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1 The health impact of substituting unprocessed red meat by
2 pulses in the Danish diet

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16

17 **Abstract:**

18 Background

19 Diets consisting of high amounts of animal-based protein have been associated with adverse
20 public health effects and are often deemed environmentally unsustainable. Therefore, replacing
21 red meat by pulses has been proposed to reduce the adverse impact on human health and
22 environment. However, unprocessed red meat is an important source of nutrients, such as vitamin
23 B₁₂, iron, zinc and selenium, and the substitution may have negative impact on nutrient adequacy.

24 Method

25 Using a risk-benefit assessment (RBA) approach, we therefore estimated the health impact of
26 substituting unprocessed red meat by pulses on the burden of non-communicable diseases in
27 Denmark, using Disability-Adjusted Life Years (DALY). Furthermore, we assessed the impact of
28 the substitution on nutrient adequacy.

29 Results

30 We found that 187 (95% UI: 209; 168) healthy years of life could be gained per 100,000 individuals
31 per year by substituting 100% of unprocessed red meat by pulses in the Danish diet. We found a
32 decrease in the intake of vitamin B₁₂, zinc and selenium due to the substitution. An additional 10%
33 of the Danish population will become at risk of vitamin B₁₂ and selenium inadequacy, and an
34 additional 20% will be at risk of zinc inadequacy due to the substitution. For iron, a small decrease
35 in the proportion at risk of inadequacy was found.

36 Conclusion

37 Substitution of unprocessed red meat by pulses was estimated to provide a beneficial health
38 impact on the burden of non-communicable disease, expressed in DALY. Additionally, it was found
39 that the complete substitution will lead to a higher risk of nutrient inadequacies.

40

41 **Keywords:** Disability-Adjusted Life Years (DALY), Risk-benefit assessment (RBA), Food
42 substitution, Health impact, Nutrient inadequacy, Non-communicable diseases

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45

46 **Declarations**

47 **Funding:** The preparation of this manuscript was funded through the Metrix II project by the
48 Ministry for Environment and Food in Denmark. The Ministry for Environment and Food in
49 Denmark had no role in the design, analysis or writing of this article.

50 **Conflicts of interest/Competing interests:** The authors declare that they have no conflict of
51 interest

52 **Ethics approval:** The DANSDA survey has been conducted in accordance with the guidelines laid
53 down in the Declaration of Helsinki and has been approved by the Danish Data Protection Agency.
54 The Danish National Committee on Health Research Ethics has decided that, according to Danish
55 Law, DANSDA does not require approval.

56 **Consent to participate:** Passive consent were given by participants

57 **Consent for publication:** The DANSDA survey has been approved by the Danish Data Protection
58 Agency and inform participants of purpose of survey.

59 **Availability of data and material:** All data are freely available within the manuscript and
60 appendices. No additional data are available.

61 **Code availability:** Code is available in Online Resource 3.

62 **Authors' contribution:** The study was framed by FAF, STT and MN. The model development was
63 performed by FAF under guidance of STT and MN. The consumption data (DANSDA) was
64 prepared by SF. The first draft of the manuscript was written by FAF and all authors commented on
65 previous versions of the manuscript. All authors read and approved the final manuscript.

66 **Acknowledgements:**

67 **Abbreviations:** AR: average requirements, CI: confidence interval, CRC: Colorectal cancer, CVD:
68 cardiovascular diseases, DALY: Disability-Adjusted Life Years, DANSDA: Danish National Survey
69 of Diet and Physical Activity, EPIC: European Prospective Investigation into Cancer and Nutrition
70 study, FAO: Food and Agriculture Organization, FRIDA: food database, GBD: Global Burden of
71 Disease, IHD: ischaemic heart disease, NNR: Nordic Nutrition Recommendation, PIF: potential

72 impact fraction, RBA: risk-benefit assessment, RR: relative risk, sd: standard deviation, UI:
73 uncertainty interval, UL: upper intake level, WCRF: World Cancer Research Fund, WHO: World
74 Health Organization, YLD: Years lived with disability, YLL: Years of life lost

75

76 **1. Introduction:**

77 Poor dietary habits caused more than 10 million deaths worldwide in 2017 according to the Global
78 Burden of Disease (GBD) Study [1]. Furthermore, current dietary habits, in particular in many
79 Western countries, have been deemed environmentally unsustainable [2]. In 2019, the EAT Lancet
80 Commission published guidelines for a more healthy and sustainable diet. These guidelines
81 recommended a shift towards more plant-based diets by e.g. limiting the consumption of meat, in
82 particular red meat, and increasing consumption of vegetables and pulses [2]. The same year, the
83 Food and Agriculture Organization (FAO) of the United Nations and World Health Organization
84 (WHO) raised the need to promote diets that are both healthy and have low environmental impacts
85 [3] .

86 Foods and diets have a high level of complexity, consisting of many components. Therefore,
87 consumption of food can cause both adverse and beneficial health effects [4]. Risk-benefit
88 assessment (RBA) is a multidisciplinary approach that allows for weighing the adverse and
89 beneficial health effects associated with a given change in consumption of food [5,6]. The overall
90 health impact may be quantified using a composite health metric that incorporates both morbidity
91 and mortality into one measure, allowing for a comparison across diseases [5,7]. One such metric
92 is the Disability-Adjusted Life Year (DALY), a composite health metric that compares a given health
93 status with an ideal state of health. One DALY equals one healthy life year lost. This metric is the
94 sum of the Years Lived with Disability (YLD) and the Years of Life Lost (YLL) due to premature
95 death [8]. [Using disability weights and life expectancy tables, it integrates incidence with duration,](#)
96 [mortality, and severity of disease \[8,9\].](#)

97 Most existing RBAs have considered single foods [10] or food components [11]. However, changes
98 in consumption of one food is expected to change the consumption of other foods in the diet [12].
99 Still, only few existing RBAs have investigated food substitutions [13–16].

100 The Danish population consumes more than the recommended maximum consumption of red and
101 processed meat [17]. Substituting red meat by pulses is one way for the Danish population to move
102 towards a more plant-based and sustainable diet. [The focus is on unprocessed red meat because,](#)
103 [in the Danish diet, processed red meat is typically used in relatively small amounts for lunch where](#)
104 [unprocessed red meat is typically used in larger quantities for dinners.](#) Furthermore, based on

105 Danish food culture, substituting pulses for unprocessed red meat was deemed more realistic than
106 for processed meat. Consumption of unprocessed red meat, defined as unprocessed mammalian
107 muscle meat including beef, veal, pork, lamb, mutton, horse, and goat [18] has been associated
108 with an increased risk of colorectal cancer (CRC) [18] and type-2 diabetes mellitus [19]. However,
109 red meat is also an important source of vitamin B₁₂, haem-iron, zinc, and selenium in the Danish
110 diet [17,20]. Consumption of pulses, defined as the dried edible seeds of the leguminous plant,
111 including beans, lentils, and peas [21], has been associated with a decreased risk of ischaemic
112 heart disease (IHD) [22]. However, pulses are a less rich source of zinc and selenium, only contain
113 non-haem iron and are not a source of vitamin B₁₂. Thus, the overall public health impact of
114 substituting red meat by pulses in the Danish population is unclear.

115 The aim of this study was to estimate the overall health impact of substituting unprocessed red
116 meat by pulses in the Danish population. We quantified the consequential change in disease
117 burden attributable to nutritional risk factors in terms of DALYs. Furthermore, we compared the
118 prevented disease burden with the potential changes in risk of nutrient inadequacies.

119

120 **2. Methodology:**

121 In our assessment, we followed the RBA framework, consisting of an identification and
122 characterisation of adverse and beneficial health effects, an exposure assessment, and a risk and
123 benefit characterisation and comparison [5,6,23,24]. We used Danish health statistics for the year
124 of 2017 in all models. Variability and uncertainty were included using two-dimensional Monte Carlo
125 simulations, thereby separating variability and uncertainty throughout the calculations [25]. The
126 models were implemented in *R* version 3.4.1 [26].

127 **2.1 Identification and characterisation of health effects**

128 The relevant health effects associated with consumption of unprocessed red meat and pulses were
129 identified on the basis of assessments by the Nordic Nutrition Recommendations (NNR) [20], the
130 World Cancer Research Fund (WCRF) [18] and the GBD 2017 [27] study. Health outcomes were
131 included in the assessment when evidence was graded as “convincing” or “probable” according to
132 the criteria set by the WCRF [28]. The health effects included in this assessment are listed in table
133 1.

134 The WCRF found probable evidence of increased risk of CRC due to consumption of unprocessed
135 red meat [18]. The dose-response relationship used in this study was estimated by the WCRF in
136 the Continuous Update Project report updated in 2017 [29]. They estimated a relative risk (RR) of

1.12 (95% confidence interval (CI) 1.00 ; 1.25) per 100 g of red meat per day based on a meta-analysis [29]. The evidence was graded probable based on the direction of the effect together with mechanistic evidence [18]. The meta-analysis included eight studies from USA, China, Australia, Finland, Sweden, Netherlands, and the European Prospective Investigation into Cancer and Nutrition study (EPIC study) including participants from ten European countries (Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden and United Kingdom). A total number of 6,662 CRC cases were included in the meta-analysis [29].

Consumption of red meat has also been found to be associated with an increased risk of type-2 diabetes mellitus (hereafter referred to as diabetes) in several studies. Red meat consumption was included as a risk factor for diabetes in the GBD 2017 study [27], based on the meta-analysis by Pan *et al.* (2011) [19]. Pan *et al.* (2011) estimated an RR of 1.19 (95% CI 1.04 ; 1.37) per 100 g of red meat per day [19]. The updated meta-analysis included nine studies from USA, China, Finland, and for Europe (the EPIC study).

