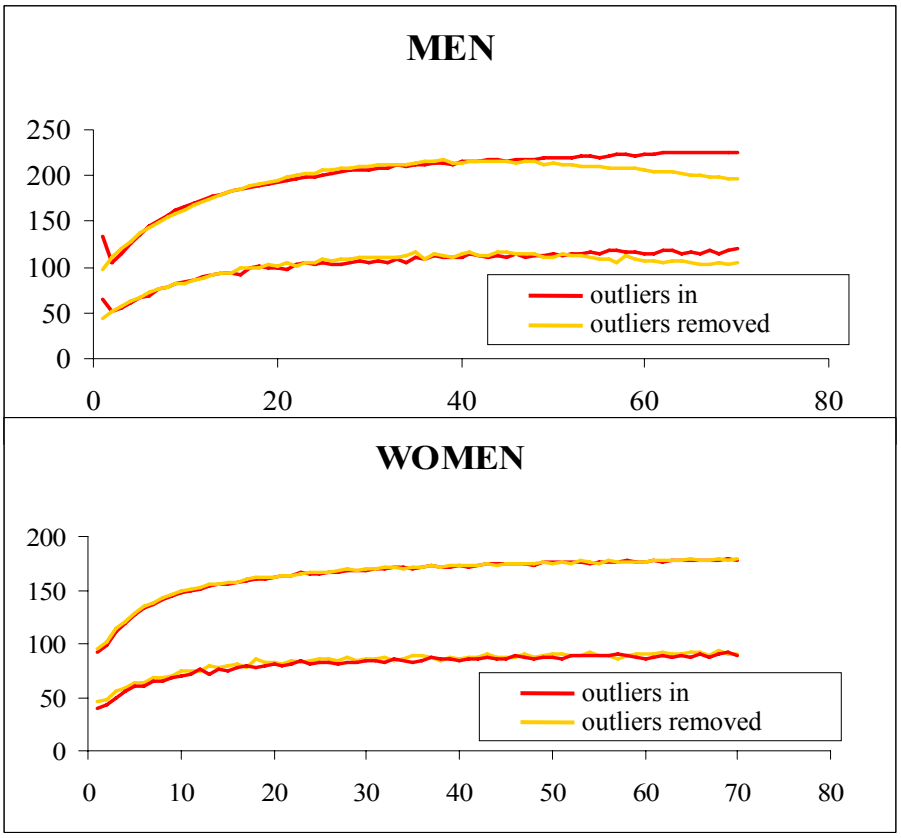


Figure 3.10: Effect of removal of outliers on the estimated mean habitual intake and 10th percentile.

[1] tuinbonen

several other products with high folate content (strawberries, orange juice, beer) resulted in the observation being judged as a statistical outlier.
The high outliers may influence the estimated habitual intakes, and it may therefore be desirable to remove them. However, it is questionable whether it can be decided to do so as these high intakes really occur and seem not due to anomalous consumption.

The effect of leaving outliers in, or removing them has been examined. The results are presented in Figure 3.10. It can be seen that for women removal of outliers does not influence the resulting habitual intake estimates. For men however, removal of outliers does seriously affect the estimates. In fact, the course of the habitual intake as a function of age seems more logical after removal of statistical outliers, as it expected that in older men intakes decrease rather than increase.

In this example most high outliers are caused by consumption of liver. A possibility would be to consider liver consumers separately. However there are several liver products with varying folate content (Table 3.4). For example: chicken liver contains 1385 µg folate per 100 g, whereas liver sausage only contains 207 µg/100 g. This raises the question how to define consumers and non-consumers. And additional information on consumption frequency and the true number of consumers and non consumers of liver (products) is desired in that case. The possibility to distinguish between consumers and non-consumers has not yet been implemented in AGE MODE, but can be adopted. Methodology for this has already been developed in S-PLUS (Slob and Bakker, 2004).
Similar issues may emerge for other micronutrients. Identified outliers should always be closer examined, as well as the effect of removing the outliers. It should be further studied how these kinds of problems can be dealt with best. For now it seems best to remove the observations that were identified outliers to obtain reliable habitual intake estimates.

Table 3.4: Liver products in NEVO-2001.

CODE	Product	Folate content (µg)
333	beef liver cooked	1057
334	pork liver cooked	540
475	chicken liver raw	1385
1407	beef liver raw	1205
1426	pork liver raw	540
1439	calf liver raw	729
1542	beef liver prepared	1057
1560	beef liver prepared	540
1573	calf liver prepared	729
335	liver paste	147
356	liver haddock	300
640	liver sausage	207
1238	liver sausage ‘hausmacher’	207
1239	liver pâté	207
1771	liver pâté ‘Berliner’	147

4. Comparison with other methods

4.1 AGE MODE compared to STEM

The basic idea of AGE MODE, fitting an age dependent function, is based on the idea of Slob, implemented in 'STEM' (Slob, 1993b). However, the applied methodology differs considerably. STEM has been elaborately evaluated and compared with other methods in a previous report (Waijers et al., 2004).

To obtain symmetrically distributed observations the log-transformation from STEM is extended to the general Box-Cox transformation in AGE MODE. In our analyses we often find estimates of λ with values about 0.20-0.25, significantly different from $\lambda = 0$ (in the case of a log transformation).
In the next step STEM chooses fixed functions with several unknown parameters to fit to the log transformed data. However, no physical relations between habitual intake and age are known. Therefore we propose the more general approach by using fractional polynomial regression, in which no function underlying the data is assumed. This method simply searches for the best way to describe the data. Since the lifetime intakes are described only for the range of available years, no extrapolation is needed, one of the well known disadvantages of polynomial regression. However, the implemented version of fractional polynomial regression can easily be extended to more than two terms, which may sometimes be advisable.
Very important furthermore is the back transformation step, that, in AGE MODE, is performed by Monte Carlo Simulations. In STEM the inverse of the forward transformation is used, which results in the medians instead of the mean and are too low. In a few iterations our method results in consistent estimates.

4.2 AGE MODE compared to the Nusser method

4.2.1 Methodological comparison

A nowadays frequently used method to estimate habitual intakes is the Nusser method. The Nusser method estimates habitual intake distributions for pre-specified gender and age groups. The methodology consists of several steps: preliminary adjustments of the data, a semi parametric transformation to normality, estimation of the habitual intake parameters, and back transformation to the normal scale (Nusser et al., 1996). As it requires considerable computational effort, special software packages have been developed at Iowa State University for the application of this method (Iowa State University, 1996a).
Each method has its strengths and weaknessess. In Table 4.1 these strengths and weaknesses of AGE MODE compared to the Nusser method are summarized.

Advantages AGE MODE

The feature of age dependency in AGE MODE shows clear advantages above creating subgroups which is done in the Nusser-method. Consider for example a group of children aged 4 to 8 years. Consumption levels may differ considerably between 4 and 8 years old children. In other words, the variation in intakes can to a large extent be explained through age. Therefore, does an estimated habitual intake distribution really represent a habitual intake distribution for this subgroup? This is the first and most obvious reason to consider intakes age dependently.

Secondly, intake data need to be transformed before habitual intake parameters can be estimated. In Nusser this is achieved separately for all pre-specified groups. Consequently, transformation parameters can show important differences between adjacent subgroups, which is not logical. This is not the case in AGE MODE, as parameter estimates are obtained age dependently.

Furthermore, numbers of individuals in distinct subgroups may be small, affecting the reliability of the estimated habitual intake distribution, especially if high variations in intake exist. In an age dependent model all data are used to estimate habitual intake parameters. In Figure 3.8 mean (observed) folate intakes are depicted. Even though these mean intakes are based on two observations for at least 20 up to 59 individuals (in the adult age range), it is clear that large fluctuations exist. For example, it is not likely that mean intake for 19 years old men is truly 20% higher than that of 20 and 21 years olds and that when individuals reach the age of 22 their folate intake goes up again with 12%. However on the longer run, from the age of 20 to 60 years a true tendency may exist. By calculating a (non-linear) regression function, age being the dependent variable, all the data are used. This means that power of precision can be lend from adjacent ages. The large fluctuations in mean intakes per age year show the high uncertainty in the measurement (Figure 3.8) and the importance of large numbers to obtain a reliable estimate of the true intake. When smaller subgroups are taken the reliability of the estimate may be poor.

Another important advantage of the method arises when intakes are related to requirements. Just as for intakes, also for requirements it would be much more logical to consider them age dependently. In that case prevalences of inadequate intakes can also be expressed as a function of age.

The back transformation step is also conducted differently in AGE MODE and the Nusser method. In Nusser it is obtained with a complex formula, whereas in AGE MODE Monte Carlo Simulations are applied for this purpose. The advantage of applying Monte Carlo Simulations may be that it is much simpler and therefore lucid. A disadvantage is the high number of simulations required to obtain consistent habitual intakes and therefore the longer duration of the analysis.

The Nusser method is operational in statistical software packages SIDE and C-SIDE, developed at Iowa State University (Iowa State University, 1996a; Iowa State University, 1996b). The available software could be considered a 'black box'. It generally works well with customary intake data, but not always with less habitual data, which may be a severe limitation for users. For example for dietary components that are not habitually consumed or for nutrient intakes from enriched products the software is not always able to produce estimates of the habitual intake. As the methodology and software are rather nontransparent, there is no insight in why problems arise and what can be done to solve them, nor is it possible to adapt or extent the method to meet ones own additional requirements. AGE MODE on the other hand is transparent and consecutive steps in the model are understandable and lucid. And as the model has been developed at the RIVM it can be adapted to meet new demands if necessary.

Advantages Nusser

The Nusser method contains some features or options that are not (yet) present in AGE MODE. In the first place it has the possibility to adjust observations to the first sample day, as it is assumed that day 1 observations are most reliable. In addition is it possible to adjust for correlation between intakes of consecutive days. However, a correlation coefficient is not available for the Dutch population. The Nusser method also provides the possibility to adjust for other variables associated with either the observations, for example weekday versus weekend, month of the year, interview sequence, or with the individual.

Secondly, within the Nusser method there is a possibility to estimate the proportion of consumers and non-consumers of certain nutrients of foods and then estimates habitual intakes for consumers only. AGE MODE does not (yet) contain this feature. This feature is

Table 4.1: Comparing AGE MODE with the Nusser method.

	AGE MODE	**Nusser**
model	age dependent	population subgroups (age categories)
software	S-PLUS program, developed at RIVM	(C-)SIDE-software, managed by IOWA State University
transparency	clear	black box
power when numbers are small	high	low
transformation	uniform	might differ from one age group to the next
back transformation	simulations	formula
dealing with outliers	gives clear insight	outliers are not considered
weighting	not (yet) implemented	weighting factors can be used
adjustments of the data	not (yet) implemented	adjustments to remove nuisance effects
non consumers	not (yet) implemented (but technique is available)	for e.g. foods the proportion of consumers can be estimated

mainly important for estimating the habitual intake of foods or for dietary components which are present in only some specific foods. For most micronutrients this feature is not essential as most micronutrients are consumed by all individuals in lesser or higher amounts. However, at the RIVM a methodology has been developed, called STEM II, that estimates the proportion of consumers and non-consumers (Slob and Bakker, 2004). In addition, rather than considering consumed quantities, it may be better to consider consumption frequencies of products. STEM II also estimates consumption frequencies. As STEM II has been programmed in S-PLUS it can easily incorporated in AGE MODE.

4.2.2 Comparing habitual intake estimates

The former paragraph has provided a theoretical comparison of AGE MODE and the Nusser method. In the current paragraph we will compare habitual intake distributions estimated with both methods. Direct comparison of estimates from both methods is difficult as estimates with the Nusser method can only be obtained for specified gender and age groups, whereas AGE MODE generates age dependent habitual intake distributions.

Habitual folate intake estimates by the Nusser method were calculated in C-SIDE (Iowa State University, 1996a). For this purpose generally used gender and age groups were specified. For a fair comparison between results from the Nusser method and AGE MODE outliers identified by AGE MODE were removed from the data.

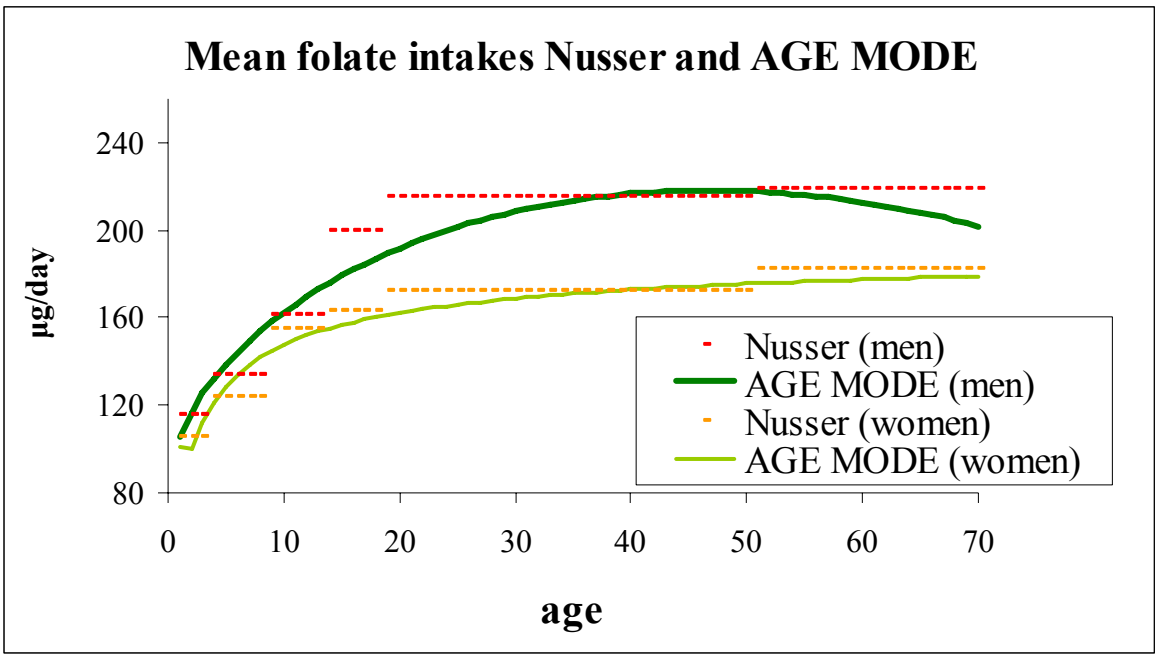


Figure 4.1: Estimated mean habitual intakes from AGE MODE (continuous line) and the Nusser method (discontinuous line) for men (upper lines) and women (lower lines).

Mean habitual intake estimates according to age for AGE MODE and the Nusser method are presented in Figure 4.1. The continuous age dependent estimate produced by AGE MODE is clearly appealing. In Figure 4.2 estimated habitual intake probability density distributions from AGE MODE and Nusser are presented.
The estimated (inter-individual) variation in habitual intakes and the shape of the estimated requirement distributions are comparable for AGE MODE and the Nusser method. For children estimated habitual intake distributions from AGE MODE are wider than those from Nusser.

From these results, obtained with two very different methodologies, it may be concluded that although we do not know the true habitual intake distribution, it can be estimated with statistical methods. Which method produces the estimates that are closest to the true habitual intake distributions cannot be ascertained.