Consumption of pulses has been associated with a decreased risk of IHD in several studies. The risk of IHD due to low pulse consumption was considered in the GBD 2017 study [27], based on the meta-analysis conducted by Afshin *et al.* (2014) [22]. An RR of 0.86 (95% CI 0.78 ; 0.94) per 400 g of pulses per week was estimated, corresponding to 57 g of pulses per day [22]. The RR was based on five studies with a total of 6,514 IHD events. The studies were conducted in USA, Japan, Spain, and Europe (the EPIC study). The RR was estimated for legumes and pulses, and was assumed to apply to pulses only as well.

For all these three health outcomes, the RR describes the increased or decreased risk per amount of food. This was used to describe the RR per gram consumed food, based on the assumption of a log-linear relation [30],

$$\ln(RR_h) = \beta \cdot I_n \quad (1)$$

where RR_h is the RR for health outcome h , obtained from the literature, β is a model parameter and I_n is the intake of food n (associated to health outcome h), in grams per day. Using this equation, a normal distribution for β was derived based on the estimated mean and 95% CI for RR_h , as found in the literature. This distribution was implemented as variability between consumers with variable intakes, to calculate individual relative risks.

Deficiency of vitamin B₁₂ and iron has been linked with megaloblastic and microcytic anaemia, respectively [20]. Selenium has been found to be related to protection of proteins and lipids from oxidative damage and thyroid hormone metabolism [20]. Zinc has, among other functions, been found to be essential for normal function of the immune system and normal DNA synthesis and cell

170 division [20]. Both zinc and selenium have been found to be necessary for normal body function
171 [20]. However, the intake of these elements has not been linked with specific health outcomes.
172 Due to lack of dose-response relationships, we could not quantify the health impact of potential
173 changes in intake of these nutrients as a result of substituting red meat by pulses in terms of
174 DALY. Instead, the impact was investigated by comparing intake of these nutrients with the
175 respective average requirements (AR) set by the NNR [20] before and after substitution. The AR is
176 defined as the lowest long-term intake of a nutrient that is sufficient to cover the physiological
177 requirements for half of the specified population group [20].

178 2.2 Consumption scenarios

179 We compared the current consumption of red meat and pulses in the Danish population with an
180 extreme scenario in which all red meat was substituted by pulses. We used data from the Danish
181 National Survey of Diet and Physical Activity (DANSDA), 2011-2013 [17] to model the substitution.
182 DANSDA is a nationwide, cross-sectional survey of diet and physical activity in a representative
183 sample of the Danish population from the age of 4 to 75 years. Dietary intake was estimated for 7
184 days of consecutive dietary recording, using food diaries with pre-coded response categories and
185 open answer options. The dietary record was structured according to the typical Danish meal
186 pattern (i.e. breakfast, lunch, dinner, and in-between meals) and food items were categorized
187 according to food groups. The pre-coded response options included food items most commonly
188 consumed in Denmark, with the possibilities of adding additional in an open field. For our study,
189 data were restricted to individuals at or above the age of 18 years, who reported food intake for all
190 seven consecutive days and for whom information on measured body weight was available.
191 Children below the age of 18 years were excluded due to limitations of the data on long-term
192 health outcomes. The total population sample considered included 2,716 individuals. We estimated
193 the observed individual mean consumption of red meat and pulses per day by taking the individual
194 average daily consumption over seven days and modelled the substitution at the individual level. A
195 gram-to-gram substitution was applied based on the assumption that individuals substituting red
196 meat by pulses would substitute by a similar portion size. The reported consumption of pulses in
197 DANSDA comprised chickpeas, white beans, brown beans and mature yellow peas. It was
198 assumed that the substitution with pulses would be equally distributed among the four pulse types,
199 independently of individual preferences. Consumption data were converted into prepared amounts
200 before modelling the substitution. Since meat loses weight during preparation in the form of water
201 and fat, and pulses gain weight, a weight change factor was used to estimate the weight of the
202 prepared food based on Ygil (2013) [31]. The included food items and their respective weight
203 change factor can be found in Online Resource 1.

204 2.3 Intake of nutrients

205 We combined data on food consumption in the reference and substitution scenarios with
206 concentration data (Online Resource 1) for nutrients in foods of both Danish and non-Danish origin
207 on the Danish market [32] to assess the change in intake of nutrients as a result of the substitution.

208 Concentration data were given for raw meat and pulses. Nutrients in foods may be lost upon
209 cooking. Thus, the effect of cooking on the concentration of nutrients was considered by means of
210 retention factors. Based on common culinary practices in Denmark, red meat was assumed fried
211 and pulses were assumed boiled. We used retention factors for minerals (for iron, zinc, and
212 selenium) in meat and vegetables, and for vitamin B₁₂ in meat, estimated by Pedersen *et al.* (2015)
213 to account for nutrient loss during cooking [17]. Vegetables were assumed to be representative of
214 pulses.

215 Intake of nutrients was expressed as absolute intakes by the following equation:

$$216 \quad x_i = \sum_n I_{n,i} \cdot c_n \quad (2)$$

217 where x_i is the observed individual mean intake of nutrients for individual i , I_n is the observed
218 individual mean consumption of food n in g/day for individual i , and c_n is the mean concentration of
219 the nutrient in food n in µg/g for vitamin B₁₂ and selenium, and in mg/g for iron and zinc.

220 Background nutrient intakes was estimated by accounting for intakes from other dietary sources in
221 both the reference and substitution scenarios. The bioavailability of nutrients is accounted for in
222 the AR. However, iron may be present in food as either haem iron or non-haem iron, which have
223 been found to differ in bioavailability [20]. Therefore, the bioavailability of both types of iron was
224 accounted for and the intakes of both types of iron was estimated. The absorbed iron was
225 estimated based on the proportion of the type of iron present in the food. The NNR (2012)
226 estimated that half of the iron in meat products is haem iron and that the other half is non-haem
227 iron. Non-animal derived products were assumed to contain only non-haem iron [20]. NNR
228 assumed that the absorption of haem iron (Abs_{hFe}) was 25%, and that the absorption of non-haem
229 iron (Abs_{nhFe}) was lower [20]. NNR also estimated that approximately 10% of iron in the Nordic diet
230 consist of haem iron ($Diet_{hFe}$) and that the absorption of total iron (Abs_{total}) (both haem iron and
231 non-haem iron) is 15% [20]. Based on this, the absorption of non-haem iron will be 13.9%.

$$232 \quad Abs_{nhFe} = \frac{Abs_{total} - Abs_{hFe} \cdot Diet_{hFe}}{Diet_{nhFe}} \rightarrow \frac{0.15 - 0.25 \cdot 0.10}{0.90} = 0.139 \quad (3)$$

233 2.4 Risk of nutrient inadequacy

Intakes of vitamin B₁₂, iron, zinc and selenium before and after substitution were compared with the respective ARs set by the NNR [20] to estimate the change in the proportion below AR and thus at risk of inadequate intakes. For vitamin B₁₂, an AR of 1.4 µg/day for both men and women has been set [20]. The ARs for the remaining nutrients distinguished between men and women. ARs of 6 and 5 mg/day for zinc and 30 and 35 µg/day for selenium, for men and women, respectively, have been established [20]. For iron, requirement distributions have been specified for men above the age of 18 (mean: 1.05 mg/day, standard deviation (sd): 0.195), menstruating women above the age of 18 (mean: 1.46 mg/day, sd: 0.614) and post-menopausal women (mean: 0.87 mg/day, sd: 0.158) [20]. The iron requirements for men and post-menopausal women were assumed to be normally distributed [33], whereas the distribution is known to be skewed for menstruating women and can be approximated by a log-normal distribution [20,33]. The female population was expected to reach menopause at the age of 52 based on Danish national statistics [34]. In addition, upper intake levels (UL) of 60 mg/day for iron and 300 µg/day for selenium have been established to assess the risk of toxicity of excessive intakes [20].

2.5 Disability-Adjusted Life Years

The individual daily consumption was combined with dose-response relationships to quantify the health impact of a full substitution of unprocessed red meat by pulses. For each risk factor-health outcome pair, we calculated the potential impact fraction (PIF), which is a measure for the proportion of disease incidence, prevalence, mortality or burden that can be prevented as a result of a shift to a counterfactual (alternative) exposure to a risk factor [35]. The PIF was estimated to investigate the impact of the alternative scenario on the risk of CRC, diabetes and IHD due to the change in red meat and pulse consumption. We estimated the PIF at the individual level ($PIF_{h,i}$), based on the current intake of each individual i as reported in the data set, as well as its intake after substitution of red meat by pulses. This resulted in an estimate of the change in probability of health outcome h for individual i due to the substitution:

$$PIF_{h,i} = \frac{RR_{ref,h,i} - RR_{alt,h,i}}{RR_{ref,h,i}} \quad (4)$$

where $RR_{ref,h,i}$ and $RR_{alt,h,i}$ are the RR for health outcome h and individual i in the reference scenario and the alternative scenario, respectively. It was assumed that the current incidence of health outcome h was reflecting the current red meat and pulse consumption. The current incidence of CRC, diabetes and IHD was found in the Danish Cancer Registry [36], the Danish Registry of Selected Chronic Diseases and Severe Mental Disorders [37], and on the portal Hjertetal.dk developed by the Danish National Institute of Public Health and the Danish Heart

266 Association [38] for the year 2017. The individual PIF was multiplied with the per capita incidence
 267 ($Inc_{h,s,a}$) to estimate the change in individual probability of disease:

$$268 \quad \Delta P_{h,i} = PIF_{h,i} \cdot Inc_{h,s,a} \quad (5)$$

269 Where ($\Delta P_{h,i}$) is the change in individual probability of disease and $Inc_{h,s,a}$ is the current per capita
 270 incidence of health outcome h with sex s and age a . The health impact of the substitution was
 271 quantified in the terms of DALYs. The DALY is the sum of YLD (morbidity) and YLL (mortality) [8].
 272 The GBD regularly estimates the incidence and disease burden of CRC, diabetes and IHD at
 273 Global and national level [39]. We used the GBD's estimates for YLD, YLL and incidence rates for
 274 CRC, diabetes and IHD in Denmark for the year 2017 to estimate the average YLD and YLL per
 275 case for each health outcome. The YLD, YLL and incidence rates were obtained for 5-year age
 276 groups between age 20 and 75 years for each gender for CRC, for 5-year age groups between age
 277 25 and 75 years for each gender and for 10-year age groups between age 35 and 75 years for
 278 each gender (Online Resource 2). The 95% CIs around these estimates were assumed to
 279 represent uncertainty; the uncertainty was assumed to be normally distributed. The individual PIFs
 280 were multiplied with the YLD and YLL per case to estimate the expected change in individual YLDs
 281 and YLLs:

$$282 \quad \Delta YLD_{h,i} = PIF_{h,i} \cdot YLD/case_{h,s,a} \quad (6)$$

$$283 \quad \Delta YLL_{h,i} = PIF_{h,i} \cdot YLL/case_{h,s,a} \quad (7)$$

284 where $YLD/case_{h,s,a}$ and $YLL/case_{h,s,a}$ are the YLD and YLL per case for health outcome h , sex s ,
 285 and age a . The change in individual DALYs was estimated by adding the change in YLDs and
 286 YLLs:

$$287 \quad \Delta DALY_{h,i} = \Delta YLD_{h,i} + \Delta YLL_{h,i} \quad (8)$$

288 $\Delta DALY_{h,i}$ should be interpreted as the average potential health impact for subgroups of same age,
 289 sex and dietary habits with the burden experienced by those falling ill averaged over a large group
 290 of similar individuals [24]. We took the average of the individual DALYs over the 2,716 individuals
 291 in DANSDA and multiplied by 100,000 to get an estimate of the change in DALYs ($\Delta DALY_h$) per
 292 100,000 individuals for each of the health outcomes.

293

294 **3. Results:**

295 **3.1 Substitution of red meat by pulses**

296 Mean and median of consumption of red meat, excluding processed red meat, in the Danish
297 population were 60.2 and 51.5 g/day in prepared amounts before substitution (table 2). [As a direct](#)
298 [consequence of the full substitution of unprocessed red meat by pulses, mean red meat](#)
299 [consumption decreased to zero, 0.0 g/day.](#) The mean and median consumption of pulses for the
300 Danish population was 1.6 and 0.0 g/day, in prepared amounts, before substitution, and only 8.6%
301 of the population consumed pulses. The mean consumption of pulses increased to 61.8 g/day after
302 substitution.

303 3.2 Intake of nutrients

304 The intake of the investigated nutrients in the reference and alternative scenarios is presented in
305 table 3. The mean intake of vitamin B₁₂ decreased from 1.9 µg/day in the reference scenario to 1.5
306 µg/day in the alternative scenario. The mean intake of zinc and selenium also decreased due to
307 the substitution, from 8.2 to 6.7 mg/day and from 35.3 to 30.9 µg/day, respectively. In contrast,
308 intake of iron increased from 1.1 to 1.2 mg/day.

309 Table 4 shows the proportion of the Danish population below the AR for vitamin B₁₂, iron, zinc, and
310 selenium. We observed a marked increase in the proportion of individuals below the AR for vitamin
311 B₁₂ (women: 7% to 16%, men: 2% to 10%), zinc (women: 27% to 47%, men: 16% to 36%) and
312 selenium (women: 55% to 67%, men: 41% to 57%). For iron, a small decrease in the proportion of
313 individual below the AR was estimated for men and post-menopausal women (women>51: 35% to
314 33%, men: 32% to 30%) whereas no change was estimated for menstruating women (women<52:
315 75%). No individuals exceeded the UL for selenium or iron in any of the scenarios (results not
316 shown).

317 3.3 Health impact

318 Substituting red meat by pulses in the Danish adult population would result in a decrease in the
319 number of cases and disease burden due to CRC, IHD, and diabetes (table 5 and figure 1). The
320 highest number of averted cases was found for IHD in the male population with 82 (95% UI: 124;
321 34) cases/100,000 averted. The highest number of averted DALYs was estimated for IHD in the
322 male population with 163 (95% UI: 254; 63) DALYs/100,000 averted. The largest contributor to
323 averted YLD was diabetes. Meanwhile, the largest contributor to YLL was IHD. Our quantitative
324 model predicted a larger benefit of the substitution for the male population than for the female
325 population.

326

327 4. Discussion:

328 The concept of a sustainable diet is high on the global political agenda. Achieving healthy diets for
329 everyone from sustainable food systems will require substantial shifts in dietary patterns. This shift
330 includes moving towards a more plant-based diet which compared to the current diet contain lower
331 amounts of animal-source foods, such as meat, and higher amounts plant-based foods, such as
332 pulses [40]. Denmark has a tradition for a high consumption of meat compared to other Nordic
333 countries and is therefore a relevant country to investigate for such substitution of red meat by
334 pulses [41]. We estimated the health impact of substituting red meat by pulses in the Danish adult
335 population and found that 187 (95% UI: 209 ; 168) healthy years of life could be gained per
336 100,000 individuals per year by substituting 100% of unprocessed red meat by pulses. An increase
337 to 61.8 g of pulses might not be realistic for many, however, social factors were not considered in
338 this study. With a lower proportion of substitution, the health gain decreases proportionally (results
339 not shown). The health impact varied between different sub-populations. Men would experience
340 the highest potential health benefit due to substitution of red meat by pulses. The difference in
341 health impact estimated for men and women is expected to originate from differences in dietary
342 patterns along with the difference in the background incidences of CRC, diabetes and IHD, which
343 are higher for men than for women. We also assessed the impact of the substitution on nutrient
344 adequacy. We found a decrease in the intake of vitamin B₁₂, zinc and selenium due to the
345 substitution. An additional 10% of the population would become at risk of vitamin B₁₂ and selenium
346 inadequacy, whereas an additional 20% would become at risk of zinc inadequacy. For iron, a small
347 decrease in the proportion below the AR was found.

348 We estimated the health impact of the substitution in terms of DALYs and made an assessment of
349 nutrient inadequacy for the Danish adult population aged 18 to 75 years. Particularly nutrient
350 inadequacies may pose a higher risk to the population groups that we did not include in our
351 assessment, i.e. children, adolescents, and elderly > 75 years of age. We did not include children
352 and adolescents below the age of 18 years due to limitations in the data on the long-term effects of
353 food intake in this subpopulation. Furthermore, we were not able to include data on dietary habits
354 in Danish individuals > 75 years in our assessment. The health impact estimated in our study
355 should not be extrapolated to other population groups. Indeed, it should be emphasized that a full
356 substitution of red meat by pulses may have severe consequences for these subpopulations.

357 The bioavailability of the nutrients largely influences these estimates. The bioavailability of zinc has
358 been found to decrease in the presence of phytic acids, which may be present in pulses, where
359 animal-based meals have been found to increase the bioavailability. The bioavailability of the two
360 types of iron, haem iron and non-haem iron, appeared to be important for the results. The total
361 intake of iron increased by the shift to the alternative scenario, but the proportion of haem iron was

362 reduced. We based our calculations on the bioavailability estimates for haem iron and non-haem
 363 iron, reported by the NNR (2012) [20]. They based the bioavailability of non-haem iron on a review
 364 by Bothwell *et al.* (1989) [42] that underlines the uncertainty around this estimate and states that
 365 many factors are affecting the bioavailability of non-haem iron. The main enhancers are known to
 366 be the MPF-factor (meat, poultry, and fish), vitamin C, and organic acids, such as citric acid, lactic
 367 acid, and ascorbic acid, where the main inhibitors are known to be calcium, phytates, and the
 368 dietary protein complex (most plant-based protein) [20,42]. The substitution investigated in this
 369 study leads to a decrease in the presence of MPF-factors while it may increase the presence of
 370 potentially inhibiting plant-based proteins. However, data are too scarce to conclude on the
 371 potential implication for the overall impact on iron adequacy.

372 De Oliveira Mota *et al.* (2019) investigated the impact of increasing red meat consumption on iron
 373 deficiency anaemia in the French population and estimated a decrease in the disease burden [11].
 374 However, they did not account for substitution of other foods, as was done in our study. They
 375 quantified the burden of iron deficiency anaemia in the French population from dietary iron intake
 376 expressed in DALYs [11]. They estimated that iron deficiency anaemia causes a burden of 16
 377 (95% CI: 11 ; 20) DALYs/100,000 based on the current iron intake in the French population [11].
 378 They used the AR as a threshold of an effect, thereby assuming that an intake below the AR would
 379 result in iron deficiency. Further, depending on age and sex, a fixed proportion of iron deficient
 380 individuals was assumed to get iron deficiency anaemia. The severity of the anaemia is assumed
 381 to depend on the haemoglobin status as an independent factor. As previously mentioned, the AR is
 382 a measure of maintenance of nutritional status, not a threshold value for deficiency or occurrence
 383 of a health effect [20]. Thus, using the AR together with the probability of anaemia as a measure of
 384 an effect may overestimate the attributable disease burden.