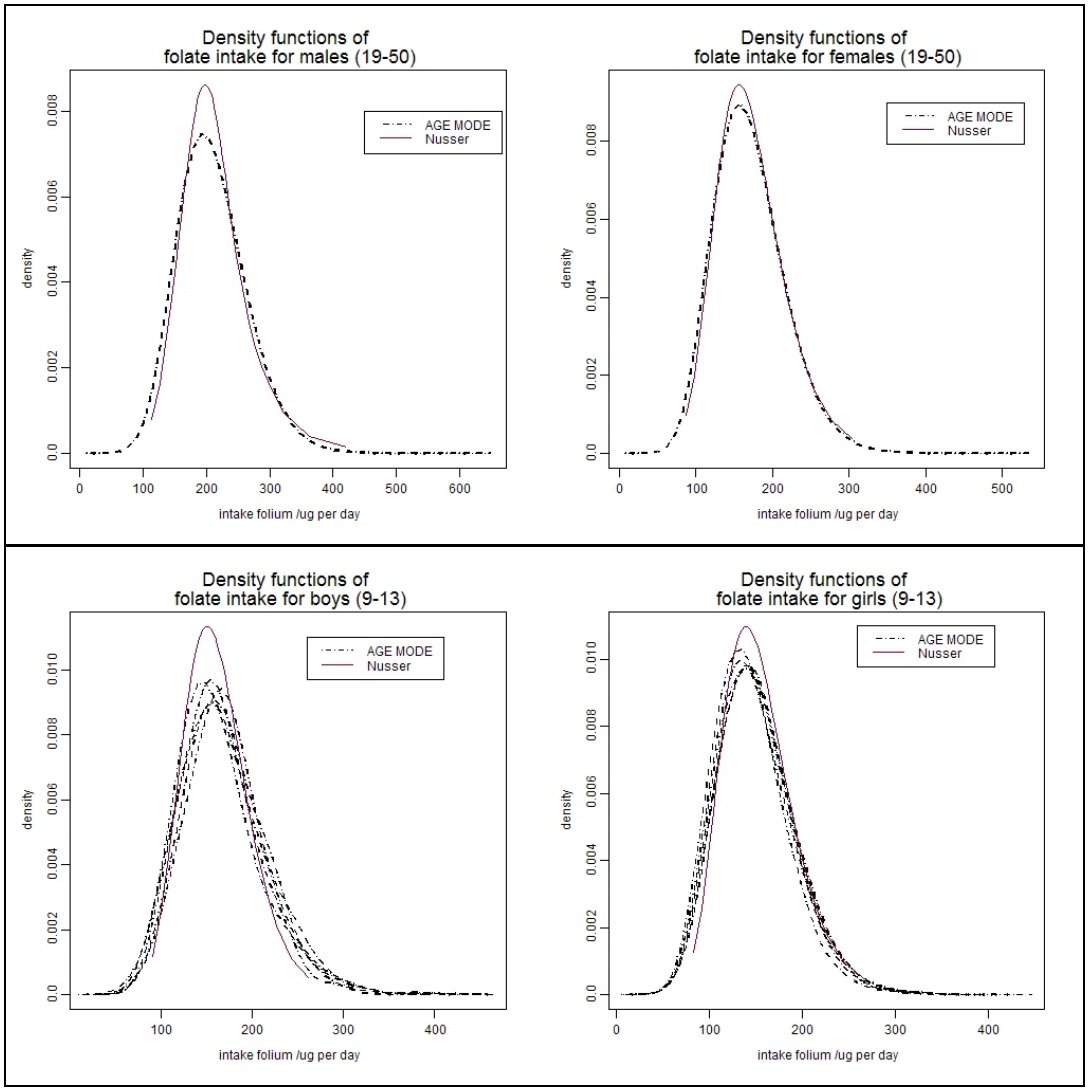


Figure 4.2: Comparison of estimated habitual intake distributions for several age ranges from AGE MODE and the Nusser method. For adults the intakes of individuals from 19 to 50 years have been averaged.

5. Evaluating folate intake with AGE MODE

In contrast to the preceding chapter in which we concentrated on explaining the working of the model. The focus of this chapter will be to explain the use of the model for the prediction of adequate e.g. inadequate intake of certain micronutrients . In this chapter the micronutrient folate is used as an example . As folate intake has been used to exemplify the model, earlier presented figures will be referred to in the current chapter.

5.1 Habitual folate intakes from AGE MODE

Folate intake data were obtained from DNFCS-3, carried out in 1997/98. DNFCS-3 comprises 6,250 non-institutionalized persons aged 1–97 years in 2,564 households selected from a stratified random sample in the Netherlands. Information on food consumption was obtained with a 2-day dietary record on 2 consecutive days.(Voedingscentrum, 1998). Pregnant women (N=50) were excluded. Folate intake was calculated using the 2001 Dutch food composition table (Voedingscentrum, 2001). For 179 products for which folate content was missing and that were regularly consumed, folate content was estimated through comparison with similar products.

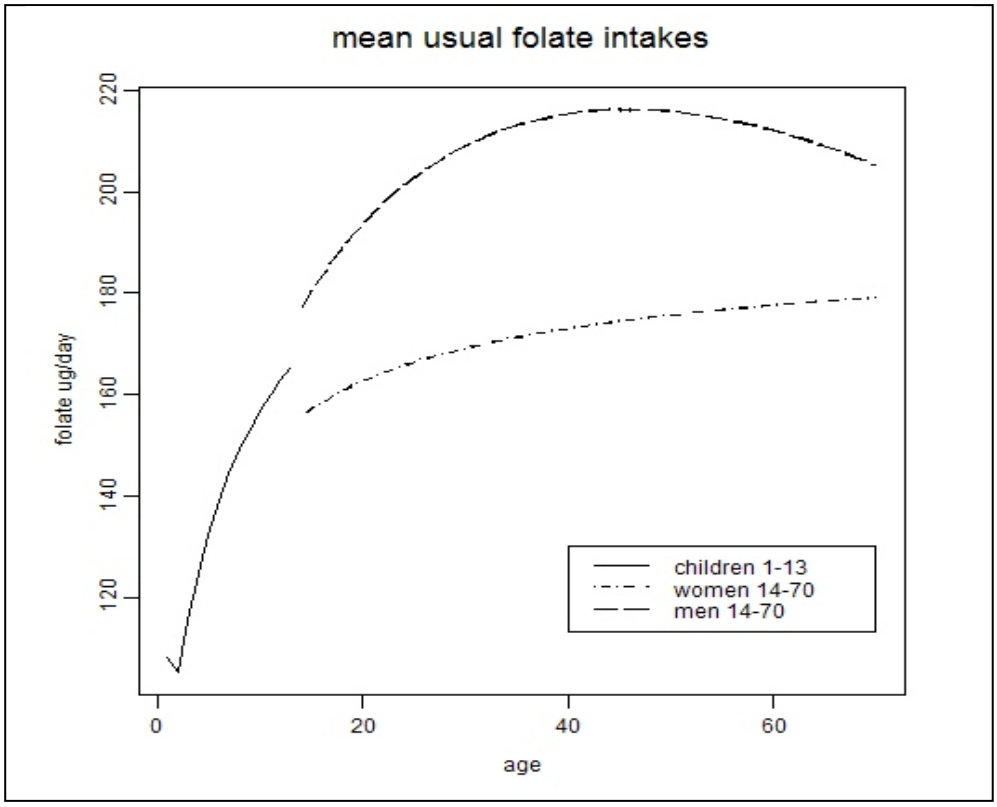


Figure 5.1: Estimated mean habitual folate intakes for the Dutch population as a function of age. To estimate habitual intakes for children until 13 analyses have been performed on all individuals together.

Habitual folate intakes were estimated with AGE MODE. As explained in paragraph 3.3, from the age of 14 men and women need to be considered separately. Therefore, we estimated habitual folate intakes using the following data as input:

- for children from 1 to 13 years: all individuals from 1 to 70 years
- for men aged 14 till 70 years: men from 1 to 70 years
- for women aged 14 till 70 years: women from 1 to 70 years

Another possibility is to just consider males and females separately. This is actually less complex. As children are often considered together, dietary reference intakes for folate are the same for boys and girls, and to be in line with the previous report on folate (Waijers et al., 2004) we chose to describe intakes for children as suggested. In addition we also present the results for males and females in younger ages separately.

We refer to Figure 3.4 and Appendix 3 for means and percentiles of the habitual folate intake distributions. Mean habitual folate intakes for children from 1 to 13 years, and men and women from 14 to70 years are depicted in Figure 5.1. Examples of habitual folate intake distributions for several ages are given in Figure 5.2.

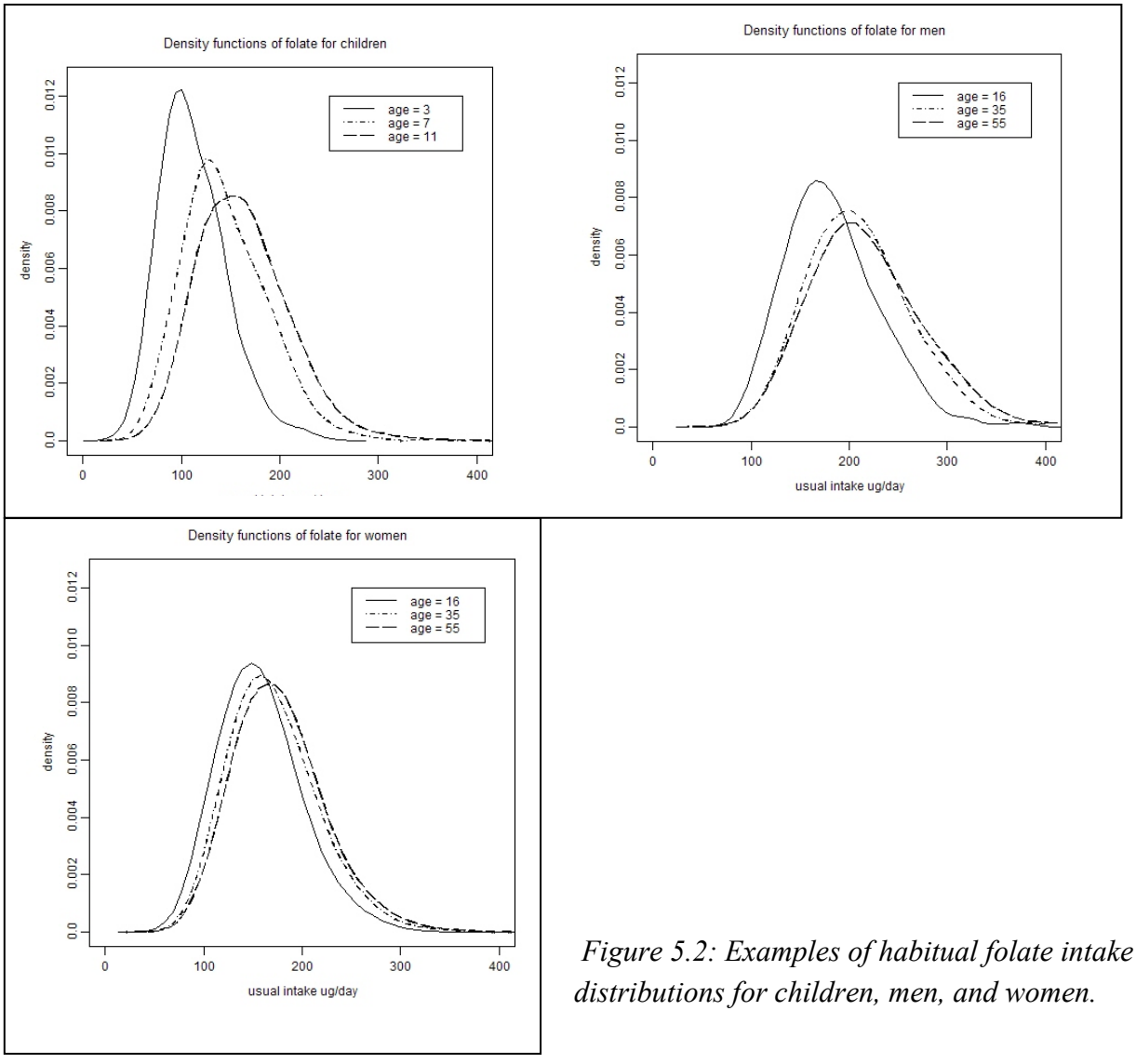


Figure 5.2: Examples of habitual folate intake distributions for children, men, and women.

5.2 Folate requirements

As mentioned in Chapter 2, two approaches can be used to estimate the prevalence of inadequate intakes: the EAR cut point approach and the probability approach. For the EAR-cut point approach an EAR should be available, while for the probability approach an requirement distribution should be specified. In the following paragraphs is described the rationale behind the used EAR and the used requirement distribution.

5.2.1 EAR

The Dutch DRIs for folate have been updated in 2003 (Gezondheidsraad, 2003). For adults the EAR for folate has been set at 200 µg/day. For children (<19 years) only an AI is given by linearly interpolating the AI of breastfed infants to the RDA for adults. As the proportion of the population below the AI can not be used as an indicator of the percentage of the population whose intakes are inadequate, we found it informative in this example to include also the younger age groups and therefore we have tried to derive an EAR for children.

We have employed a similar procedure as used for AIs to obtain EARs for children, departing from the EAR for adults and assuming that the RDA and EAR do not differ importantly in (young) infants, as breast milk is considered the optimal nutrition for infants. Based on this assumption the folate content of breast milk could also be considered the EAR for infants. Although this choice may be arbitrary, it is the most practical. Besides, the variation in requirements can be expected to be small for infants and therefore the RDA and the EAR will not differ importantly. Figure 5.3 demonstrates the derivation of the EAR analogous to the AI. The results are presented in the accompanying table.

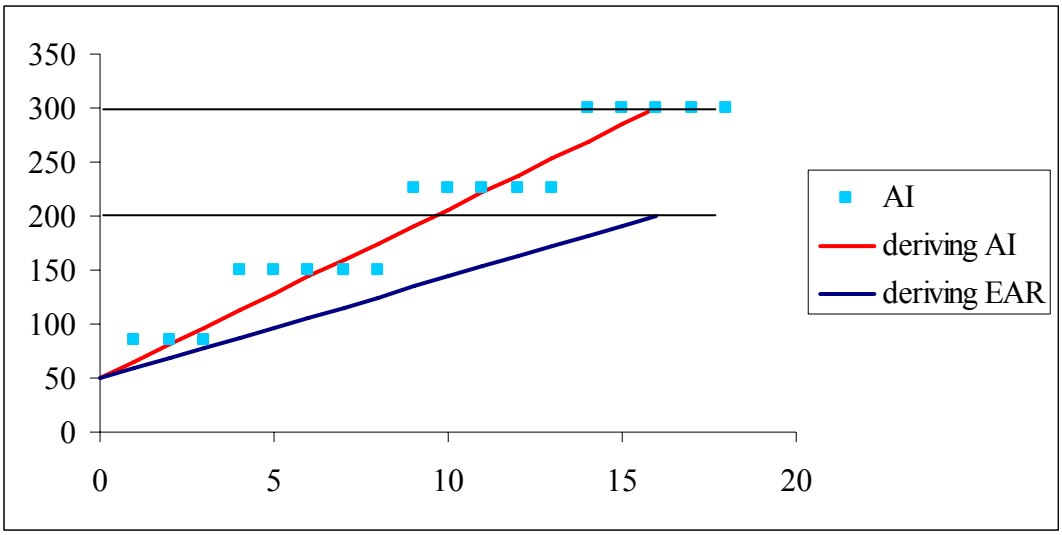


Figure 5.3: The AI for folate for children derived by the Health Council and analogous the EAR for children as a function of age, derived by interpolating between the EAR for adults and infants.

Table 5.1: Derived EARs for folate for children.

age	EAR	age	EAR
1	59	10	144
2	69	11	153
3	78	12	163
4	88	13	172
5	97	14	181
6	106	15	191
7	116	16	200
8	125	17	200
9	134	18	200

5.2.2 Requirement distribution

The DRIs do not give enough information about an requirement distribution for folate, and thus the probability approach can not be performed. However, to exemplify this option in AGE MODE, we found it informative to work with the best guess for this requirement distribution. The process of coming to this choice of distribution is described below.

The DRIs for folate provide a coefficient of variation (CV) of 25%. No explicit statement is made on the shape of the requirement distribution. In contrast, the US Institute of Medicine has decided on a CV of 10% for folate, as there is no information available on the variation in folate requirements between individuals.
In its report, the National Health Council has mentioned the MTHFR-gene mutation that may influence folate requirement. Twelve percent of Caucasians is carrier of the C667 TT-genotype of the MTHFR-enzyme (Gezondheidsraad, 2003). This group may have an increased folate requirement compared to carriers of the CC-genotype or heterozygotes. Implicit it is suggested that the population consists of two subgroups with differing folate requirements, so that in fact two distinct (but overlapping) requirement distributions exist. The occurrence of this mutation was a main argument for the Health Council to set the CV at 25%, in order to ensure the RDA to be high enough to cover the increased needs for carriers of the TT-genotype.

If the probability approach is used for dietary evaluation at the population level, the specified requirement distribution needs to reflect the *true* distribution of requirements in the population, though. Therefore, based on the above, it may be more in accordance with reality to specify two distinct distributions instead of one distribution with a large variation. The key question is then, if the requirement for carriers of the TT-genotype for the MTHFR-enzyme is indeed increased, how much is it increased compared to individuals with the CC- and CT-genotype? And what is the 'true' variation in requirements within the two subgroups? But even more important: do carriers of the TT-genotype indeed have increased needs for folate?[1]

[1] Petra Verhoef, an expert in this area, has provided important input for the reasoning following this question.