385 To our knowledge, our study is the first to quantify the health impact of substituting red meat by
 386 pulses. Temme *et al.* (2013, 2015) investigated the impact of substituting meat and dairy by plant-
 387 derived foods on iron and saturated fatty acid intake in Dutch young adult females and children,
 388 respectively [14,15]. Both studies found an increased intake of iron, however of lower
 389 bioavailability, which is in line with the results of our study. Temme *et al.* (2015) furthermore
 390 compared vitamin B₁₂ and zinc intake in the reference scenario with a full substitution of meat and
 391 dairy products. They found that the proportion of girls of 4-6 years with an intake below the AR
 392 would increase from 0% to 10% for vitamin B₁₂ and decrease from 9% to 6% for zinc. Our results
 393 show similar results for vitamin B₁₂ but a markedly higher proportion and an increase in individuals
 394 with an intake below the AR for zinc (vitamin B₁₂: from 7% and 2% to 16% and 10% for adult men

395 and women respectively, zinc: from 16% and 27% to 36% and 47% for adult men and women,
396 respectively) when substituting 100% of unprocessed red meat by pulses in the Danish diet.

397 In our study, the substitution of red meat by pulses was specified as a gram-to-gram substitution of
398 prepared food, i.e. the amount of prepared red meat was substituted with the same amount of
399 prepared pulses. Temme *et al.* (2013, 2015) took a similar approach [14,15]. However, other
400 options exist. Springmann *et al.* (2018) investigated the health impact of shifting to a more
401 sustainable diet using isocaloric substitution, keeping the total energy intake constant [43]. An
402 isocaloric substitution was deemed unrealistic for our study, since the energy content of prepared
403 red meat is up to three times the energy content of prepared pulses (data not shown), which would
404 lead to unreasonably high amounts of pulses replacing red meat. Due to the differences in energy
405 content between red meat and pulses, the substitution investigated in this study would lead to an
406 overall decrease in energy intake. It is likely that individuals will add other foods to their diet as a
407 consequence of the substitution to reach the energy balance [20]. Optimally, individuals should add
408 foods with high content of vitamin B₁₂, zinc and selenium, for which the intake decreased as a
409 result of the substitution. Thus, an extension of our substitution model, including also other foods,
410 could be relevant to investigate further, such as fruit, vegetables and dairy products. Another
411 option is to substitute by amounts of protein. However, the protein content of prepared red meat is
412 up to four times the amount of prepared pulses (data not shown). As for an isocaloric substitution,
413 this would lead to unreasonably high amounts of pulses replacing the red meat and was therefore
414 deemed unrealistic. Thomsen *et al.* (2018) investigated the impact of substituting red and
415 processed meat by fish in the Danish diet [13]. Specified substitution factors were applied for
416 substituting by portion size. In that way, cultural eating patterns for unprocessed red meat,
417 processed red meat, and fish were accounted for. The substitution modelled in our study
418 corresponds to a substitution factor of 1, based on the assumption that an equal amount of cooked
419 pulses would replace cooked unprocessed red meat.

420 In another study, De Oliveira Mota *et al.* (2019) estimated the burden attributable to red meat
421 consumption due to CRC and cardiovascular diseases (CVD) in France [10]. They estimated a
422 burden of 19 (95% UI: 8; 33) DALYs/100,000 for CRC and 21 (95% UI: 12; 32) DALYs/100,000 for
423 CVD, for the French population. The estimated burden for CRC was close to our estimated
424 potential health gain of 18 (95% UI: 0;18) DALYs/100,000 for the alternative scenario. CRC was
425 based on the same evidence as in our study, whereas CVD was included due to its large
426 contribution to mortality in France [10]. CVD was included even though strong enough evidence
427 has not yet been established for the association with red meat consumption. Ruan *et al.* (2019)
428 also included health outcomes with limited evidence in the estimation of the burden of cancer

429 attributable to red and processed meat consumption in Canada [44]. In addition to CRC, stomach
 430 and pancreatic cancer were included. However, the association between stomach cancer and
 431 consumption of red meat has not been assessed by the WCRF [18]. Meanwhile, the association
 432 between red meat consumption and pancreatic cancer was graded *limited - suggestive* by the
 433 WCRF [18]. Health outcomes with lower level of evidence could be included but introduce large
 434 uncertainties. One way to deal with this is to include such health outcomes as model scenarios.
 435 We only included health outcomes with strong evidence (“convincing” and “probable” evidence
 436 according to the WCRF criteria scheme) in our study.

437 Springmann *et al.* (2018) investigated the impact of replacing animal-derived foods with plant-
 438 derived foods on nutrient intakes, premature mortality and various environmental parameters [43].
 439 They found that nutrient levels would be adequate except for calcium and vitamin B₁₂, and
 440 premature mortality would decrease by up to 12% when all animal-based foods were substituted
 441 by plant-based foods. We also found a reduction in premature mortality (expressed in YLL) and
 442 lower intakes of vitamin B₁₂ due to the substitution investigated in our study. However, in addition,
 443 we estimated a decrease in intake of zinc and selenium. We only considered unprocessed red
 444 meat and pulses in our study, whereas Springmann *et al.* (2018) included several foods including
 445 red meat, fish, legumes and pulses, nuts and seeds, fruits and vegetables [43]. Thus, potential
 446 increases in consumption of other zinc- and selenium-containing foods may have compensated for
 447 the decrease in zinc and selenium intake due to decreased red meat consumption.

448 In our study, the RRs were assumed to follow a log-linear association. However, the association
 449 may be described by a different model shape. This could affect the estimated individual RR and
 450 thereby affect the estimated health impact. Also, the level at which the association is established,
 451 i.e. for whole foods or food components, may affect the dose-response relationship. The RRs used
 452 in this study were describing the association between the whole foods (red meat and pulses,
 453 respectively) and CRC, diabetes, and IHD. Thomsen (2019) stressed the importance of specifying
 454 substitution in nutritional epidemiological studies [45]. The RRs used in this study for CRC,
 455 diabetes and IHD were established for red meat and pulses individually without specifying
 456 substitution with or of other foods. Thus, our health impact estimates may also represent other
 457 underlying substitutions than those we investigated [45].

458 We accounted for some uncertainties in the quantitative analysis, but not for all. The quantified
 459 uncertainties were introduced from the RRs and the estimates derived from the GBD results tool
 460 (YLD, YLL and incidence estimates). However, also unquantified uncertainties were introduced.
 461 One way to deal with unquantified uncertainties is by assessing them qualitatively. EFSA (2006)
 462 suggests such an approach, where the unquantified uncertainties are described and scored by the

team of researchers to show the direction and magnitude of the potential impact on the final estimate (table 6). Based on this approach, the uncertainty around the substitution model is expected to have the largest impact on the total DALY difference. As dietary trends may have changed since year 2013, the reference scenario may not reflect the current diet of the Danish population. A change in the reference scenario would affect the estimated health impact of the substitution and to the uncertainty around our results. It is expected to affect the magnitude rather than the direction of the health impact. However, non-communicable diseases such as CRC, IHD and diabetes have a latency stage between exposure and onset of disease. Thus, the four-year gap between the reported dietary patterns (from 2013) and YLD, YLL, and incidence data (from 2017) may reduce this uncertainty. Misreporting (over- and underreporters) were not accounted for in our study. However, it has previously been found, by comparing with objectively measured energy expenditure, that energy intake was underreported by 12% in adults aged 20-59 years. Therefore, it could possibly affect the magnitude of the impact of the substitution [46]. The uncertainty around the YLD and YLL per case estimates based on the GBD Results Tool [39] is also expected to introduce additional uncertainties due to assumptions in the methodological approach.

5. Conclusion:

We took an RBA approach in assessing the risks and benefits of substituting unprocessed red meat by pulses in the Danish adult population. In total, 344 (95% UI: 425; 251) DALYs/100,000 could be averted per year by substituting unprocessed red meat by pulses in the Danish adult population. Men would experience the highest health gain from this substitution with 540 (95% UI: 683; 386) averted DALYs/100,000 per year. IHD was found to be the main contributor to the YLL, whereas diabetes was the main contributor to the YLD. Although our quantitative assessment of disease burden found an overall health gain, we also found an overall decrease in intakes of vitamin B₁₂, zinc and selenium leading to higher proportions of the population at risk of inadequate intakes. A small increase in iron intake and thus a decrease in the risk of iron inadequacy was estimated. The impact of the substitution for children and adolescents (< 18 years of age) remain to be assessed. Further development of our study could be done to include environmental parameters and thereby estimating the impact of such substitution on the environment.

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- 623
- 624

625 **Table 1** Health outcomes associated with consumption of unprocessed red meat and pulses included in the
626 assessment and the population at risk. The type of assessment applied for each health outcome (Disability-
627 Adjusted Life Year (DALY) or risk of inadequacy) is indicated under Health impact estimation.

Food	Component	Health outcome	Population at risk	Health impact estimation	Reference
Red meat	Whole food	Increased risk of colorectal cancer	20-75 years	DALY	[29]
Red meat	Whole food	Increased risk of diabetes mellitus	25-75 years	DALY	[19]
Pulses	Whole food	Decreased risk of ischaemic heart disease	20-86 years	DALY	[22]
Red meat	Vitamin B ₁₂	Decreased risk of megaloblastic anaemia	All	Risk of inadequacy	[20]
Red meat pulses	Iron	Decreased risk of microcytic anaemia	All	Risk of inadequacy	[20]
Red meat and pulses	Zinc	Zinc deficiency	All	Risk of inadequacy	[20]
Red meat and pulses	Selenium	Selenium deficiency	All	Risk of inadequacy	[20]

628

629

630 **Table 2** Consumption of unprocessed red meat and pulses (g/day) in the Danish population for the reference
 631 and alternative scenario. The proportion of the population consuming the specific food in the reference and
 632 the alternative scenario. Abbreviations: P2.5: 2.5th percentile, P50: 50th percentile, P97.5: 97.5th percentile,
 633 sd: standard deviation

Scenario	Mean	sd	P2.5	P50	P97.5	Proportion
Red meat						
Reference	60.20	41.94	6.02	51.49	168.73	99.6%
Alternative	0.00	0.00	0.00	0.00	0.00	0.0%
Pulses						
Reference	1.62	7.82	0.00	0.00	21.00	9.5%
Alternative	61.82	42.12	7.24	53.36	170.93	99.8%

634

635

636 **Table 3** Daily intake of vitamin B₁₂, iron, zinc and selenium in the Danish population for the reference and the
 637 alternative scenario. Abbreviations: P2.5: 2.5th percentile, P50: 50th percentile, P97.5: 97.5th percentile, sd:
 638 standard deviation

Scenario	Mean	sd	P2.5	P50	P97.5
Vitamin B₁₂ (µg/day)					
Reference	1.90	1.15	0.59	1.67	4.47
Alternative	1.52	0.93	0.37	1.32	3.72
Iron (mg/day)					
Reference	1.14	0.41	0.49	1.09	2.05
Alternative	1.16	0.41	0.49	1.11	2.09
Zinc (mg/day)					
Reference	8.21	2.93	3.53	7.83	15.07
Alternative	6.70	2.37	2.89	6.45	12.39
Selenium (µg/day)					
Reference	35.29	14.13	14.61	33.14	67.41
Alternative	30.89	13.41	11.47	28.76	62.07

639

640

641 **Table 4** Proportion of Danish population below the average requirements (AR) for vitamin B₁₂, iron, zinc and
642 selenium in the reference and alternative scenarios. Abbreviations: sd: standard deviation.

Nutrient	sex	AR ^a	Reference (%)	Alternative (%)
Vitamin B ₁₂	Women	1.4 µg/day	7	16
	Men	1.4 µg/day	2	10
Iron	Women<52 years	Mean: 1.46, sd: 0.614 mg/day	75	75
	Women>51 years	Mean: 0.87, sd: 0.158 mg/day	35	33
	Men	Mean: 1.05, sd: 0.195 mg/day	32	30
Zinc	Women	5.7 mg/day	27	47
	Men	6.4 mg/day	16	36
Selenium	Women	35 µg/day	55	67
	Men	30 µg/day	41	57

643 a: AR from the NNR [20].

644

645 **Table 5** Health impact of substituting red meat by pulses in the Danish adult population, in terms of
646 difference in Years Lived with Disability (YLD), Years of Life Lost due to premature death (YLL) and
647 Disability-Adjusted Life Years (DALY) between the reference scenario and the alternative scenario by health
648 outcome. Estimates are given per 100,000 individuals (total population, women only, and men only) and for
649 the year 2017 with 95% uncertainty intervals (UI) in brackets. Abbreviations: CRC: colorectal cancer, IHD:
650 ischaemic heart disease

Food	Health outcome	Extra cases/100,000 (95% UI)	Δ YLD/100,000 (95% UI)	Δ YLL/100,000 (95% UI)	Δ DALY/100,000 (95% UI)
Danish adult population					
Red meat	CRC	-2.07 (-4.05 ; -0.02)	-1.13 (-2.22 ; -0.01)	-17.29 (-34.73 ; -0.17)	-18.43 (-37.00 ; -0.18)
	Diabetes	-33.34 (-57.14 ; -8.14)	-53.44 (-92.74 ; -12.99)	-12.64 (-21.96 ; -3.05)	-66.07 (-114.23 ; -15.91)
Pulses	IHD	-53.34 (-80.86 ; -21.78)	-19.01 (-29.58 ; -7.35)	-240.81 (-365.93 ; -92.89)	-259.82 (-394.70 ; -100.32)
Total			-73.58 (-104.15 ; -41.69)	-270.74 (-372.70 ; -152.63)	-344.32 (-425.08 ; -251.78)
Women					
Red meat	CRC	-1.19 (-2.34 ; -0.01)	-0.66 (-1.33 ; -0.01)	-9.96 (-20.34 ; -0.10)	-10.62 (-21.70 ; -0.10)
	Diabetes	-19.68 (-34.12 ; -4.72)	-30.32 (-54.58 ; -7.29)	-4.24 (-7.66 ; -0.98)	-34.56 (-62.01 ; -8.29)
Pulses	IHD	-24.92 (-38.29 ; -9.98)	-12.47 (-20.22 ; -4.80)	-95.84 (-147.67 ; -38.23)	-108.31 (-166.11 ; -42.97)
Total			-43.45 (-61.77 ; -26.39)	-110.04 (-150.67 ; -64.20)	-153.49 (-186.77 ; -119.36)
Men					
Red meat	CRC	-2.98 (-5.80 ; -0.03)	-1.64 (-3.22 ; -0.02)	-25.19 (-49.20 ; -0.25)	-26.83 (-52.35 ; -0.27)
	Diabetes	-47.35 (-80.74 ; -11.64)	-77.13 (-133.36 ; -18.65)	-21.25 (-36.81 ; -4.97)	-98.38 (-169.81 ; -23.95)
Pulses	IHD	-82.47 (-124.52 ; -33.88)	-25.73 (-40.15 ; -10.08)	-389.46 (-602.57 ; -149.48)	-415.18 (-640.38 ; -159.76)
Total			-104.50 (-151.90 ; -58.40)	-435.89 (-612.19 ; -241.64)	-540.39 (-682.68 ; -385.69)

651

652 **Table 6** The source of unquantified uncertainties together with the magnitude and direction of the impact on
653 the total DALY difference estimate, presented qualitatively and with a score. +, ++, +++ indicate a small,
654 medium or large overestimation. -, - - and - - - indicate a small, medium or large underestimation.

	Source of uncertainty	Magnitude and direction of influence on health impact	Score
Health outcomes	Identification of relevant compounds	There may be other relevant compounds with adverse/beneficial effects in red meat and pulses not accounted for	++/- -
	Identification of relevant health outcomes	There may be other relevant health effects associated with consumption of red meat and pulses	++/- -
	Identification of relevant sub-populations	There may be other relevant sub-populations relevant to the health effects considered	+/-
	Dose response relationship	Assuming a log-linear shape of model	+/-
Exposure assessment	Consumption data	over- and under-reporters were not excluded	+/-
	Concentration data	Measurement of nutrients and contaminants in food	+/-
	Substitution model	A gram to gram substitution may not be the realistic, energy balance is not kept constant	-
		Dietary trends have changed since the year of 2013 when consumption data was gathered. This may affect the reference scenario and thereby the health impact	++/-
CRC model	YLD and YLL per case approach	Methodological uncertainties	++/- -
Diabetes model	YLD and YLL per case approach	Methodological uncertainties	++/- -
IHD model	YLD and YLL per case approach	Methodological uncertainties	++/- -

655

656

657

658

659 **Fig. 1** Difference in Disability-Adjusted Life Years (DALY) per 100,000 for the total Danish adult population,
660 Danish women, and Danish men by health outcome for the year 2017. Each bar represents a health
661 outcome. The error bars indicate the 95% uncertainty interval (UI) and reflects the uncertainty introduced by
662 the relative risk (RR) and DALY/case estimates.

663

664 **Online Resource 1:**

665 **Table 7** The food items included in the Danish dietary survey (DANSDA) with the respective DANSDA id and
666 Food data id (database for concentration of nutrients in foods of both Danish and non-Danish origin on the
667 Danish market) [32]. The weight change factor is indicated together with the concentration of vitamin B₁₂,
668 iron, zinc and selenium.