They do show increased serum homocysteine concentrations and their serum folate is decreased (Frosst et al., 1995). Serum homocysteine can be decreased and serum folate increased by folate supplementation or nutrition high in folate (Ashfield-Watt et al., 2002; Guinotte et al., 2003). But although increased plasma homocysteine concentrations can be considered a marker for a disturbed folate metabolism, little is known about functional consequences of increased serum homocysteine concentrations.

Dietary reference intakes and therefore folate requirements are based on the level required to prevent diseases. As little is known on functional consequences of the polymorphism, it is questionable whether carriers of the TT-genotype in the MTHFR-enzyme do actually have increased requirements and therefore whether it is realistic to discern a distinct requirement distribution for this subgroup. For this reason it may be better to assume the requirements to be lognormally distributed, maintaining a CV of 25% as the tail of the distribution will be to the right.

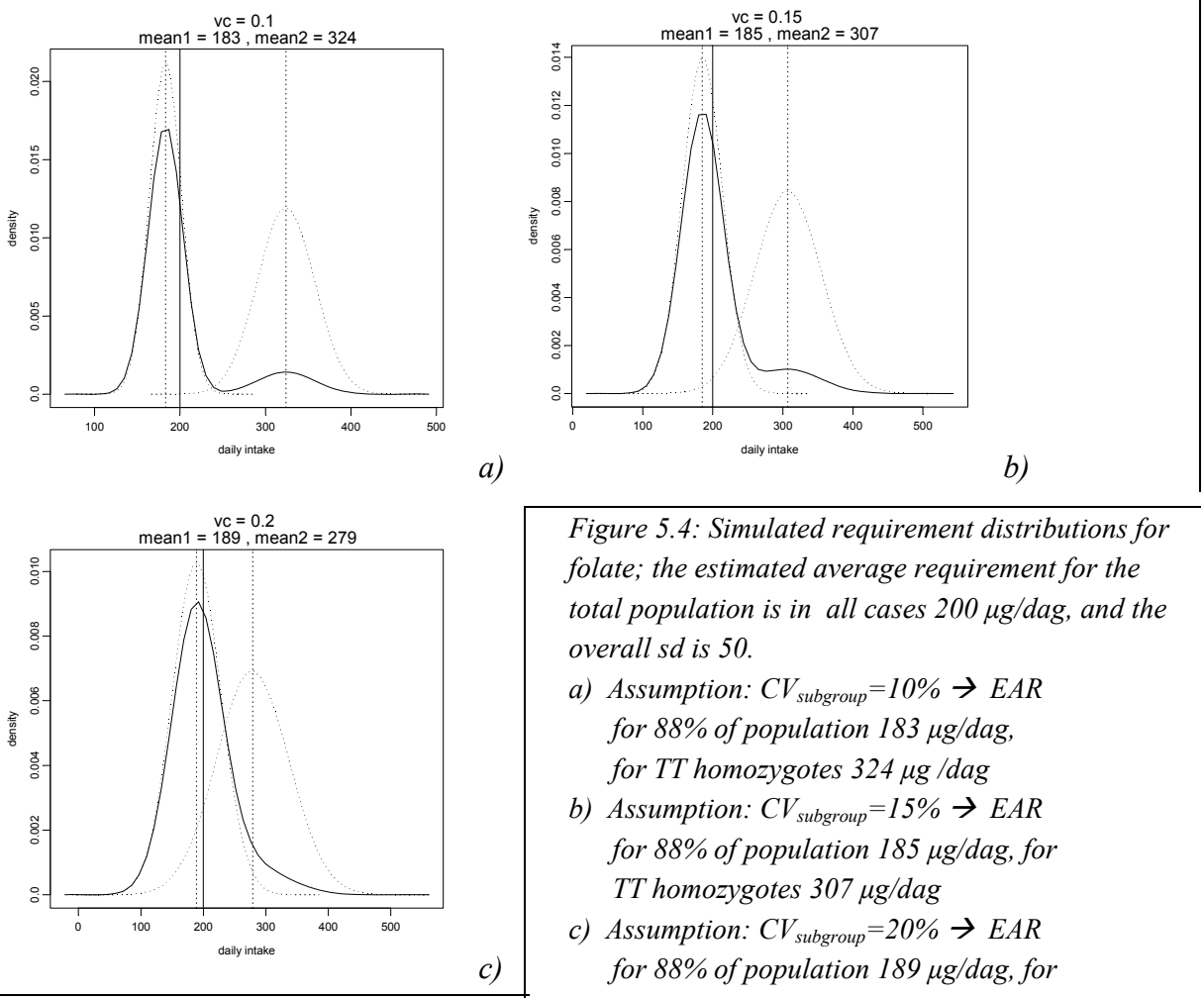


Figure 5.4: Simulated requirement distributions for folate; the estimated average requirement for the total population is in all cases 200 µg/dag, and the overall sd is 50.

a) Assumption: $CV_{subgroup}$=10% → EAR for 88% of population 183 µg/dag, for TT homozygotes 324 µg /dag

b) Assumption: $CV_{subgroup}$=15% → EAR for 88% of population 185 µg/dag, for TT homozygotes 307 µg/dag

c) Assumption: $CV_{subgroup}$=20% → EAR for 88% of population 189 µg/dag, for TT homozygotes 279 ug/dag.

Together with some other possible distributions (Figure 5.4), the resulting lognormal folate requirement distribution is depicted in Figure 5.5. With this lognormal distribution the possibly increased requirement for individuals with the TT-genotype is somewhat covered, the variance is particularly present at the higher site of the distribution (and not at the lower site), no choice need to be made regarding the exact EAR for the different genotypes, so that can be stuck most closely to the recommendations of the national Health Council.

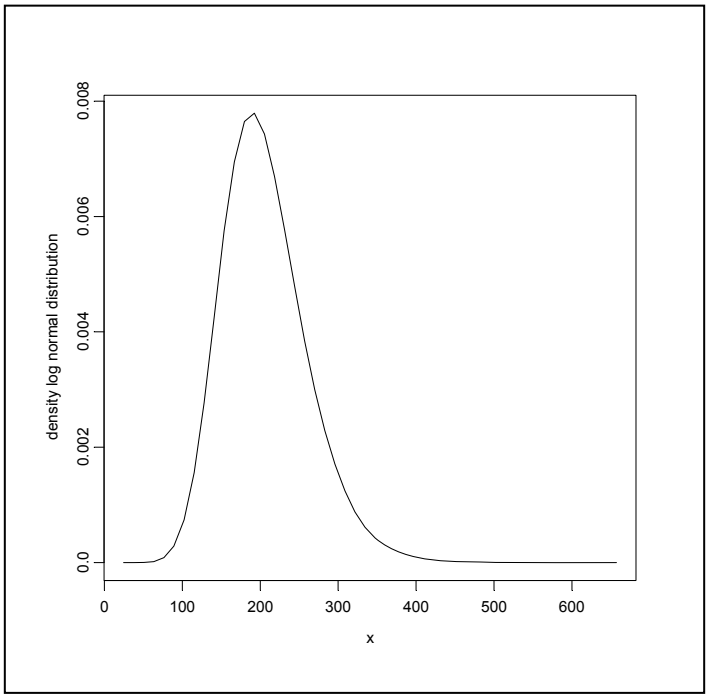


Figure 5.5 : Simulated requirement distribution for folate: lognormal distributions, the EAR being 200 µg/day with a CV of 25%.

5.3 Evaluating folate intake in relation to requirements

At this moment the EAR cut-point approach is the only 'workable' approach, as the DRIs do not provide enough information to specify a requirement distribution. Nevertheless we have also calculated prevalence estimates using the probability approach based on the rationale in paragraph 5.2. The results are presented in the two panes of Figure 5.6 (and numerically in Appendix 4).

Resulting estimates from the EAR cut-point approach in comparison to the probability approach are close for men but differ notably (about 10%) for women. The explanation for this phenomenon has been given in a previous report (Waijers et al., 2004): if the median intake is closer to the estimated average requirement the estimates will become more reliable and this is the case for men, but not for women. Assuming a normal or a lognormal

distribution with equal means and variances does not make a noteworthy difference in prevalence estimates for the case of folate.

As, at this moment, we suggest the EAR cut-point approach, as explained in paragraph 2.3. In Figure 5.7, the prevalence estimates obtained with this approach are depicted for children, men, and women. It suggest that dependent on the age, 60 to 80% of adolescent women has an inadequate folate intake from foods. For men the prevalence is about 20% lower, but still high. For children the estimated prevalence of inadequacy is much lower. It increases with age from 6% at an age of one year till about 60 % at the age of 13. Prudence is called for the interpretation for the interpretation of these prevalences among children. These estimated prevalences for children are based on the in this report derived EAR. In fact, for these low age groups the median habitual intake can only be quantitatively compared with the AI.

The findings in this report correspond with those presented in a former report on the adequacy of folate intake in which the probability approach and the cut-point approach is used for the habitual intakes derived with the Nusser method and with STEM. (Waijers et al., 2004). However, especially for children the estimates are lower compared to the estimates derived with the other methods.

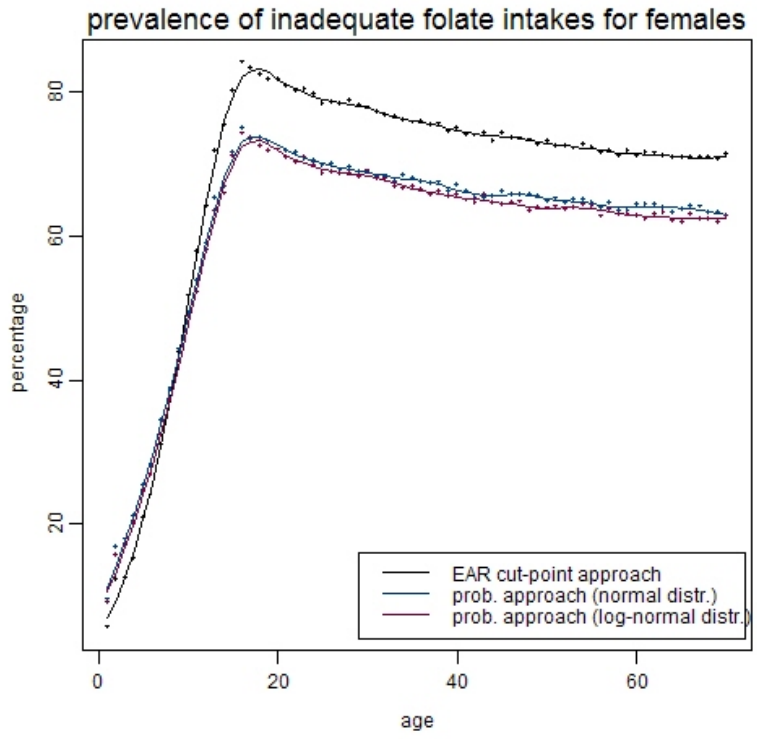


Figure 5.6: Estimates for the prevalence of inadequate folate intakes for males and females, applying the EAR cut-point approach and the probability approach. For the probability approach it was assumed that the requirements showed a normal or a lognormal distribution and a CV of 25%.

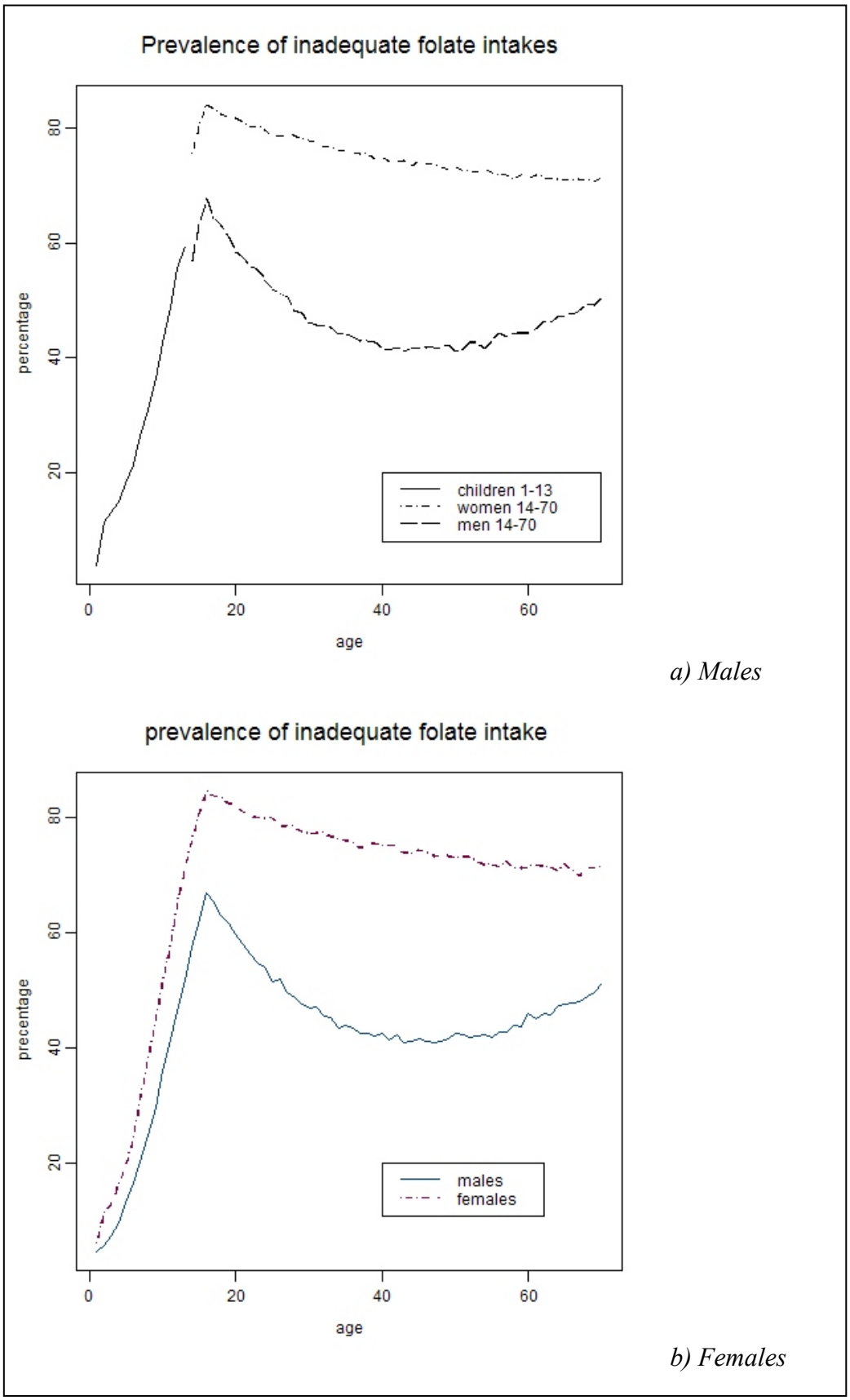


Figure 5.7: Estimates for the prevalence of inadequate folate intakes in Dutch children, men, and women (a) and in males and females (b).

Thus, with AGE MODE it is possible to evaluate the intake of folate. Based on the DFCS-3, the evaluation of the habitual folate intake compared with the dietary reference intakes suggests that the intake might not be adequate for a high percentage of the population. This is in line with a study from Brussaard et al, in which they concluded that according to criteria derived from homocysteine metabolism as related to cardiovascular disease, folate status may not be adequate in more than 60% of the adults.(Brussaard et al., 1997) However, for several reasons one should be cautious with undertaking policies based on the figures in this report. For example, this survey was based on data from already more than eight years ago. In addition, in these intakes the intake of folate by supplements or folate enriched foods were not used yet.
Finally, evaluation of dietary intakes is good method to indicate possible problems with the intake of folate. But before policies can be undertaken, verification of such a problem with actual data on the population's folate status with biochemical parameters or with studies on clinical symptoms is desired.

6. Evaluating vitamin A intake with AGE MODE

6.1 Habitual vitamin A intakes from AGE MODE

Vitamin A is a generic term for retinol and provitamin A carotenoids, the most important being beta-carotene. Intake and requirements for vitamin A are expressed in equivalents of retinol. The formerly used equivalence ratios for dietary provitamin A carotenoids are now considered to be too low, meaning that a higher amount of provitamin A carotenoids is needed to obtain a certain amount of retinol equivalents, referred to as Retinol Activity Equivalents (RAE) (Institute of Medicine, 2001). Table 6.1 shows the former and revised equivalence ratios.