DANSDA id	Food data id	Food item	Weight change factor	Vitamin B ₁₂ (µg/g)	Iron (mg/g)	Zinc (mg/g)	Selenium (µg/g)
Pulses							
25	568	White beans, dried	2.40	0.000	0.055	0.028	0.088
29	19	Brown beans, dried	2.40	0.000	0.050	0.020	0.088
345	592	Peas, mature, dried	2.10	0.000	0.055	0.038	0.140
484	741	Chickpeas, dried	2.10	0.000	0.064	0.010	0.020
Red meat							
80	644	Pork, heart, raw	0.65	0.027	0.060	0.021	0.121
112	798	Veal, lean, raw	0.80	0.013	0.014	0.043	0.084
113	984	Veal, medium fat, raw	0.80	0.013	0.016	0.042	0.030
138	1234	Lamb, meat, average, raw	0.80	0.012	0.015	0.034	0.061
139	994	Lamb, shoulder, raw	0.80	0.012	0.015	0.034	0.061
146	781	Liver, pig, raw	0.80	0.400	0.134	0.068	0.476
189	547	Kidney, calf, raw	0.80	0.023	0.068	0.017	1.200
191	574	Kidney, pig, raw	0.60	0.017	0.033	0.026	1.820
199	818	Beef, meat, <5% fat, raw	0.80	0.014	0.021	0.036	0.065
201	909	Beef, meat, 5-10% fat, raw	0.80	0.014	0.021	0.048	0.068
374	1124	Pork, thin belly with rind, raw	0.35	0.008	0.005	0.015	0.104
378	771	Pork, tenderloin trimmed, raw	0.75	0.006	0.010	0.018	0.104
379	1117	Pork, lion with rind, raw	0.65	0.009	0.004	0.014	0.072
380	1003	Pork, defatted, raw	0.80	0.008	0.005	0.014	0.108
381	949	Pork, collar, defatted, raw	0.65	0.008	0.010	0.027	0.092
382	74	Pork, collar with rind, raw	0.65	0.009	0.008	0.021	0.089
419	770	Beef, top side, cap off, raw	0.80	0.014	0.024	0.047	0.065
420	879	Beef, outside round, raw	0.80	0.014	0.021	0.045	0.097

424	966	Beef, rumpsteak, cap on, raw	0.80	0.014	0.022	0.034	0.065
429	1109	Beef, striplion, cap on, raw	0.80	0.014	0.017	0.042	0.089
431	871	Beef, striplion, cap off, raw	0.80	0.014	0.018	0.046	0.102
436	1040	Beef, brisket anterior part, raw	0.80	0.016	0.020	0.035	0.080
438	1233	Beef, brisket posterior part, raw	0.80	0.014	0.016	0.039	0.077
927	739	Pork, lion, lean, raw	0.80	0.007	0.007	0.036	0.069
941	796	Lamb, leg defatted, raw	0.80	0.012	0.022	0.033	0.061

669

670

671 **Online Resource 2:**

672 **Table 8** mean and standard deviation (sd) of Years Lived with Disability (YLD) and Years of Life Lost due to
673 premature death (YLL) extracted from the Global Burden of Disease (GBD) results tool for Denmark for the
674 year 2017 [39]. The data is health outcome specific, age groups specific and gender specific. Abbreviations:
675 CRC: colorectal cancer, IHD: ischaemic heart disease, m: men, w: women

Age group	Gender	YLD/ Mean (sd)	YLL/ Mean (sd)
CRC			
20-24	M	0.59 (0.13)	9.37 (1.51)
	W	0.86 (0.20)	13.18 (2.73)
25-29	M	1.46 (0.29)	20.95 (3.25)
	W	1.56 (0.35)	22.42 (3.91)
30-34	M	2.58 (0.62)	37.91 (5.31)
	W	2.77 (0.68)	39.75 (6.46)
35-39	M	4.55 (1.17)	68.97 (9.99)
	W	4.93 (1.13)	73.41 (10.23)
40-44	M	7.87 (2.04)	123.90 (16.62)
	W	8.10 (1.97)	125.68 (16.65)
45-49	M	16.17 (3.42)	274.46 (29.53)
	W	14.55 (2.99)	246.59 (26.92)
50-54	M	29.78 (6.68)	539.41 (55.45)
	W	28.17 (6.45)	477.55 (49.32)
55-59	M	58.96 (11.27)	1013.21 (100.00)
	W	44.80 (9.41)	747.13 (74.93)
60-64	M	98.03 (17.92)	1607.14 (143.84)
	W	74.37 (14.34)	1182.11 (110.86)
65-69	M	136.92 (24.79)	1989.12 (182.38)
	W	95.58 (18.95)	1368.77 (130.28)
70-74	M	202.73 (34.91)	2807.38 (248.05)
	W	134.13 (25.09)	1807.14 (165.89)
75-79	M	250.56 (45.68)	3236.40 (303.33)
	W	172.39 (30.86)	2230.57 (197.09)
IHD			
35-39	M	15.72 (3.77)	159.88 (21.99)
	W	11.25 (3.13)	32.08 (4.90)
40-44	M	30.84 (6.91)	400.52 (44.96)
	W	20.31 (4.67)	68.10 (9.88)
45-49	M	55.85 (11.22)	841.05 (89.21)

	W	34.36 (7.21)	162.91 (21.68)
50-54	M	89.87 (16.27)	1456.32 (127.49)
	W	52.27 (10.54)	353.44 (42.92)
55-59	M	136.13 (25.14)	2467.79 (182.69)
	W	75.25 (14.46)	601.94 (65.03)
60-64	M	210.83 (38.34)	3618.68 (277.00)
	W	109.28 (21.04)	1035.59 (107.52)
65-69	M	329.13 (58.95)	4463.53 (328.17)
	W	165.28 (29.94)	1398.07 (131.85)
70-74	M	451.30 (79.24)	6096.61 (446.50)
	W	231.57 (79.24)	2310.29 (209.40)
75-79	M	547.69 (93.23)	8178.02 (592.00)
	W	291.03 (51.30)	3821.91 (326.90)
Diabetes			
25-29	M	401.22 (85.28)	2.25 (0.51)
	W	349.89 (73.29)	5.43 (1.25)
30-34	M	465.64 (93.75)	10.18 (2.06)
	W	384.59 (77.83)	7.30 (1.39)
35-39	M	540.75 (109.85)	20.25 (3.45)
	W	420.08 (84.88)	10.62 (1.90)
40-44	M	632.29 (126.70)	35.76 (6.40)
	W	478.26 (95.25)	12.86 (2.53)
45-49	M	873.93 (172.32)	130.26 (20.48)
	W	626.46 (124.87)	36.69 (6.63)
50-54	M	1253.67 (252.76)	256.33 (35.71)
	W	846.56 (169.70)	85.96 (15.40)
55-59	M	1727.48 (335.48)	378.96 (49.93)
	W	1147.04 (230.43)	154.27 (24.25)
60-64	M	2225.28 (421.20)	647.64 (81.05)
	W	1493.20 (293.29)	266.09 (35.47)
65-69	M	2536.81 (476.52)	886.53 (98.66)
	W	1748.93 (341.99)	338.20 (47.92)
70-74	M	2718.81 (510.54)	1177.39 (155.85)
	W	1985.64 (379.80)	516.95 (63.25)
75-79	M	3041.97 (549.10)	1404.51 (172.12)
	W	2347.50 (431.45)	791.88 (94.14)

677 Online Resource 3

678 R code

679 Preparation

```
680 # Packages
681 library(tidyr)
682 library(dplyr)
683 library(data.table)
684 library(mc2d)
685
686 # Helpers
687 mean_median_ci <-
688   function(x) {
689     c(mean = mean(x),
690       sd = sd(x),
691       quantile(x, probs = c(0.025, 0.25, 0.5, 0.75, 0.975)))
692   }
693
694 # bioavailability of haem and non-haem iron
695 bio_av_fe_m <-
696   function(cons_m) {
697     a <- 0.25*(0.5*cons_m)+0.1389*(0.5*cons_m) #50% of iron in meat is haem iron, 25% haem iron is
698     absorbed, 15% non-haem iron is absorbed (NNR,2014)
699     return(a)
700   }
701
702 ## Data Loading
703 ### Consumption data in raw amounts
704 cons_rm <- read.csv("consumption_redmeat.csv") #red meat
705 cons_rm <- tbl_df(cons_rm)
706 cons_rm <- filter(cons_rm, age>=18)
707 cons_p <- read.csv("consumption_pulses.csv") #pulses
708 cons_p <- tbl_df(cons_p)
709 cons_p <- filter(cons_p, age>=18)
710 cons_pp <- subset(cons_p, select=-c(ID,sex,age,weight,height,BMI)) #removing the columns that would
711 be duplicates
712 cons_total <- cbind(cons_rm,cons_pp) #total consumption, used for total exposure
713 cons_back <- read.csv("consumption_background.csv") #for background exposure
714 cons_back <- tbl_df(cons_back)
715 cons_back <- filter(cons_back, age>=18)
716
717 #Retention factor for nutrients
718 retention_nut <- read.csv("retention.csv") #retention factors for vitamin B12, iron, zinc, selenium
719 for red meat and pulses (Pedersen et al. 2015)
720
721 ##weight change factor
722 change_weight <- read.csv("change_factor.csv")
723 change_weight <- as.data.frame(change_weight)
724
725 change_rf <- change_weight[, grepl("RF",colnames(change_weight)) | grepl("Row.Names",colnames(change_weight))]
726 change_100 <- change_weight[, grepl("100p",colnames(change_weight)) | grepl("Row.Names",colnames(change_weight))]
727
728 ### GBD results
729 GBD <- read.csv("gbd_results_m_sd.csv")
730
731 ## Settings
732 set.seed(123)
```

```

736 nunc <- 1000
737 nvar <- nrow(cons_total)