In the 2001 Dutch food composition (NEVO) table the 'old' retinol equivalences have still been used. For the analyses presented here the new equivalences, RAEs, have been estimated for all products in the 2001 NEVO table. For more details we refer to a previous report on vitamin A (Waijers and Feskens, 2004)[1].

Just as for folate, food consumption data were obtained from DNFCS-3 (1997/98). These data were combined with the (revised) 2001 NEVO table to calculate vitamin A intakes, expressed in RAEs, for all individuals in DNFCS-3.

Table 6.1: Formerly used and new retinol equivalence ratios.

'old' eq ratio 1 RE ~	new eq ratio 1 RAE ~	
1	1	µg all-trans retinal
2	2	µg β-carotene from supplements
6	12	µg dietary β-carotene
12	24	µg other dietary provit. A carotenoïds

As requirements are different for males and females in all ages, habitual intake estimates were obtained separately for males and females. Estimates for the habitual vitamin A intake distribution obtained with AGE MODE are shown in the 2 panes of Figure 6.1 (and listed in Appendix 5). A summarizing figure with mean habitual vitamin A intakes for men and women is presented in Figure 6.2. Examples of habitual vitamin A intake distributions for several ages are given in Figure 6.3. These are much more skewed than habitual folate intake distributions, which is not remarkable as vitamin A content in foods is highly variable, being extremely high in some foods and absent in many other foods.

[1] In this report, written in Dutch, the new RAEs are referred to as 'RE-IOM' (retinol equivalences established by the Institute of Medicine)

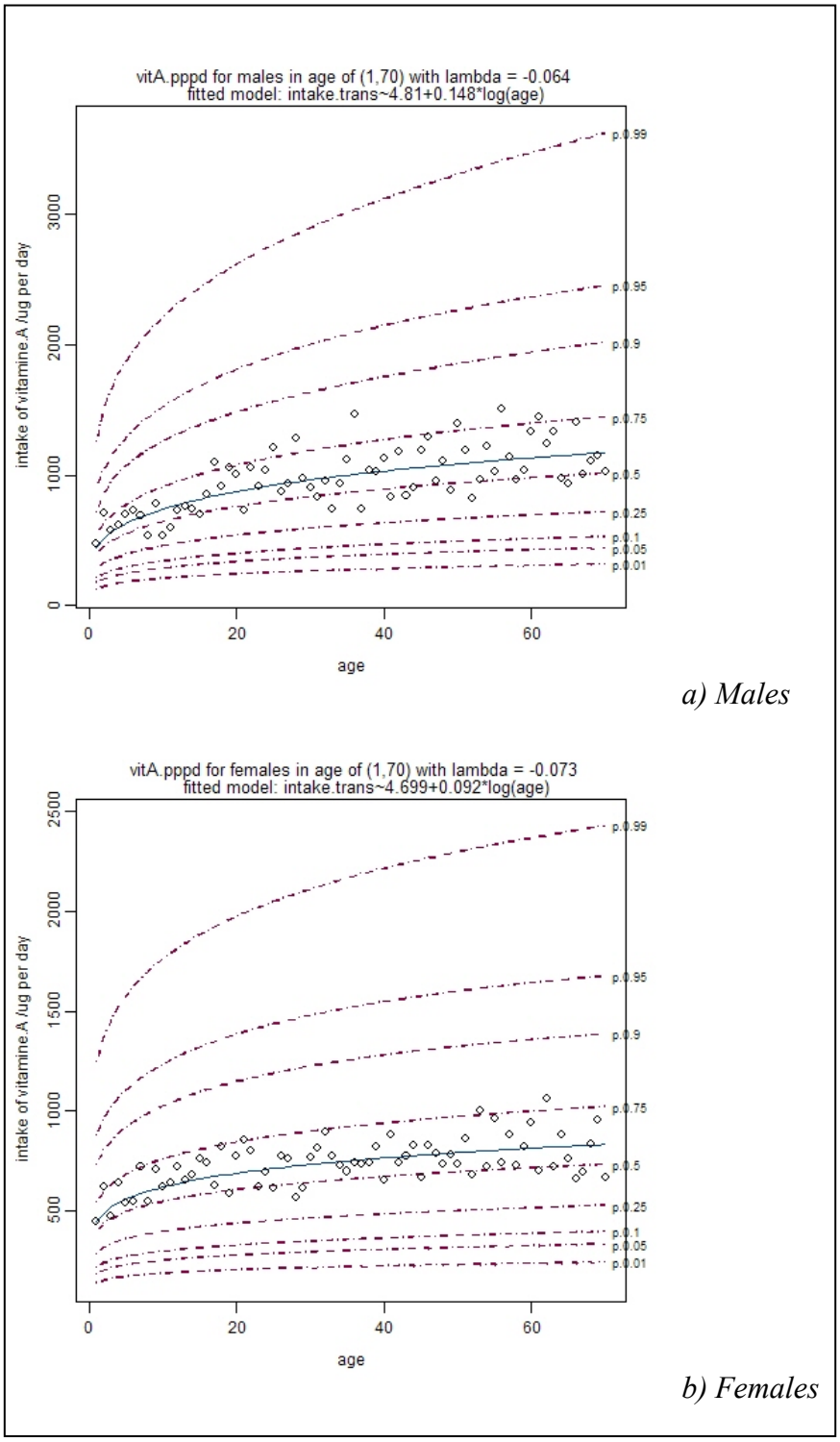


Figure 6.1: Habitual vitamin A intakes (RAE/day) as a function of age. Mean (continuous line) and percentiles for the habitual intake distribution. The dots represent the mean observed vitamin A intakes for each age year.

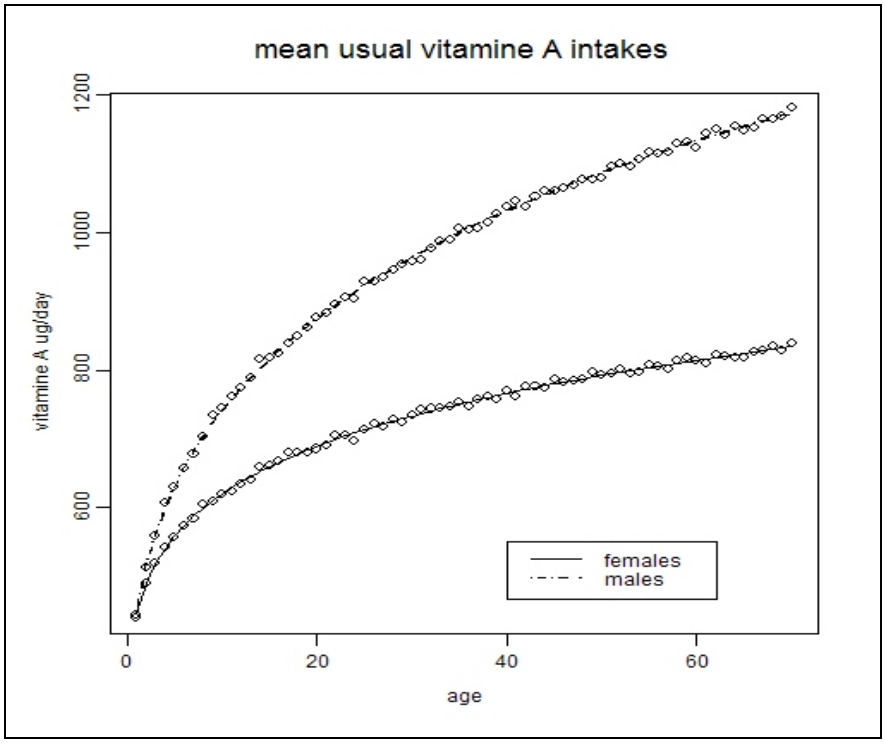


Figure 6.2: Estimated mean habitual vitamin A intakes (RAE/day) for the Dutch population as a function of age.

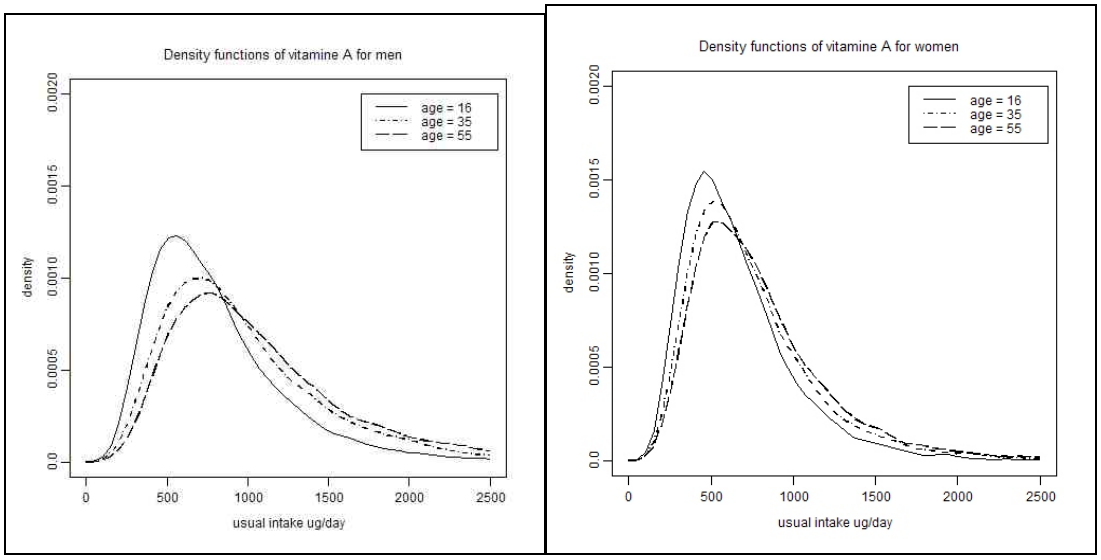


Figure 6.3: Examples of habitual vitamin A intake distributions for men and women.

Reported mean habitual intake estimates are lower than estimates in the previous report on vitamin A (Waijers and Feskens, 2004). In the previous report the Nusser method was used. Comparison of density distributions of the habitual vitamin A intake from AGE MODE and Nusser (Figure 6.4) shows that the shape and variance of estimated habitual intake distributions highly correspond.

For a correct comparison we removed the outliers identified by AGE MODE and recalculated Nusser estimates. Also we calculated again observed means (and P50), as it is expected that mean habitual intakes correspond with mean observed intake estimates. Habitual intake estimates from AGE MODE are somewhat lower than observed means, whereas estimates from the Nusser method are higher (Table 6.2). Except for adolescent females the AGE MODE estimates are closer to the observed means than the Nusser estimates. As mentioned earlier, the true habitual intake distribution is unknown, so it is not possible to do a statement on which estimate is better. The Nusser method produces 'black-box estimates', whereas our method is transparent. For adolescents the fit of the age dependent curve may not yet be optimal, causing the estimates to be somewhat low.

Additionally, it can be seen from Figure 6.4 and Table 6.2 that removal of outliers has only a minor effect on estimated habitual intakes.

6.2 Vitamin A requirements

The most recent dietary reference intakes for vitamin A in the Netherlands date from 1989 (Voedingsraad, 1992). The EAR for vitamin A has been set at 600 RE/day for adults. For children and adolescents only an AI has been determined.
Since 1989 scientific knowledge on vitamin A requirements has accumulated. In 2001 the US Institute of Medicine has published its most recent report with DRIs for vitamin A (Institute of Medicine, 2001). In the IOM-report vitamin A requirements have been estimated with a formula (Box 6.1), which allows to calculate the amount of vitamin A required to maintain a given body-pool size of vitamin A in well-nourished subjects (Olson, 1987). In this way both for children in all ages as for adults an EAR can be obtained. As the Dutch DRIs for vitamin A are dated, and an EAR has only been established for adults, it has been decided to use the Olson-formula to determine the EAR for adults and children (similar as in a previous report on vitamin A (Waijers and Feskens, 2004)).
For this purpose Dutch reference weights and growth factors were needed. These data have been obtained from the fourth national growth study (1997) (TNO/LUMC, 1998). For children reference weights were copied and growth factors have been obtained by determining the tangent to the growth curve. The reference weights for adults (older than 18 years) have been calculated departing from the average height and a desired Body Mass Index of 22.5 kg/m^2 for individuals aged 18 to 50 years, and 24 kg/m^2 for 51 to 70 years old

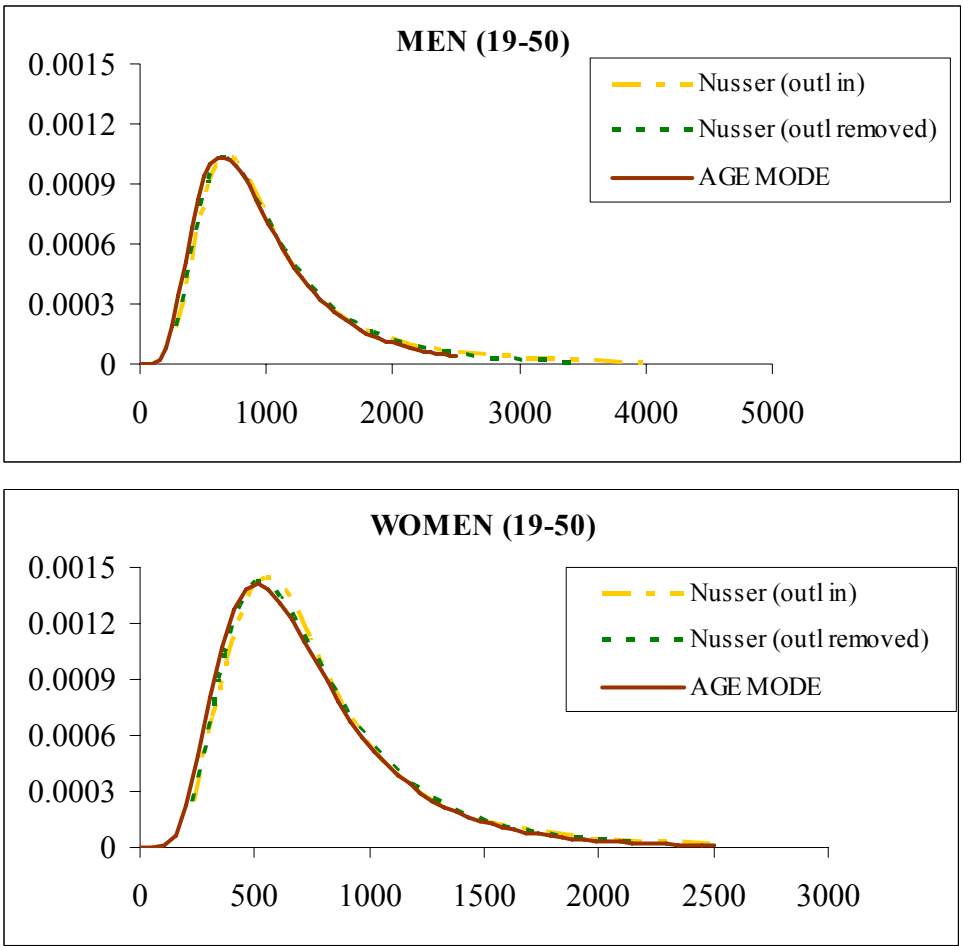


Figure 6.4: Comparison of estimated habitual vitamin A intake distributions from AGE MODE and the Nusser method.

Table 6.2: Comparison of habitual intake estimates (mean and 50th percentile in RAE/day) from AGE MODE and Nusser.

	Report 2005 (Nusser)		**AGE MODE**		**Nusser (outl removed)**		**Observed (outl removed)**	
	Mean	P50	Mean	P50	Mean	P50	Mean	P50
males 14-18 (16)[1]	960	817	825	715	975	831	865	615
females 14-18 (16)[1]	741	662	667	591	741	662	725	483
males 19-50 (35)[1]	1096	899	1007	868	1061	894	1027	644
females 19-50 (35)[1]	787	676	753	658	766	672	743	502

[1]The Nusser estimates reflect estimated habitual intake parameters for all individuals in the age group, The AGE MODE estimates reflect the habitual intake of the age in brackets.

persons. These are reference values used in recent reports from the Health Council of the Netherlands (Gezondheidsraad, 2003).
The obtained EARs and the reference weights and growth factors used in the calculation are presented in Table 6.3. For children also pooled estimates are given for certain age classes in accordance with the former RIVM-report on vitamin A (Waijers and Feskens, 2004).

To apply the probability approach a requirement distribution for vitamin A needs to be determined. In addition to the EAR information on the variation in requirements and the shape of the distribution is needed. Based on the study of Olson the IOM has set the VC for the vitamin A requirements in the population at 20% (Olson, 1987; Institute of Medicine, 2001). As in the Dutch DRIs from 1989 nothing is mentioned concerning the variation in requirements, we will adopt this CV of 20%. No statement is made on the shape of the requirement distribution. Therefore, we will assume it to be normally distributed.

Table 6.3: EARs for vitamin A (in RAE/day), calculated with Olson's formula using reference weights and growth factors for the Dutch population.

Age	Reference weight (W)		Growth factor (G)		EAR for vitamin A	
	boys/ men	girls / women	boys/ men	girls / women	boys/ men	girls / women
1	10.2	9.6	0.40	0.44	195	184
2	13	12.3	0.29	0.28	214	197
3	15.2	14.7	0.24	0.23	232	217
1-3	*14*	*13.5*	*0.27*	*0.27*	*220*	
4	17.4	16.9	0.19	0.21	247	237
5	19.8	19.2	0.19	0.20	273	258
6	22.4	21.8	0.19	0.19	298	280
7	25	24.7	0.16	0.18	316	305
8	27.9	27.8	0.16	0.17	344	332
4-8	*24*	*23.5*	*0.18*	*0.18*	*300*	
9	30.8	31	0.14	0.16	363	358
10	33.8	34.5	0.14	0.16	387	388
11	37.2	38.5	0.14	0.16	418	422
12	41.5	43.2	0.17	0.16	467	460
13	46.8	48.3	0.20	0.13	521	485
9-13	*40*	*41*	*0.16*	*0.15*	*440*	
14	52.9	52.7	0.19	0.08	569	496
15	58.8	56	0.15	0.06	593	506
16	63.8	58.4	0.10	0.03	603	510
17	67.4	60	0.05	0.02	602	515
18	70.1	61.3	0.03	0.02	606	522
14-18	*65*	*59*	*0.08*	*0.03*	*600*	*510*
19-30	***75 (W_{aver})***	***64 (W_{aver})***			***620***	***530***
31-50	*72*	*62*			*600*	*520*
51-70	*74*	*64*			*610*	*530*
>71	*74*	*63*			*610*	*520*

Box 6.1: The Olson formula to estimate the EAR for vitamin A for adults (Olson, 1987; Institute of Medicine, 2001).

*EAR vitamin A ~ A * B * C * D * E * F*

A = % of body vitamin A stores lost per day when ingesting a vitamin A-free diet
~ 0.5% per day (0.005)
based on the rate of excretion of radio-activity from radio labeled vitamin A and by the calculation of the half-life of vitamin A

B = Minimum acceptable liver vitaminA reserve
20,000 µg/kg
concentration at which (1) no clinical signs o f a deficiency are observed, (2) adequate plasma retinol concentrations are maintained, (3) induced biliary excretion of vitamin A is observed, and (4) there is a protection against a vitamin A-deficiency for approximately 4 months while the person consumes a vitamin A-deficient diet.

C = The liver weight : body weight ratio
1:33 (0.03)
average of children and adults

D = Reference weight for a specific age group and gender

E = Ratio of total body : liver vitamin A reserves
10:9 (1.1)
based on individuals with adequate vitamin A status

F = Efficiency of storage of ingested vitamin A (40%)
100:40 (2.5)
determined by isotope dilution methods

The EAR for children and adolescents is extrapolated from adults by using metabolic body weight ($kg^{0.75}$) and a growth factor (Institute of Medicine, 2001):

*EAR child = EAR adult * F*
*F = (weight child (W)/average weight adult (W_{aver})) ^0.75 * 1+growth factor(G))*

6.3 Evaluating vitamin A intake in relation to requirements

Like in the previous chapter on folate, prevalence estimates describing the proportion of individuals in the population with inadequate intakes for vitamin A, are given. Again, estimates from the EAR cut-point approach and the probability approach, are depicted in one figure to compare the results (Figure 6.5). Although there is no reason to assume that vitamin A requirements are lognormally distributed, these results are also depicted in accordance with the folate results.
Resulting prevalence estimates are very close. This can be explained by the fact that the variation in intakes is far larger than the variation in requirements, making the estimates more reliable (Waijers et al., 2004). Therefore, in the case of vitamin A, the choice for the approach used to estimate the prevalence of inadequate intakes does not importantly influence the results.

The final prevalence estimates, obtained with the EAR cut-point approach can be found numerically in Appendix 6. Especially in adolescents intake inadequacy appears to be high. 25% to 39% of adolescent women seem not meet the vitamin A requirements. The findings are in line with the conclusions in the previous report, although prevalence estimates are somewhat higher, up to 10% in adolescents. This can be explained by the slightly lower estimated habitual intake estimates, due to the methodology used, as explained in paragraph 6.1.

Thus, based on the DFCS-3 and the recommendations, the evaluation of the vitamin A intake suggests that the intake is inadequate for a 25 to 40% of the population. For children this is possibly lower. Similar to the findings of folate, policies should not be based on these findings only. It would be interesting what the new data of the Food Consumption Surveys will show, as the data on intake used in this example is already gathered 8 years ago. And also for vitamin A eventually problems should be verified with biochemical analyses..

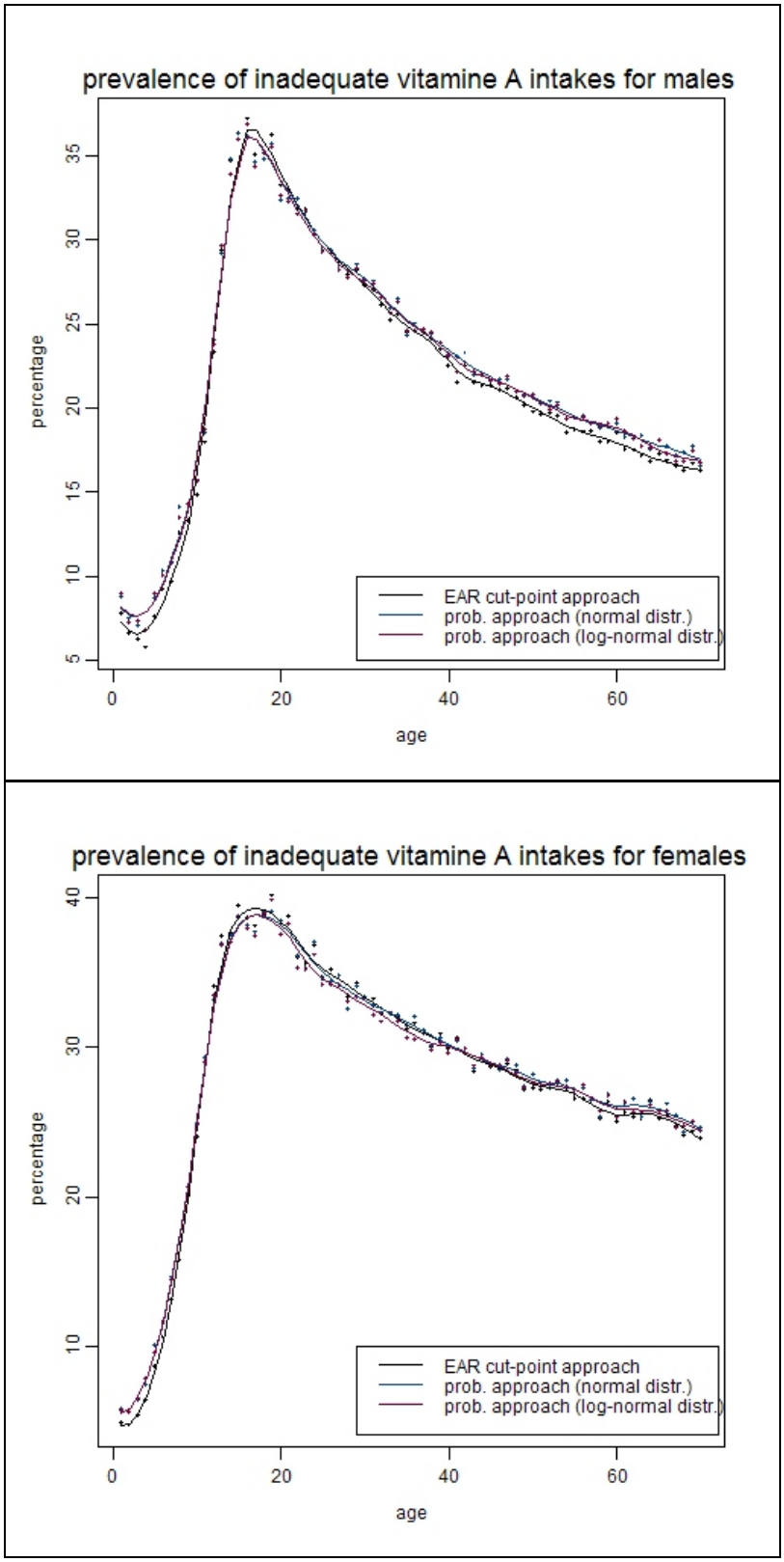


Figure 6.5: Estimates for the prevalence of inadequate vitamin A intakes for males and females, applying the EAR cut-point approach and the probability approach. For the probability approach it was assumed that the requirements showed a normal or a lognormal distribution and a CV of 20%.

7. Discussion

In this report a new method to evaluate the intake of micronutrients has been presented, called AGE MODE. As the acronym indicates, the model assesses intakes of micronutrients and other dietary components in an age dependent manner.

The use of AGE MODE fits in a general framework for the evaluation of micronutrient intakes in relation to requirements, consisting of three parts. First the habitual intake of the micronutrient must be estimated from the observed intakes. This first part is statistically the most complex. Then the (distribution of) requirements for the micronutrient need to be described, which is actually performed outside AGE MODE. Although this may sound straightforward, as the description of the requirements in the population can be based on the dietary reference intakes, this is complicated by the inadequacy of information on requirements. Subsequently the habitual intakes can be related to the requirements to obtain estimates for the prevalence of inadequate intakes. For this purpose the EAR cut-point approach or probability approach can be used. AGE MODE produces habitual intake distributions from short-term measurements (first part) and can be applied to obtain estimates for the prevalence of inadequate intakes in a population (third part).

7.1 Bias and uncertainties in dietary evaluation

Before considering AGE MODE and the 3 steps in dietary evaluation some general comments need to be made. The procedure and statistical methods proposed in this report aims to assess intakes of, in the first place, micronutrients in relation to requirements. However, it should be realized that intake data are subject to uncertainties and bias. Bias can arise in the first place from misreporting or underreporting of specific foods, but can be minimized by a good study design and the most optimal method of food consumption survey. In addition, the validity of the calculated micronutrient intakes depends to a large extent on the validity of the food composition table. Furthermore, as can be seen from the folate and vitamin A data, intakes itself are subject to large day-to-day *and* inter-individual variations. The proposed methodology aims to estimate these variations, but the importance of adequately large sample sizes is evident.

In addition, for not al nutrients or subgroups an EAR and or a requirement distribution is defined. In addition if it is defined, it can only be estimated with large uncertainty, a reason for the Health Council to choose a high coefficient of variation. In this report we made some arbitrary assumptions about the EAR and for the probability approach for the requirement distribution. This was mainly done for showing in what way AGE MODE can deal with the EAR cutpoint approach and the probability approach. However, these assumptions can of course have affected the estimates of inadequacy. For standardization reasons it would be better to use only EARs or EAR-distributions which are defined by the Health Council. This

means that if no EAR is available in fact no estimate for the proportion with an inadequate intake can be calculated, independent whether AGEMODE, Nusser or STEM is used.

7.2 AGE MODE: strengths and limitations (as compared to the Nusser method)

In this report AGE MODE has been described, and applied to and exemplified by folate and applied also to vitamin A. Currently in the Netherlands the so-called Nusser method, developed at Iowa State University, is used to estimate habitual intake distributions from short-term measurements. As described in one of the previous chapters, each method has its own advantages and disadvantages.

The feature of age dependency shows clear advantages above the creation of subgroups, as has been discussed in paragraph 3.6. It is not only more appealing, but also for subgroups of children variation in intakes can to a large extent be explained by age. AGE MODE overcomes this problem. Furthermore, it produces consistent estimates across ages, and habitual intake estimates may be more reliable, especially for smaller population samples. Another important strength of AGE MODE is its transparency. The input data become visible, all steps in the estimation of the habitual intakes are clearly described and illustrated, and the final estimates are depicted in one figure with the original observations. This allows gaining insight into the data. In contrast, the Nusser method is rather a ‘black box’, which may bring about incorrect use. Furthermore, there is no insight in why problems arise and what can be done to solve them. Therefore, resulting habitual intake estimates should be considered with the greatest care, especially if little intake data are available, if the data contain influential outliers, or if intakes of less habitual substances is considered. In fact this is a general plea to pay more attention to the data before just starting the analyses. Too little attention may be paid to this aspect, whereas it is highly important to look before one leaps. On the other hand, the Nusser method contains some features, like the possibility to estimate the proportion of consumers and non-consumers for less frequently consumed dietary compounds. These issues should be developed in AGE MODE.

7.3 AGE MODE: further developments

Although AGE MODE is now applicable, the model can be further developed. Several issues have been pointed out to improve the model. Most important may be to study the use of higher order polynomials or options to make the age dependent polynomial more flexible, so that it may even better describe the data. Furthermore, at this moment, variances are assumed to be the same for all ages. This assumption may not be valid, and could be relaxed by estimating inter- and intra-individual variances as a function of age. This will not greatly influence the results, but may optimize the model. And, as mentioned, it should be investigated how an additional module can be incorporated in AGE MODE to discern

between consumers and non consumers and to estimate consumption frequency. The methodology for this has already been developed and is available in S-PLUS. Additionally, the inclusion of covariates in the model should be studied, as well as further adjustments of the data before analysis. A next step could be to incorporate the calculation of micronutrient intakes from food consumption data, in the methodology. This would to a great extent facilitate calculations and detection of irregularities.
Furthermore, AGE MODE may not only be used to assess prevalences of inadequate intakes, but can also be applied for other purposes. For example, to estimate habitual intakes of micronutrients from enriched products and relating these intakes to upper safe levels of intake may pose new analytical challenges.
A broader application of AGE MODE may lead to new insights to further adapt, extent, and/or optimize the model and make it more convenient for use, for the Dutch users, but possibly also for other users.

7.4 The EAR cut-point approach or the probability approach?

For step 3 of the overall evaluation procedure two different approaches to relate intakes to requirements are considered: the EAR cut-point approach and the probability approach. The latter approach was favoured in a previous report (Waijers et al., 2004). With the probability approach an accurate estimate of the number of individuals with an inadequate intake can be obtained if the specified requirement distribution reflects the true distribution of requirements in the population. However, the information necessary to specify the requirement distribution is generally not available, making it impossible to specify a requirement distribution without doing additional assumptions that may or may not be valid.

To apply the EAR cut-point approach only the EAR is needed. Therefore, although application of the EAR cut-point approach involves assumptions that are not tested nor made visible, it is much more practical, and therefore recommended for use, at least until the DRIs have been adapted to provide all the information necessary to specify requirement distributions. In this respect, the uncertainties in the DRIs must be borne in mind. Therefore, efforts should be directed to upgrade the DRIs to also include information on the (true) variation in requirements in the population and the shape of the requirement distribution. Furthermore, the DRIs are specified for age groups, whereas the proposed methodology works age dependently and therefore demands the DRIs also to be specified in this way.

7.5 AGE MODE in international perspective

To establish a sound dietary evaluation procedure is an issue not only in the Netherlands, but throughout the world. For the Netherlands the European context is important. Ideally the same procedure is used throughout Europe.

To establish a common procedure is the aim of the European Food Consumption Validation (EFCOVAL) project, that has been launched within the EU Sixth Framework Programme. EFCOVAL aims to further develop and validate a trans-European food consumption methodology. One of the project's main objectives is to improve the methodology and statistical aspects, one of the goals being to provide an improved statistical tool for estimating habitual intake distributions from two 24h dietary recalls. Within this work package a so-called Simplified Nusser method for estimating habitual intake distributions has already been proposed. In addition, a comparison between the different available methods, including AGE MODE will be made. Ideally, the new harmonized method would be a combination of all strengths of the different methods.