```

738 Scenarios

```

739 #Pulses:
740 # Reference
741 cons_p_rf <- cons_p[ , grepl("RF",colnames(cons_p)) | grepl("ID",colnames(cons_p)) | grepl("sex",
742 colnames(cons_p)) | grepl("age",colnames(cons_p)) |
743 grepl("weight",colnames(cons_p)) | grepl("height",colnames(cons_p)) | grep
744 l("BMI",colnames(cons_p))]
745 edi_p_rf <- cons_p_rf[ , grepl("RF",colnames(cons_p_rf))]
746 #from raw to prepared amounts
747 cons_pulses_RF2 <- mapply("?", edi_p_rf[intersect(names(edi_p_rf), names(change_rf))],
748 change_rf[intersect(names(edi_p_rf), names(change_rf))])
749 cons_total$edi_p_rf <- rowSums(cons_pulses_RF2)
750
751
752 # 100% substitution
753 cons_p_100 <- cons_p[ , grepl("100p",colnames(cons_p)) | grepl("ID",colnames(cons_p)) | grepl("se
754 x",colnames(cons_p)) | grepl("age",colnames(cons_p)) |
755 grepl("weight",colnames(cons_p)) | grepl("height",colnames(cons_p)) | gre
756 pl("BMI",colnames(cons_p))]
757 edi_p_100 <- cons_p_100[ , grepl("100p",colnames(cons_p_100))]
758 #from raw to prepared amounts
759 cons_pulses_100 <- mapply("?", edi_p_100[intersect(names(edi_p_100), names(change_100))],
760 change_100[intersect(names(edi_p_100), names(change_100))])
761 cons_total$edi_p_100 <- rowSums(cons_pulses_100)
762
763 #Red meat:
764 # Reference:
765 cons_rm_rf <- cons_rm[ , grepl("RF",colnames(cons_rm)) | grepl("ID",colnames(cons_rm)) | grepl("s
766 ex",colnames(cons_rm)) | grepl("age",colnames(cons_rm)) |
767 grepl("weight",colnames(cons_rm)) | grepl("height",colnames(cons_rm)) |
768 grepl("BMI",colnames(cons_rm))]
769 edi_rm_rf <- cons_rm_rf[ , grepl("RF",colnames(cons_rm_rf))]
770 #from raw to prepared amounts
771 cons_redmeat_RF2 <- mapply("?", edi_rm_rf[intersect(names(edi_rm_rf), names(change_rf))],
772 change_rf[intersect(names(edi_rm_rf), names(change_rf))])
773 cons_total$edi_rm_rf <- rowSums(cons_redmeat_RF2)
774
775
776
777 # Alternative (100% substitution)
778 cons_total$edi_rm_100 <- 0

```

779 Intake of nutrients - vitamin B12, zinc, selenium

```

780 #Background intakes from other food sources
781 edi_nut_back_all <- mapply("?", cons_back[intersect(names(cons_back), names(nut_back))],
782 nut_back[intersect(names(cons_back), names(nut_back))])
783 edi_nut_back_all <- edi_nut_back_all*retention_nut #including the retention factor
784
785
786 ### From red meat:
787 # Reference
788 edi_rm_nut_rf <- mapply("?", cons_rm_rf[intersect(names(cons_rm_rf), names(nut_rf))],
789 nut_rf[intersect(names(cons_rm_rf), names(nut_rf))])
790 edi_rm_nut_rf <- edi_rm_nut_rf*retention_nut
791
792
793 ### From pulses
794 # Reference
795 edi_p_nut_rf <- mapply("?", cons_p_rf[intersect(names(cons_p_rf), names(nut_rf))],

```

```

796         nut_rf[intersect(names(cons_p_rf), names(nut_rf))])
797 edi_p_nut_rf <- edi_p_nut_rf*retention_nut
798
799 # Alternative
800 edi_p_nut_100 <- mapply("?", cons_p_100[intersect(names(cons_p_100), names(nut_100))],
801                          nut_100[intersect(names(cons_p_100), names(nut_100))])
802 edi_p_nut_100 <- edi_p_nut_100*retention_nut
803
804
805
806 #Total intake
807 cons_total$nut_background <- cons_total$edi_nut_back_all-cons_rm$edi_nut_rf+cons_p$edi_nut_rf
808
809
810 # Reference
811 cons_total$edi_nut_rf <- cons_rm$edi_nut_rf+cons_p$edi_nut_rf+cons_total$nut_background #adding the two intakes + background intake
812 mean_median_ci(cons_total$edi_nut_rf)
813 #Proportion below the average requirement
814 edi_nut_rf_m <- cons_total[cons_total$sex %in% 1, ] # Men
815 edi_nut_rf_m <- edi_nut_rf_m$edi_nut_rf
816 mean(edi_nut_rf_m<AR)
817
818
819 edi_nut_rf_w <- cons_total[cons_total$sex %in% 2, ] # Women
820 edi_nut_rf_w <- edi_nut_rf_w$edi_nut_rf
821 mean(edi_nut_rf_w<AR)
822
823
824 # Alternative
825 cons_total$edi_nut_100 <- cons_p$edi_nut_100+cons_total$nut_background #adding the two intakes
826 mean_median_ci(cons_total$edi_nut_100)
827 #Proportion below the average requirement
828 edi_nut_100_m <- cons_total[cons_total$sex %in% 1, ] # Men
829 edi_nut_100_m <- edi_nut_100_m$edi_nut_100
830 mean(edi_nut_100_m<AR)
831
832 edi_nut_100_w <- cons_total[cons_total$sex %in% 2, ] # Women
833 edi_nut_100_w <- edi_nut_100_w$edi_nut_100
834 mean(edi_nut_100_w<AR)

```

835 ##Intake of nutrients - Iron

```

836 #Background intake from other food sources
837 edi_fe_back_all <- mapply("?", cons_back[intersect(names(cons_back), names(fe_back))],
838                          fe_back[intersect(names(cons_back), names(fe_back))])
839 edi_fe_back_all <- edi_fe_back_all*0.15 #bioavailability: 15% is assumed to be absorbed from all foods (NNR,2014)
840
841
842
843 ### Iron from red meat:
844 # Reference
845 edi_rm_fe_rf <- mapply("?", cons_rm_rf[intersect(names(cons_rm_rf), names(fe_rf))],
846                       fe_rf[intersect(names(cons_rm_rf), names(fe_rf))])
847 edi_rm_fe_rf <- bio_av_fe_m(edi_rm_fe_rf) #bioavailability of haem iron and non-haem iron (NNR,2014)
848
849
850
851 ### Iron from pulses:
852 # Reference
853 edi_p_fe_rf <- mapply("?", cons_p_rf[intersect(names(cons_p_rf), names(fe_rf))],
854                      fe_rf[intersect(names(cons_p_rf), names(fe_rf))])
855 edi_p_fe_rf <- edi_p_fe_rf*retention_nut*0.1389 #bioavailability of non-haem iron
856

```

```

857 # Alternative
858 edi_p_fe_100 <- mapply("!", cons_p_100[intersect(names(cons_p_100), names(fe_100))],
859                        fe_100[intersect(names(cons_p_100), names(fe_100))])
860 edi_p_fe_100 <- edi_p_fe_100*retention_nut*0.1389 #bioavailability of non-haem iron
861
862
863 ### Total intake
864
865 # Average requirement distributions for men, menstruating women and menopause women
866 dis_men <- rnorm(1341, 1.05, 0.195)
867 dis_women_mens_req <- rlnorm(779, 0.299, 0.403)
868 dis_women_meno_req <- rnorm(596, 0.87, 0.158)
869
870 cons_total$fe_background <- cons_total$sedi_fe_back_all-cons_rm$sedi_fe_rf+cons_p$sedi_fe_rf
871
872
873 # Reference
874 cons_total$sedi_fe_rf <- cons_rm$sedi_fe_rf+cons_p$sedi_fe_rf+cons_total$fe_background #adding the t
875 wo intakes + background intake
876 mean_median_ci(cons_total$sedi_fe_rf)
877
878 #Proportion below the average requirement distribution
879 edi_fe_rf_m <- cons_total[cons_total$sex %in% 1, ] # men
880 edi_fe_rf_m <- edi_fe_rf_m$sedi_fe_rf
881 mean(edi_fe_rf_m<dis_men)
882
883 edi_fe_rf_w <- cons_total[cons_total$sex %in% 2, ] # menstruating women
884 edi_fe_rf_w_mens <- edi_fe_rf_w[edi_fe_rf_w$age <= 51, ]
885 edi_fe_rf_w_mens <- edi_fe_rf_w_mens$sedi_fe_rf
886 mean(edi_fe_rf_w_mens<dis_women_mens_req)
887
888 edi_fe_rf_w_meno <- edi_fe_rf_w[edi_fe_rf_w$age > 51, ] # menopause women
889 edi_fe_rf_w_meno <- edi_fe_rf_w_meno$sedi_fe_rf
890 mean(edi_fe_rf_w_meno<dis_women_meno_req)
891
892
893
894 # Alternative
895 cons_total$sedi_fe_100 <- cons_p$sedi_fe_100+cons_total$fe_background #adding the two intakes
896 mean_median_ci(cons_total$sedi_fe_100)
897
898 #Proportion below the average requirement distriution
899 edi_fe_100_m <- cons_total[cons_total$sex %in% 1, ] # men
900 mean(edi_fe_100_m$sedi_fe_100<dis_men)
901
902 edi_fe_100_w <- cons_total[cons_total$sex %in% 2, ] # menstruating women
903 edi_fe_100_w_mens <- edi_fe_100_w[edi_fe_100_w$age <= 51, ]
904 edi_fe_100_w_mens <- edi_fe_100_w_mens$sedi_fe_100
905 mean(edi_fe_100_w_mens<dis_women_mens_req)
906
907 edi_fe_100_w_meno <- edi_fe_100_w[edi_fe_100_w$age > 51, ] # menopause women
908 edi_fe_100_w_meno <- edi_fe_100_w_meno$sedi_fe_100
909 mean(edi_fe_100_w_meno<dis_women_meno_req)
910
911 ##Non-communicable diseases
912
913 # The relative risk (RR) for the non-communicable diseases colorectal cancer (CRC), diabetes and
914 ischaemic heart disease (IHD)
915
916 # CRC RR: 1.12 (CI: 1.00;1.25)per 100 g red meat per day (Norat et al. 2017)
917 # Diabetes RR: 1.19 (CI: 1.04 ; 1.37) per 100 g red meat per day (Pan et al. 2011)
918 # IHD RR: 0.86 (CI: 0.78 ; 0.94) per 400 g pulses per week (Afshin et al. 2014)