To enable a proper discussion internationally about the advantages and disadvantages for the different methodologies , we presented AGE MODE at the sixth International Conference on Dietary Evaluation Methods in Copenhagen and published the description of the model in an international peer-reviewed journal in the field of nutrition (The Journal of Nutrition) (Waijers et al., 2006). Furthermore we made a manual for potential users of AGE MODE.

The developments within EFCOVAL may affect the work on AGE MODE. Harmonization of the methodologies is necessary. Therefore, developments in the European context need to be followed closely.

7.6 Conclusions on the intake of folate and vitamin A

In this report AGE MODE has been applied to folate and vitamin A. The resulting habitual intake estimates as well as the estimated proportions of individuals with an intake below the requirement have been presented in Chapters 5 and 6, respectively. For a rather high percentage of the adolescent women the folate intake seems to be inadequate (about 60 to 80%), where as for vitamin A up to 39% of adolescent women appears not to meet the dietary reference intakes.

These results are similar to those in a previous report on folate (Waijers et al., 2004). For vitamin A the findings are also in line with the conclusions in a former report (Waijers and Feskens, 2004), although prevalence estimates are up to 10% higher in adolescents. This can be explained by the slightly lower habitual intake estimates resulting from the difference in methodology.

Thus, based on the DFCS-3, the evaluation of the folate and vitamin A intake suggests that the intake is inadequate for a high percentage of the population. However, for several reasons one should be cautious when undertaking changes in the current policy based on these findings. For example, this survey was based on data from 8 years ago. In addition, in these intakes the intake by supplements were not used yet. Furthermore, the requirements were based on folate, while perhaps folate acid equivalents would be more accurate.
Finally, evaluating intakes of micronutrients from food consumption data in relation to requirements enables to detect risks of inadequacy. However, verification of the findings by assessing the population's status for the micronutrient, in this case folate and vitamin A status, with biochemical parameters is desired.

7.7 Recommendations

The following recommendations result from the findings presented in this report:

- Nationally and internationally, a common sound dietary evaluation procedure should be established.
- The (dis)advantages and potentials , such as transparency and age dependency, of all existing method should be considered in this procedure.
- A detailed comparison of the available methods used for several research questions can help in the choice for the common dietary evaluation procedure .
- If AGE MODE should be part of an internationally procedure, the method should be improved and extended on the following important methodological issues:
  - to include an additional module to discern between consumers and non consumers and to estimate consumption frequency;
  - to study the use of statistical techniques to improve the age dependent polynomial (the use of higher order polynomials, B-spline, et cetera);
  - to explore the properties of the model (simulation studies);
  - to study inclusion of covariates in the model and further adjustments of the data;
  - to explore AGE MODE to assess micronutrient intakes in relation to upper safe levels of intake, micronutrient intakes from enriched products or supplements, and intakes of other dietary components.

- The evaluation procedure needs to be prepared for other micronutrients and for the results of the food consumption survey in children in the Netherlands of which the data collection has just finished.

- The evaluation procedure needs to be fine-tuned to match with the new food consumption surveillance system.

- At this moment it is not possible to apply the probability approach to estimate the proportion of individuals with inadequate intake.
    - Until the DRIs have been adapted the EAR cut-point approach is the recommended procedure to assess intakes of micronutrients;
    - If it is desired to use the probability approach to assess intake adequacy in the future, then the DRIs should be specified in a way that is suitable for this approach.
- In an evaluation procedure which is based on an age dependent approach the DRIs also need to be specified age dependently.

- Following the recommendations in previous reports: the health consequence of the potential inadequate supply to the population especially of folate, and to a lesser extent of vitamin A, needs to be assessed and trends in intake need to be closely monitored.

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Appendix 1: Report of the workshop on micronutrient evaluation

On November 1st 2005 in Utrecht

Attendants:

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Henk vd Berg	Voedingscentrum
Karin Hulshof	TNO
Joyce de Stoppelaar	VWS
Marga Ocké	CVG, RIVM
Hendriek Boshuizen	IMA, RIVM
Jolanda Boer	CVG, RIVM
Patricia Waijers	CVG, RIVM

The workshop

The new model to assess micronutrient intakes in relation to requirements, temporarily named ADMAD (Age Dependent Model for the Assessment of Dietary components)[1] was presented and explained. This was followed by a general discussion on the model and several related issues, with special attention to the dietary reference intakes.

General

It was mentioned that the Steering Committee on Nutrition of the Health Council[2] prefers the Nusser method above STEM to estimate the habitual intake distribution. It was therefore made clear that the new model is very distinct from STEM. It only adopted the basic idea of fitting an age dependent function. The new model is statistically sound.

The strength of the new model to assess intakes in relation to requirements, as compared to the Nusser method[3], was explained.

Limitations of current practice:

- The Nusser method requires the specification of subgroups according to age. In general age groups are chosen in concordance with dietary reference intakes. However, intakes and requirements do not increase in steps, but gradually with age. In addition, consumption levels, and also requirements, may differ considerably between for example 4 and 8 year old children.

[1] ADMAD has been a temporal name for the model now and in the remainder of the report referred to as AGE MODE

[2] Beraadsgroep Voeding van de Gezondheidsraad

[3] With the Nusser method the habitual intake distribution can be estimated from observed intakes. Prevalences of inadequate intakes for specified age and gender groups can be estimated separately in a next step.

- A habitual intake distribution for 4 to 8 year olds is in fact not a habitual intake distribution. 4 year olds will be at the lower site, whereas 8 year olds will have the higher intakes.
- There is a large variation in (folate) intakes. It is not likely that mean intake for 19 year olds is truly 20% higher than that of 20 and 21 year olds and that when individuals reach the age of 22 their intake goes up again with 12%. However on the longer run, from the age of 20 to 60 a true tendency may exist. The large fluctuations in mean intakes per age year show the high uncertainty in the measurement and the importance of large numbers to gain a reliable estimate of the true intake. When smaller subgroups are taken the reliability of the estimate may be poor.
- Nusser adheres close to the data. The estimated habitual intake distribution will be greatly influenced by the sample size (a smaller sample size may produce unreliable estimates) and outliers. This can result in very distinct model assumptions and estimates for adjacent groups.

In the new model these problems are solved by calculating a (non-linear) regression function, age being the dependent variable, all the data are used. No subgroups need to be created. This means that power of precision can be lend from adjacent ages.
It was put forward that with the Nusser method aspects like the day of the week can be taken into account. This option is not implemented in the new model, but could be included. Whether this is desired is questionable as follows from the discussion below.

Outcome

1. Support for the new model
   - The general framework and use of the probability approach to relate intakes to requirement is supported. The Steering Committee on Nutrition also prefers the probability approach above the cut-point approach.
   - The idea of the estimated average requirement being specified as a function of age is supported. The construction of age categories is in fact artificial. On the other hand, there are large uncertainties in the requirement estimate. Still, an age dependent function will better describe the course of the requirements over age than a staggered course.
   - The advantages of ADMAD above the Nusser method to estimate the habitual intake distribution as a function of age are recognized, although validation and broader support is required:
     - It should be made very clear how the new model relates to the Nusser method and what the advantages of the new model are compared to the Nusser method (and estimating the prevalence of inadequate intakes for specified age and gender groups). The Nusser method is now generally accepted and in use, also internationally.

- There should be broader (international) support for the new model. Publication in an international journal is one step in this process.
- The new model should be validated. Several options were proposed. Using the Dutch food consumption survey among 2- and 3-year old children, using the 12 repeated recalls for 120 Dutch individuals from the early nineties. Also dietary data from the United States could be used. It could also be attempted to interest another group for the new model, for example Kurt Hoffmann in Potsdam or a group in Great Britain, in order to gain support and make use of their data for validation purposes.
- It was put forward that the method can also be validated by determining nutritional status. However, this is in fact not only (or not in the first place) a validation of the new model, but rather a validation of the dietary reference intakes and the dietary assessment method (data collection and calculation of nutrient intake with food consumption table).
- A general remark that came back several times during the workshop: there are many uncertainties and assumptions in the overall dietary assessment procedure (food consumption data, food consumption table, estimated average requirement). This raises the question how 'exact' a model needs to be that uses this information to estimate the prevalence of inadequate intakes. How far should we go?
- For example: in the model the variation is assumed to be homogenous over all ages. This assumption may not be valid. It would be better to estimate the variation age dependent. However, the workshop members argue that many uncertainties exist in the intake data: how far should we go in (statistically) optimizing the model?
- From what age on should intakes of men and women be assessed separately? Differences between males and females start early. Considering the mean observed intakes per age year can give insight into the age at which intakes seem to really start diverging.

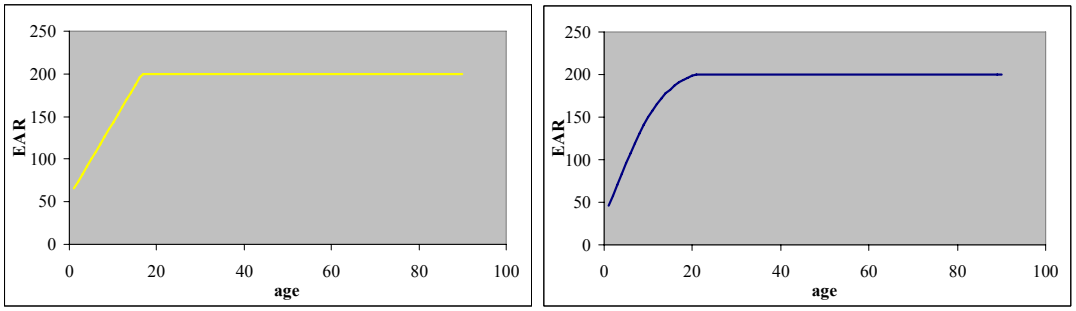
The new model had temporarily been named 'ADMAD': Age Dependent Model for the Assessment of Dietary components. However, the workshop members found this name not very appropriate. 'Assessment' would suggest that 'dietary assessment methodology' is concerned, instead of evaluating intakes in relation to requirements. All participants will reflect on an appropriate name for the model.

2. 'Estimating' the Estimated Average Requirement (EAR)[1]
   - The workshop members find it reasonable to derive an EAR for age categories that only have an Adequate Intake (AI). Although this is not correct given the definition

[1] Estimated Average Requirement = gemiddelde behoefte

of the AI, it is the only way to obtain an estimate of the prevalence of inadequate intakes. This is however not allowed if for a certain micronutrient no EAR for adults has been specified.

- The workshop members conclude that the EAR should be obtained by interpolation, departing from the EAR for adults and the AI for breast-fed babies. As a result no extra 'function' needs to be fit through the data, as this approach will already result in an age dependent curve. In doing so, an additional problem arises, that is *at what age and how* should the curve convert to the EAR for adults. For folate for example from the age of 14 the EAR is set at 200, equal to the EAR for adults. It is considered very important to stick as much as possible to the requirements set by the Health Council. But should the shift be as depicted in Figure 1a or Figure 1b? Figure 1b appeals more, as the angle in Figure 1a seems artificial. However a rounded transition demands further assumptions. This issue should be discussed and decided on in the Steering Committee on Nutrition of the Health Council. It is decided that meanwhile the approach as depicted in Figure 1a will be used (interpolation of the EAR for adults and infants, so that the level of 200 is reached at the age of 14).



a) *b)*

Figure 1: EAR as a function of age, two options: a straight (a) or rounded (b) angle.

3. The requirement distribution

- Specification of a requirement distribution based on the EAR and CV is supported
- It is not desirable to specify various requirement distributions by varying the EAR and CV. The Health Council has set the criteria and determined the EAR. If the choice for the EAR appears not to be optimal this is an issue for the Health Council.
- For folate the situation is complex. In the report on dietary reference intakes for folate it is explicitly mentioned that 12% of the population, carriers of the C667TT-genotype in the MTHFR-gene, have increased requirements. In order to also cover the needs of those individuals the CV was set at 25%. Departing from a normal distribution with a CV of 25% will not correctly describe the requirement distribution in the population. This may result in an unreliable estimate of the prevalence of inadequate intakes if the probability approach is used. It is therefore

decided that for folate the distribution of requirements should also be specified as depicted in Figure 2. The EARs for the two subgroups should be arithmetically determined. The CV can be set at 10%.

- For every micronutrient different issues that need to be decided on may be at stake when the new method is used to assess intake adequacy. It is suggested that when a new nutrient is to be assessed, a proposal to handle the requirements should be presented to the Steering Committee on Nutrition of the Health Council. With agreement of the working group results are generally supported.
- If this new model will be used to assess intake adequacy in the future, then the dietary reference intakes should be specified in a way that is suitable for this approach. This issue needs to be discussed in the Steering Committee on Nutrition of the Health Council.

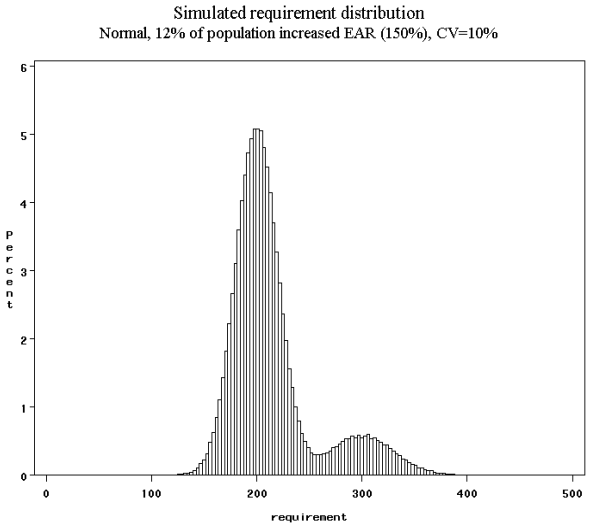


Figure 2: An example of the folate requirement distribution in the population

4. Outliers in the intake data
    - In the new model outliers are removed on the basis of a statistical test. Outliers can seriously influence the data and the estimated habitual intake distribution. However the workshop members feel that it is incorrect to remove outliers if these intakes do really occur (and can be explained). For example, liver consumption often causes extreme intakes for folate and vitamin A. Knowledge of true occurrence and frequency of (liver) consumption is of interest. It is a new challenge to incorporate such information in the model. At TNO this issue has been examined for vitamin A. Kevin Dodd (US) has also done work on this issue.

Appendix 2: Detailed description of AGE MODE

AGE MODE is a general methodology which can be used for all types of intakes. The aim is to estimate in a general way the lifetime intake as a continuous function of age. The methodology is based on ideas of Slob (Slob, 1993), generalized as much as possible. The model has been programmed in S-PLUS (Anonymous, 2005).
AGE MODE contains several steps, explained in more detail below:

1. Box-Cox transformation of the observed intakes to obtain normally distributed data.
2. Fitting a fractional polynomial to the transformed data.
3. Obtaining a Mixed Effect estimate of the fractional polynomial, providing the inter-individual variance and the intra-individual variance.
4. Identification of possible outliers.
5. Check of λ
6. Back-transformation by Monte Carlo Simulations to obtain the habitual intakes on the original scale
7. Additional steps in dietary assessment

1. Box-Cox transformation of the observed intakes to obtain normally distributed data

Intake data are generally skewed, whereas most statistical analyses require normally distributed data. Therefore, before fitting a regression function of the intakes on age, either or not stratified by gender, it is necessary to transform the data. With the Box-Cox method the transformation parameter λ is estimated so that after transformation the intake data are symmetrically and approximately normally distributed (equation 1).

$$f(x) = (x^{\lambda} - 1) / \lambda \qquad \text{(eq 1)}$$

Note that for $\lambda = 0$, $f(x) = \ln(x)$
The result of the transformation is shown in a QQ-plot. To check whether the transformation was successful an 'optimal lambda' is calculated, indicating the additional transformation required for the transformed intakes to obtain a normal distribution. Ideally, this optimal lambda should have a value of 1 (no additional transformation needed).

2. Fitting a fractional polynomial to the transformed data

With fractional polynomial regression the best polynomial function is searched to describe the data, while no underlying function is assumed. Fractional polynomial regression has been described well by Royston and Altman (Royston and Altman, 1997). Let *n* denote the number of observations and let *p* and *q* be the powers of the fractional polynomial $y(x_i)$. The fractional polynomial regression function (equation 2) is given by:

$$y_i = a + b*(x_i)^p + c*(x_i)^q + \varepsilon_I \ (i= 1,2,\ldots,n,\ p\neq q)$$

or (eq 2)

$$y_i = a + b*(x_i)^p + c*(x_i)^p*\ln(x_i) + \varepsilon_I \ (i= 1,2,\ldots,n,\ p=q)$$

where x_i is the age of individual i, and y_i the transformed intake; p and q can take the value of {-2,-1,-0.5,0,0.5,1,2}. In this way the transformed intakes are described by at most a three parameter family of curves, and the optimal fractions p and q are estimated as well as *a, b* and *c*.

3. Obtaining a Mixed Effect estimate of the fractional polynomial, providing the inter-individual variance and the intra-individual variance

Since for each person intake data for at least two days are available equation 2 is refit with a mixed effect model. Each person is seen as a group with two or more observations, allowing estimating the intra-individual day-to-day variance, τ^2, and the inter-individual variance, denoted by σ^2. We redefine equation 2 for the case $p \neq q$, and define '*a*' as a random parameter, the individuals being the grouping variable, and the intakes for an individual may differ by day so that equation 2 can be reformulated into:

$$y_{ij} = a + \alpha_i + b*(x_i)^p + c*(x_i)^q + \varepsilon_{ij} \qquad \text{(eq 3)}$$

where y_{ij} is the transformed intake for individual i on day j, $\alpha_i \sim N(0,\sigma^2)$, σ^2 being the inter-individual variance, and $\varepsilon_{ij} \sim N(0,\tau^2)$, τ^2 constituting the intra-individual variance. The overall variance has thus been split into the inter- and intra-individual variance.

4. Identification of possible outliers

Outliers can seriously influence the Box-Cox transformation and the Mixed Effect Estimate and therefore deserve special attention. Given the generally large numbers of observations it is impossible to examine the result of equation 3 manually on possible outliers or other abnormalities. Therefore Grubbs method is used to detect outliers numerically by assuming that the residuals of equation 3 are normally distributed (Grubbs, 1969; Grubbs and Beck, 1972). This test calculates cut offs beyond which occurrence of an observation is very unlikely. To check if the residuals are normally distributed diagnostic plots of the Kolmogorov Smirnov goodness of fit test from the S-PLUS module Environmental Stats are used (Millard, 2002).
Grubbs' test statistic is defined as:

$$G = (\max |y_i - \text{mean}(y_i)|)/s \qquad \text{(eq 4)}$$

where mean *(yi)* and *s* denotes the sample mean and the standard deviation, respectively.
So the Grubbs' test statistic is the largest absolute deviation from the sample mean in units of the sample standard deviation. For the two-sided test, the hypothesis of no outliers is rejected at the significance level α if

$$G > (N-1)\sqrt{t^2_{(\alpha/(2N),N-2)} / N} \qquad \text{(eq 5)}$$

with $t_{(\alpha/(2N),N-2)}$ denoting the critical value of the t-distribution with *(N-2)* degrees of freedom and a significance level of $\alpha/(2N)$.
If the researcher decides to remove the statistical outlier, both observations for the individual are removed from the sample. Elimination of the outliers results in improvement of the QQ-plots, but the goodness of fit test almost always rejects the null-hypothesis (that residuals are normally distributed) given the large number of observations.

5. Check of λ

Finally a check of normality is carried out with some graphs and a normality test, which always rejects the null-hypothesis, given the large amount of data. Therefore the Box-Cox transformation is carried out again, because the residuals, without the outliers, should be at least symmetrically distributed. The estimated Box-Cox parameter, reported as 'λ-check' should be near to one, which means that no additional transformation is needed.
If outliers have been removed, steps 1 to 4 need to be repeated until no further outliers are eliminated.

6. Back-transformation by Monte Carlo Simulations to obtain the habitual intakes on the original scale

To obtain the habitual intake distributions on the original scale Monte Carlo Simulations are performed, using the results of the fitted Mixed Effect model. In order to obtain the long-term mean intake for each individual, the intra-individual variance needs to be eliminated.
First simulated intakes are generated on the transformed scale by drawing *n* individuals of each age, and creating a time series of *k* intake days for each individual *i* with:

$\alpha \sim N(0, \sigma^2)$
$\varepsilon_{i,t} \sim N(0, \tau^2)$ for t= 1,2,…, *k*

Resulting in a time series for each individual *i*

$$y_{i,t} = a + b*(x_i)^p + c*(x_i)^q + d_i + e_{i,t} \qquad \text{(eq 6)}$$

where d_i, and $e_{i,t}$ are realizations of α_i, and $\varepsilon_{i,t}$ in equation 3.
Then each of the generated observations is back transformed to the original scale:

$$x_{i,t} = (\lambda*y_{i,t} + 1)^{1/\lambda} \qquad \text{(eq 7)}$$

These individual long-term intakes can subsequently be averaged into the population mean habitual intake for a given age. The habitual intake distribution of an age class, with a corresponding confidence interval, can be estimated from the individual mean intakes, averaging over *t*

$$x_i = \text{mean}(\{\lambda*y_{i,t} + 1\}^{1/\lambda}) \qquad \text{(eq 8)}$$

For every age class the distribution of *n* individuals, is given by $\{x_1, x_2, \ldots, x_n\}$, which implies that the mean of the population and all quantiles can be calculated.

7. Additional steps in dietary assessment

Once the habitual intake distributions have been estimated the proportion of individuals with inadequate intakes can be estimated. A cut-point approach is straightforward and does not demand any computational effort, more than counting the number of individuals with intakes lower than the cut-off. The probability approach can be carried out by Monte Carlo Simulations. For each randomly drawn observation (from step 4), or differently stated, for each simulated individual with a certain lifetime mean (habitual) intake, a requirement can be drawn from a specified requirement distribution. If the simulated habitual intake exceeds the simulated requirement for that individual, the intake is adequate, if it is lower than the requirement, it is inadequate. In this way age dependent estimates of the prevalence of inadequate intakes are obtained.

References in Appendix 2:

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Appendix 3: Habitual folate intake characteristics[1]

a) Children (males and females analyzed together)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	110	63	71	86	105	129	153	170
2	99	56	63	77	95	117	140	156
3	113	65	73	89	109	133	158	176
4	125	72	81	98	120	146	174	192
5	134	78	88	106	129	157	185	205
6	141	83	93	112	136	165	195	215
7	146	87	97	116	141	171	202	223
8	151	90	100	120	146	176	208	229
9	155	92	103	123	150	181	213	235
10	158	94	105	126	153	185	218	240
11	161	96	108	129	156	188	221	244
12	164	98	109	131	159	191	225	247
13	166	100	111	133	161	194	228	251

b) Males

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	107	63	70	85	103	125	148	163
2	116	69	77	93	112	135	160	176
3	124	75	83	99	120	144	170	186
4	131	79	88	105	127	152	179	196
5	137	84	93	111	133	159	187	204
6	143	88	97	115	139	166	194	212
7	148	91	101	120	144	172	201	219
8	153	94	105	124	149	177	207	226
9	158	98	108	128	153	182	213	232
10	162	100	111	132	157	187	218	238
11	166	103	114	135	161	192	223	244
12	170	106	117	138	165	196	228	249
13	173	108	119	141	168	200	232	254
14	176	110	122	144	172	204	236	258
15	179	112	124	147	175	207	240	262
16	182	114	126	149	178	210	244	266
17	185	116	128	151	180	214	248	270
18	188	118	130	154	183	216	251	274
19	190	120	132	156	185	219	254	277
20	192	121	134	158	188	222	257	280
21	195	123	136	159	190	224	260	283
22	197	124	137	161	192	227	262	286
23	199	126	138	163	194	229	265	289
24	200	127	140	164	195	231	267	291
25	202	128	141	166	197	233	269	293
26	204	129	142	167	199	235	271	296
27	205	130	143	168	200	236	273	298
28	207	131	144	170	201	238	275	299
29	208	132	145	171	203	239	277	301
30	209	133	146	172	204	241	278	303

[1] Mean and percentiles of the habitual folate intake distribution in µg/day

Appendix 3 (continued)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
31	210	133	147	173	205	242	280	304
32	211	134	148	174	206	243	281	306
33	212	135	149	174	207	244	282	307
34	213	135	149	175	208	245	283	308
35	214	136	150	176	208	246	284	309
36	214	136	150	176	209	247	285	310
37	215	137	151	177	210	247	286	311
38	216	137	151	177	210	248	286	312
39	216	138	152	178	211	249	287	312
40	216	138	152	178	211	249	288	313
41	217	138	152	178	211	249	288	313
42	217	138	152	179	212	250	288	314
43	217	138	152	179	212	250	289	314
44	217	138	153	179	212	250	289	314
45	217	139	153	179	212	250	289	314
46	217	139	153	179	212	250	289	315
47	217	139	153	179	212	250	289	314
48	217	138	153	179	212	250	289	314
49	217	138	152	179	212	250	289	314
50	217	138	152	179	212	250	288	314
51	217	138	152	178	211	249	288	314
52	216	138	152	178	211	249	288	313
53	216	138	152	178	211	249	287	313
54	216	137	151	177	210	248	287	312
55	215	137	151	177	210	248	286	311
56	215	137	151	177	209	247	286	311
57	214	136	150	176	209	246	285	310
58	213	136	150	176	208	246	284	309
59	213	135	149	175	207	245	283	308
60	212	135	149	174	207	244	282	307
61	211	134	148	174	206	243	282	306
62	211	134	148	173	205	242	281	305
63	210	133	147	172	204	242	280	304
64	209	133	147	172	203	241	278	303
65	208	132	146	171	203	240	277	302
66	207	132	145	170	202	238	276	300
67	206	131	144	169	201	237	275	299
68	205	130	144	168	200	236	274	298
69	204	129	143	167	199	235	272	296
70	203	129	142	166	197	234	271	295

Appendix 3 (continued)

c) Females

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	101	58	66	80	97	118	141	155
2	100	58	65	78	96	117	139	154
3	112	66	74	89	108	131	155	171
4	121	72	81	97	117	142	167	184
5	128	77	86	103	124	150	176	194
6	134	81	90	107	130	156	183	201
7	138	84	93	111	134	161	189	207
8	142	86	96	114	138	165	194	212
9	145	88	98	117	141	169	198	217
10	148	90	100	119	143	172	201	220
11	150	92	102	121	146	174	204	224
12	152	93	103	123	148	177	207	226
13	154	94	105	124	149	179	209	229
14	155	95	106	125	151	180	211	231
15	157	96	107	127	152	182	213	233
16	158	97	108	128	154	183	214	235
17	159	98	109	129	155	185	216	236
18	160	99	109	130	156	186	217	238
19	161	99	110	131	157	187	219	239
20	162	100	111	131	158	188	220	241
21	163	100	111	132	159	189	221	242
22	164	101	112	133	159	190	222	243
23	165	101	113	133	160	191	223	244
24	165	102	113	134	161	192	224	245
25	166	102	114	135	161	193	225	246
26	167	103	114	135	162	193	226	247
27	167	103	114	136	163	194	226	247
28	168	104	115	136	163	195	227	248
29	168	104	115	137	164	195	228	249
30	169	104	116	137	164	196	228	250
31	169	105	116	137	165	196	229	250
32	170	105	116	138	165	197	230	251
33	170	105	117	138	165	197	230	252
34	171	105	117	138	166	198	231	252
35	171	106	117	139	166	198	231	253
36	171	106	118	139	167	199	232	253
37	172	106	118	139	167	199	232	254
38	172	106	118	140	167	199	233	254
39	173	107	118	140	168	200	233	255
40	173	107	119	140	168	200	233	255
41	173	107	119	141	168	201	234	256
42	173	107	119	141	169	201	234	256
43	174	108	119	141	169	201	235	256
44	174	108	119	141	169	202	235	257
45	174	108	120	142	169	202	235	257

Appendix 3 (continued)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
46	175	108	120	142	170	202	236	258
47	175	108	120	142	170	202	236	258
48	175	108	120	142	170	203	236	258
49	175	109	120	142	170	203	237	259
50	176	109	121	143	171	203	237	259
51	176	109	121	143	171	203	237	259
52	176	109	121	143	171	204	237	259
53	176	109	121	143	171	204	238	260
54	176	109	121	143	171	204	238	260
55	177	109	121	143	172	204	238	260
56	177	110	121	144	172	205	239	261
57	177	110	122	144	172	205	239	261
58	177	110	122	144	172	205	239	261
59	177	110	122	144	172	205	239	261
60	178	110	122	144	173	206	239	262
61	178	110	122	144	173	206	240	262
62	178	110	122	145	173	206	240	262
63	178	110	122	145	173	206	240	262
64	178	110	122	145	173	206	240	263
65	178	111	123	145	173	206	241	263
66	179	111	123	145	174	207	241	263
67	179	111	123	145	174	207	241	263
68	179	111	123	145	174	207	241	263
69	179	111	123	145	174	207	241	264
70	179	111	123	146	174	207	241	264

Appendix 4: Estimates for the prevalence of inadequate folate intakes

a) Children (males and females analyzed together)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
1	110	59	**6**	9	10
2	99	69	**9**	13	13
3	113	78	**11**	16	16
4	125	88	**15**	19	19
5	134	97	**18**	23	22
6	141	106	**22**	26	25
7	146	116	**26**	30	28
8	151	125	**31**	34	32
9	155	134	**36**	38	37
10	158	144	**42**	43	41
11	161	153	**48**	47	46
12	164	163	**55**	52	51
13	166	172	**61**	57	55

b) Males

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
1	107	59	**5**	8	8
2	116	69	**6**	10	10
3	124	78	**8**	13	12
4	131	88	**10**	15	15
5	137	97	**13**	19	18
6	143	106	**16**	22	21
7	148	116	**20**	26	25
8	153	125	**25**	30	29
9	158	134	**30**	34	33
10	162	144	**36**	38	37
11	166	153	**42**	42	41
12	170	163	**47**	46	45
13	173	172	**53**	50	49
14	177	181	**58**	54	53
15	181	191	**62**	57	55
16	184	200	**64**	59	57
17	185	200	**64**	59	57
18	189	200	**64**	58	57
19	191	200	**62**	57	56
20	193	200	**60**	56	54

Appendix 4 (continued)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
21	195	200	**58**	54	53
22	197	200	**56**	53	52
23	199	200	**55**	52	51
24	200	200	**53**	51	49
25	203	200	**52**	50	48
26	203	200	**51**	49	47
27	205	200	**49**	48	47
28	207	200	**49**	48	46
29	209	200	**48**	47	45
30	209	200	**47**	46	45
31	209	200	**46**	46	44
32	211	200	**45**	45	44
33	212	200	**45**	45	43
34	213	200	**44**	44	43
35	213	200	**44**	44	42
36	214	200	**44**	44	42
37	215	200	**43**	44	42
38	215	200	**43**	43	41
39	215	200	**43**	43	41
40	215	200	**42**	43	41
41	216	200	**42**	43	41
42	216	200	**42**	43	41
43	217	200	**42**	43	41
44	216	200	**42**	42	41
45	216	200	**42**	42	41
46	217	200	**42**	42	41
47	217	200	**42**	42	41
48	217	200	**42**	43	41
49	216	200	**42**	43	41
50	216	200	**42**	43	41
51	216	200	**42**	43	41
52	215	200	**42**	43	41
53	215	200	**42**	43	41
54	215	200	**42**	43	42
55	215	200	**43**	43	42
56	215	200	**43**	43	42
57	214	200	**43**	44	42
58	213	200	**44**	44	43
59	214	200	**44**	44	43
60	211	200	**45**	45	43
61	212	200	**45**	45	44
62	211	200	**45**	46	44
63	211	200	**46**	46	44
64	209	200	**46**	46	45
65	209	200	**47**	46	45

Appendix 4 (continued)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
66	208	200	**48**	47	45
67	208	200	**48**	47	46
68	206	200	**49**	48	46
69	206	200	**50**	48	47
70	205	200	**51**	49	47

[1]The requirements are assumed to be lognormally distributed, with an EAR of 200 and a CV of 25%
[2]The requirements are assumed to be normally distributed, with an EAR of 200 and a CV of 25%

c) Females

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
1	107	59	**7**	11	11
2	116	69	**10**	14	14
3	124	78	**13**	18	17
4	131	88	**16**	21	20
5	137	97	**21**	25	24
6	143	106	**26**	29	28
7	148	116	**31**	34	33
8	153	125	**37**	39	38
9	158	134	**44**	44	43
10	162	144	**51**	49	48
11	166	153	**58**	54	53
12	170	163	**65**	59	58
13	173	172	**71**	64	63
14	177	181	**76**	68	67
15	181	191	**80**	70	70
16	184	200	**82**	73	72
17	185	200	**83**	74	73
18	189	200	**83**	74	73
19	191	200	**83**	74	73
20	193	200	**82**	73	72
21	195	200	**81**	72	71
22	197	200	**81**	72	71
23	199	200	**80**	71	70
24	200	200	**80**	70	70
25	203	200	**79**	70	69
26	203	200	**79**	70	69
27	205	200	**79**	69	69
28	207	200	**78**	69	69
29	209	200	**78**	69	68
30	209	200	**78**	69	68

Appendix 4 (continued)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(µg/day)		*EAR cut-point approach*	*Prob approach (normal)*[1]	*Prob approach (lognormal)*[2]
31	209	200	**77**	69	68
32	211	200	**77**	68	68
33	212	200	**77**	68	67
34	213	200	**76**	68	67
35	213	200	**76**	67	67
36	214	200	**76**	67	67
37	215	200	**76**	67	66
38	215	200	**75**	67	66
39	215	200	**75**	67	66
40	215	200	**75**	66	65
41	216	200	**74**	66	65
42	216	200	**74**	66	65
43	217	200	**74**	66	65
44	216	200	**74**	66	65
45	216	200	**74**	66	65
46	217	200	**74**	66	65
47	217	200	**74**	66	65
48	217	200	**73**	65	65
49	216	200	**73**	65	64
50	216	200	**73**	65	64
51	216	200	**73**	65	64
52	215	200	**73**	65	64
53	215	200	**73**	65	64
54	215	200	**72**	65	64
55	215	200	**72**	65	64
56	215	200	**72**	65	64
57	214	200	**72**	65	64
58	213	200	**72**	64	63
59	214	200	**72**	64	63
60	211	200	**71**	64	63
61	212	200	**71**	64	63
62	211	200	**71**	64	63
63	211	200	**71**	64	63
64	209	200	**71**	64	63
65	209	200	**71**	64	62
66	208	200	**71**	64	62
67	208	200	**71**	64	62
68	206	200	**71**	64	62
69	206	200	**71**	64	63
70	205	200	**71**	64	63

1The requirements are assumed to be normally distributed, with an EAR of 200 and a CV of 25%

[2]The requirements are assumed to be lognormally distributed, with an EAR of 200 and a CV of 25%

Appendix 5: Habitual vitamin A intake characteristics[1]

a) Children (males and females analyzed together)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	457	179	213	279	389	543	747	937
2	511	200	238	320	446	625	859	1042
3	548	214	255	344	482	676	929	1118
4	578	225	268	363	508	714	981	1178
5	602	234	278	377	528	744	1022	1228
6	622	241	287	390	546	769	1058	1272
7	641	248	295	400	561	791	1088	1310
8	657	254	302	410	575	811	1115	1345
9	672	259	309	418	587	828	1140	1376
10	685	264	315	426	598	844	1162	1405
11	698	268	320	433	608	859	1183	1431
12	709	273	325	439	617	873	1202	1456
13	720	276	330	445	626	885	1220	1479

b) Males

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	449	179	212	285	395	549	715	903
2	515	204	242	324	452	631	858	1044
3	562	221	262	352	491	688	949	1142
4	599	235	279	374	523	734	1016	1221
5	630	246	293	392	549	773	1072	1287
6	657	256	304	408	572	806	1118	1344
7	681	265	315	422	592	836	1159	1395
8	702	273	325	435	611	863	1196	1441
9	722	280	333	447	628	887	1229	1484
10	740	286	341	458	643	910	1260	1523
11	757	293	349	468	658	931	1288	1559
12	773	298	356	477	671	950	1314	1593
13	788	304	362	486	684	969	1339	1625
14	803	309	368	495	696	986	1363	1655
15	816	314	374	503	707	1003	1385	1683
16	829	318	380	510	718	1019	1406	1711
17	841	323	385	518	729	1034	1426	1737
18	853	327	390	524	739	1048	1445	1761
19	864	331	395	531	748	1062	1464	1785
20	874	335	399	537	757	1075	1482	1808
21	885	338	404	544	766	1088	1499	1830
22	895	342	408	550	774	1100	1516	1851
23	904	345	412	555	783	1112	1532	1872
24	914	349	416	561	790	1124	1548	1892
25	923	352	420	566	798	1135	1563	1911

[1] Mean and percentiles of the habitual vitamin A intake distribution in RAE/day

Appendix 5 (continued)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
26	931	355	424	571	806	1146	1577	1930
27	940	358	428	576	813	1156	1592	1948
28	948	361	431	581	820	1166	1606	1965
29	956	364	435	586	826	1176	1619	1982
30	964	367	438	591	833	1186	1633	1999
31	971	369	441	595	839	1195	1646	2015
32	979	372	444	600	846	1204	1659	2031
33	986	374	447	604	852	1213	1671	2046
34	993	377	450	608	858	1222	1683	2061
35	1000	379	453	612	864	1230	1695	2076
36	1007	382	456	616	869	1238	1707	2090
37	1013	384	459	620	875	1246	1718	2104
38	1019	386	462	624	880	1254	1730	2118
39	1026	388	464	628	886	1262	1741	2131
40	1032	391	467	632	891	1270	1752	2144
41	1038	393	469	635	896	1277	1762	2157
42	1044	395	472	639	901	1284	1773	2170
43	1050	397	474	642	906	1291	1783	2182
44	1055	399	477	646	911	1298	1794	2194
45	1061	401	479	649	915	1305	1804	2206
46	1066	403	481	652	920	1312	1814	2218
47	1072	404	484	655	925	1318	1823	2229
48	1077	406	486	658	929	1325	1833	2241
49	1082	408	488	662	933	1331	1843	2252
50	1087	410	490	665	938	1338	1852	2263
51	1092	412	492	668	942	1344	1861	2273
52	1097	413	494	671	946	1350	1870	2284
53	1102	415	496	673	950	1356	1879	2294
54	1107	417	498	676	954	1362	1888	2304
55	1111	418	500	679	958	1367	1897	2315
56	1116	420	502	682	962	1373	1906	2324
57	1120	421	504	685	966	1379	1914	2334
58	1125	423	506	687	970	1384	1923	2344
59	1129	424	508	690	973	1389	1931	2353
60	1134	426	509	693	977	1395	1939	2362
61	1138	427	511	695	981	1400	1948	2372
62	1142	429	513	698	984	1405	1956	2381
63	1146	430	515	700	988	1410	1964	2390
64	1150	432	516	703	991	1415	1972	2398
65	1154	433	518	705	995	1420	1980	2407
66	1158	434	520	707	998	1425	1987	2416
67	1162	436	521	710	1001	1430	1995	2424
68	1166	437	523	712	1005	1435	2003	2432
69	1170	438	525	714	1008	1439	2010	2441
70	1174	440	526	717	1011	1444	2018	2449

Appendix 5 (continued)

c) Females

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
1	446	184	218	286	389	544	734	877
2	489	203	240	316	433	598	803	961
3	518	214	253	335	460	634	850	1020
4	540	223	263	349	480	661	888	1066
5	558	229	271	360	495	683	918	1103
6	574	235	278	369	509	702	945	1136
7	587	240	283	377	520	719	968	1165
8	599	244	288	384	530	734	989	1190
9	610	248	293	390	539	747	1008	1213
10	620	252	297	396	547	759	1025	1235
11	629	255	301	401	555	770	1041	1254
12	637	258	305	406	562	781	1056	1273
13	645	261	308	411	568	790	1070	1290
14	652	263	311	415	574	799	1083	1306
15	659	266	314	419	580	808	1095	1321
16	666	268	317	423	585	816	1107	1335
17	672	270	320	427	590	823	1118	1348
18	678	273	322	430	595	830	1128	1361
19	684	275	325	433	600	837	1138	1373
20	689	277	327	436	605	844	1148	1385
21	694	279	330	440	609	850	1157	1396
22	699	280	332	442	613	856	1165	1407
23	704	282	334	445	617	862	1174	1417
24	708	284	336	448	621	868	1182	1427
25	713	286	338	451	625	873	1189	1436
26	717	287	340	453	628	879	1197	1445
27	721	289	342	456	632	884	1204	1454
28	725	290	344	458	635	889	1211	1463
29	729	292	345	461	639	893	1218	1471
30	733	293	347	463	642	898	1224	1479
31	737	295	349	465	645	902	1231	1487
32	740	296	350	467	648	907	1237	1494
33	744	297	352	469	651	911	1243	1501
34	747	299	354	471	654	915	1248	1508
35	750	300	355	473	657	919	1254	1515
36	754	301	357	475	660	923	1259	1522
37	757	302	358	477	662	927	1265	1528
38	760	304	360	479	665	931	1270	1535
39	763	305	361	481	668	935	1275	1541
40	766	306	362	483	670	938	1280	1547
41	769	307	364	485	673	942	1284	1553
42	772	308	365	487	675	945	1289	1558
43	774	309	366	488	678	948	1293	1564
44	777	310	368	490	680	952	1298	1569
45	780	311	369	492	683	955	1302	1574

Appendix 5 (continued)

Age	*Mean*	*p.0.05*	*p.0.10*	*p.0.25*	*p.0.50*	*p.0.75*	*p.0.90*	*p.0.95*
46	782	312	370	493	685	958	1306	1580
47	785	313	371	495	687	961	1310	1585
48	787	314	373	497	689	964	1314	1590
49	790	315	374	498	692	967	1318	1594
50	792	316	375	500	694	970	1322	1599
51	795	317	376	501	696	973	1326	1604
52	797	318	377	503	698	976	1330	1608
53	799	319	378	504	700	979	1333	1613
54	802	320	380	506	702	982	1337	1617
55	804	321	381	507	704	984	1340	1621
56	806	322	382	509	706	987	1344	1625
57	808	323	383	510	708	990	1347	1629
58	810	324	384	511	710	992	1350	1633
59	812	325	385	513	712	995	1353	1637
60	814	325	386	514	714	997	1356	1641
61	817	326	387	515	716	1000	1359	1645
62	819	327	388	517	718	1002	1362	1649
63	821	328	389	518	719	1005	1365	1652
64	822	329	390	519	721	1007	1368	1656
65	824	330	391	521	723	1010	1371	1659
66	826	330	392	522	725	1012	1374	1663
67	828	331	393	523	727	1014	1377	1666
68	830	332	394	524	728	1016	1379	1669
69	832	333	395	525	730	1019	1382	1672
70	834	333	396	527	732	1021	1385	1676

Appendix 6: Estimates for the prevalence of inadequate vitamin A intakes

a) Males

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(RAE/day)		*EAR cut-point approach*	*Prob approach (normal)[1]*	*Prob approach (lognormal)[2]*
1	457	195	**7**	8	8
2	511	214	**7**	8	8
3	548	232	**7**	8	8
4	578	247	**7**	8	8
5	602	273	**7**	9	8
6	622	298	**8**	10	10
7	641	316	**10**	11	11
8	657	344	**11**	12	12
9	672	363	**13**	14	14
10	685	387	**16**	17	17
11	698	418	**20**	21	20
12	709	467	**24**	25	25
13	720	521	**29**	29	29
14	652	593	**32**	33	32
15	659	603	**35**	35	34
16	666	602	**37**	36	36
17	672	606	**37**	36	36
18	678	593	**36**	36	35
19	684	620	**35**	35	34
20	689	620	**34**	34	34
21	694	620	**33**	33	33
22	699	620	**32**	32	32
23	704	620	**31**	31	31
24	708	620	**31**	31	31
25	713	620	**30**	30	30
26	717	620	**29**	29	29
27	721	620	**29**	29	29
28	725	620	**28**	28	28
29	729	620	**28**	28	28
30	733	620	**27**	28	27
31	737	600	**27**	27	27
32	740	600	**26**	27	26
33	744	600	**26**	26	26
34	747	600	**25**	26	25
35	750	600	**25**	25	25
36	754	600	**25**	25	25
37	757	600	**24**	25	25
38	760	600	**24**	24	24
39	763	600	**23**	24	24
40	766	600	**23**	23	23

Appendix 6 (continued)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(RAE/day)		*EAR cut-point approach*	*Prob approach (normal)*[1]	*Prob approach (lognormal)*[2]
41	769	600	**22**	23	23
42	772	600	**22**	23	23
43	774	600	**22**	22	22
44	777	600	**21**	22	22
45	780	600	**21**	22	22
46	782	600	**21**	22	21
47	785	600	**21**	22	21
48	787	600	**21**	21	21
49	790	600	**20**	21	21
50	792	600	**20**	21	20
51	795	610	**20**	20	20
52	797	610	**19**	20	20
53	799	610	**19**	20	20
54	802	610	**19**	20	20
55	804	610	**19**	20	19
56	806	610	**19**	19	19
57	808	610	**18**	19	19
58	810	610	**18**	19	19
59	812	610	**18**	19	19
60	814	610	**18**	19	18
61	817	610	**18**	19	18
62	819	610	**18**	19	18
63	821	610	**17**	18	18
64	822	610	**17**	18	18
65	824	610	**17**	18	18
66	826	610	**17**	18	18
67	828	610	**17**	17	17
68	830	610	**17**	17	17
69	832	610	**16**	17	17
70	834	610	**16**	17	17

[1]The requirements are assumed to be lognormally distributed, with a CV of 20%

[2]The requirements are assumed to be normally distributed, with a CV of 20%

Appendix 6 (continued)

b) Females

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(RAE/day)		*EAR cut-point approach*	*Prob approach (normal)*[1]	*Prob approach (lognormal)*[2]
1	449	184	**5**	6	5
2	515	197	**5**	6	6
3	562	217	**5**	7	7
4	599	237	**7**	8	8
5	630	258	**8**	10	9
6	657	280	**10**	12	12
7	681	305	**13**	14	14
8	702	332	**17**	18	17
9	722	358	**20**	21	21
10	740	388	**25**	26	25
11	757	422	**29**	30	29
12	773	460	**33**	33	33
13	788	485	**36**	36	35
14	803	506	**38**	38	37
15	816	510	**39**	38	38
16	829	515	**39**	39	38
17	841	522	**39**	39	39
18	853	506	**39**	39	38
19	864	530	**39**	39	38
20	874	530	**38**	38	38
21	885	*530*	**38**	38	37
22	895	530	**37**	37	37
23	904	530	**36**	36	36
24	914	530	**36**	36	35
25	923	530	**35**	35	35
26	931	530	**35**	35	34
27	940	530	**35**	34	34
28	948	530	**34**	34	33
29	956	530	**34**	33	33
30	964	530	**33**	33	33
31	971	520	**33**	33	33
32	979	520	**33**	33	32
33	986	520	**32**	32	32
34	993	520	**32**	32	32
35	1000	520	**32**	32	31
36	1007	520	**31**	31	31
37	1013	520	**31**	31	31
38	1019	520	**31**	31	31
39	1026	520	**30**	31	30
40	1032	520	**30**	30	30

Appendix 6 (continued)

Age	*Mean habitual intake*	*EAR*	*Estimated prevalence of inadequate intakes (%)*		
	(RAE/day)		*EAR cut-point approach*	*Prob approach (normal)*[1]	*Prob approach (lognormal)*[2]
41	1038	520	**30**	30	30
42	1044	520	**30**	30	30
43	1050	520	**29**	30	30
44	1055	520	**29**	29	29
45	1061	520	**29**	29	29
46	1066	520	**29**	29	29
47	1072	520	**28**	29	29
48	1077	520	**28**	28	28
49	1082	520	**28**	28	28
50	1087	520	**28**	28	28
51	1092	*530*	**27**	28	28
52	1097	530	**27**	28	27
53	1102	530	**27**	28	27
54	1107	530	**27**	27	27
55	1111	530	**27**	27	27
56	1116	530	**27**	27	27
57	1120	530	**26**	27	27
58	1125	530	**26**	26	26
59	1129	530	**26**	26	26
60	1134	530	**26**	26	26
61	1138	*530*	**26**	26	26
62	1142	530	**26**	26	26
63	1146	530	**26**	26	26
64	1150	530	**26**	26	26
65	1154	530	**25**	26	26
66	1158	530	**25**	26	25
67	1162	530	**25**	26	25
68	1166	530	**25**	25	25
69	1170	530	**24**	25	25
70	1174	530	**24**	24	25

[1]The requirements are assumed to be lognormally distributed with a CV of 20%

[2]The requirements are assumed to be normally distributed, with a CV of 20%