```

```

918
919
920 # The uncertainty around the RR was assumed to follow a log-normal distribution.
921 # For extrapolation of the RR per 1 g, the beta parameter was estimated from the upper and lower
922 bound of the 95% UI of the RR.
923 # For each outcome, the following was done:
924
925 RR_beta_low <- log(low)/100 #Low is the lower bound of the 95% UI of the RR
926 RR_beta_up <- log(up)/100 #up is the upper bound
927
928 mu <- (RR_beta_low+RR_beta_high)/2
929 mu
930
931 sigma <- (RR_beta_high-RR_beta_low)/(qnorm(0.975,0,1)-qnorm(0.025,0,1))
932 sigma
933
934
935 beta <- rnorm(nunc,mu,sigma)
936
937
938
939
940 # Individual RR estimated for the two scenarios:
941 #Reference
942 RR_rf <- apply(t(beta),2,function(x) exp(x * cons_total$edi_food_rf)) #where food is red meat (rm
943 ) for CRC and diabetes and pulses (p) for IHD
944
945 #Alternative
946 RR_100 <- apply(t(beta),2,function(x) exp(x * cons_total$edi_food_100)) #where food is red meat (
947 rm) for CRC and diabetes and pulses (p) for IHD
948
949
950 # PIF (potential impact fraction):
951 PIF_100 <- (RR_rf - RR_100)/RR_rf
952
953
954 # Incidence
955 # number of cases per 100,000
956 # CRC: https://www.esundhed.dk/home/registre/cancerregisteret/nye%20kraefttilfaelde number of aff
957 ected in 2017
958 # Diabetes: https://www.esundhed.dk/Registre/Register-for-udvalgte-kroniske-sygdomme number of af
959 fected in 2017
960 # IHD: hjertetal.dk number of affected in 2017
961
962 # CRC:
963 #male
964 p_20_24_male <- 5e-05
965 p_25_29_male <- 5e-05
966 p_30_34_male <- 5e-05
967 p_35_39_male <- 5e-05
968 p_40_44_male <- 6e-05
969 p_45_49_male <- 1.3e-04
970 p_50_54_male <- 2.2e-04
971 p_55_59_male <- 4.9e-04
972 p_60_64_male <- 7.4e-04
973 p_65_69_male <- 1.23e-03
974 p_70_74_male <- 1.39e-03
975 p_75_79_male <- 1.41e-03
976
977 #female
978 p_20_24_female <- 5e-05
979 p_25_29_female <- 5e-05
980 p_30_34_female <- 5e-05

```

```

981 p_35_39_female <- 5e-05
982 p_40_44_female <- 5e-05
983 p_45_49_female <- 1e-04
984 p_50_54_female <- 1.9e-04
985 p_55_59_female <- 4.2e-04
986 p_60_64_female <- 3.9e-04
987 p_65_69_female <- 5.6e-04
988 p_70_74_female <- 7e-04
989 p_75_79_female <- 6.9e-04 #same for diabetes and IHD
990
991
992 ## Diabetes (DM):
993 ##male
994 # p_25_29_male <- 5e-04
995 # p_30_34_male <- 1e-03
996 # p_35_39_male <- 1.5e-03
997 # p_40_44_male <- 2.5e-03
998 # p_45_49_male <- 4.25e-03
999 # p_50_54_male <- 5.5e-03
1000 # p_55_59_male <- 6.75e-03
1001 # p_60_64_male <- 7.5e-03
1002 # p_65_69_male <- 7e-03
1003 # p_70_74_male <- 7e-03
1004 # p_75_79_male <- 6.5e-03
1005 #
1006 ##female
1007 # p_25_29_female <- 1.25e-03
1008 # p_30_34_female <- 7.5e-04
1009 # p_35_39_female <- 1e-03
1010 # p_40_44_female <- 1.25e-03
1011 # p_45_49_female <- 2e-03
1012 # p_50_54_female <- 3.25e-03
1013 # p_55_59_female <- 4e-03
1014 # p_60_64_female <- 4.5e-03
1015 # p_65_69_female <- 4.5e-03
1016 # p_70_74_female <- 4.75e-03
1017 # p_75_79_female <- 4.75e-03
1018 #
1019 #
1020 ## IHD:
1021 ##male
1022 # p_34_male <- 0
1023 # p_35_44_male <- 1.18e-03
1024 # p_45_54_male <- 3.83e-03
1025 # p_55_64_male <- 8.52e-03
1026 # p_65_74_male <- 1.297e-02
1027 # p_75_84_male <- 1.848e-02
1028 #
1029 #
1030 ##female
1031 # p_34_female <- 0
1032 # p_35_44_female <- 4.9e-04
1033 # p_45_54_female <- 1.68e-03
1034 # p_55_64_female <- 3.66e-03
1035 # p_65_74_female <- 5.51e-03
1036 # p_75_84_female <- 9.51e-03
1037
1038
1039
1040
1041
1042 #For Loop for creating new column for the probability of Background incidence of CRC for the indi
1043 vidual

```

```

1044 cons_total$p_rf <- 0
1045
1046
1047 for (i in 1:nrow(cons_total)) {
1048
1049   if(cons_total$sex[i] == 1){ #male
1050
1051     if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1052       cons_total$p_rf[i] <- p_20_24_male
1053     }
1054     if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1055       cons_total$p_rf[i] <- p_25_29_male
1056     }
1057     if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1058       cons_total$p_rf[i] <- p_30_34_male
1059     }
1060     if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1061       cons_total$p_rf[i] <- p_35_39_male
1062     }
1063     if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1064       cons_total$p_rf[i] <- p_40_44_male
1065     }
1066     if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1067       cons_total$p_rf[i] <- p_45_49_male
1068     }
1069     if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1070       cons_total$p_rf[i] <- p_50_54_male
1071     }
1072     if(cons_total$age[i] > 54 & cons_total$age[i] < 60){
1073       cons_total$p_rf[i] <- p_55_59_male
1074     }
1075     if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1076       cons_total$p_rf[i] <- p_60_64_male
1077     }
1078     if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1079       cons_total$p_rf[i] <- p_65_69_male
1080     }
1081     if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1082       cons_total$p_rf[i] <- p_70_74_male
1083     }
1084     if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1085       cons_total$p_rf[i] <- p_75_79_male
1086     }
1087   }
1088
1089   if(cons_total$sex[i] == 2){ #female
1090
1091     if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1092       cons_total$p_rf[i] <- p_20_24_female
1093     }
1094     if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1095       cons_total$p_rf[i] <- p_25_29_female
1096     }
1097     if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1098       cons_total$p_rf[i] <- p_30_34_female
1099     }
1100     if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1101       cons_total$p_rf[i] <- p_35_39_female
1102     }
1103     if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1104       cons_total$p_rf[i] <- p_40_44_female
1105     }
1106   }

```



```

1107   if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1108     cons_total$p_rf[i] <- p_45_49_female
1109   }
1110   if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1111     cons_total$p_rf[i] <- p_50_54_female
1112   }
1113   if(cons_total$age[i] > 54 & cons_total$age[i] < 60){
1114     cons_total$p_rf[i] <- p_55_59_female
1115   }
1116   if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1117     cons_total$p_rf[i] <- p_60_64_female
1118   }
1119   if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1120     cons_total$p_rf[i] <- p_65_69_female
1121   }
1122   if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1123     cons_total$p_rf[i] <- p_70_74_female
1124   }
1125   if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1126     cons_total$p_rf[i] <- p_75_79_female
1127   }
1128 }
1129 }
1130
1131
1132
1133
1134 # Change in incidence of CRC for the alternative scenario
1135 delta_p_100 <- apply(PIF_100, 2, function(x) x*cons_total$p_rf)
1136 delta_p_100_unc <- apply(delta_p_100, 2, function(x) mean(x)*100000) #mean over population keeping
1137 g uncertainty per 100,000 individuals
1138 mean_median_ci(delta_p_100_unc) # finding the mean, sd and quantiles over the uncertainty dimensi
1139 on
1140
1141
1142
1143 # DALY Estimations
1144 #YLD per case, YLL per case from GBD results tool.
1145
1146 #YLD and YLL per case per sex and age group for health outcome CRC:
1147 # 20 - 24 years
1148 inc_20_24_m <- rnorm(nunc, 0.77, 0.13)
1149 inc_20_24_w <- rnorm(nunc, 1.14, 0.25)
1150 yld_20_24_m <- rnorm(nunc,0.59,0.13)
1151 yld_20_24_w <- rnorm(nunc,0.86,0.20)
1152 yll_20_24_m <- rnorm(nunc,9.37,1.51)
1153 yll_20_24_w <- rnorm(nunc,13.18,2.73)
1154
1155 yldcase_20_24_m <- yld_20_24_m/inc_20_24_m
1156 yldcase_20_24_w <- yld_20_24_w/inc_20_24_w
1157 yllcase_20_24_m <- yll_20_24_m/inc_20_24_m
1158 yllcase_20_24_w <- yll_20_24_w/inc_20_24_w
1159
1160
1161 # 25 - 29 years
1162 inc_25_29_m <- rnorm(nunc,2.01,0.32)
1163 inc_25_29_w <- rnorm(nunc,2.16,0.38)
1164 yld_25_29_m <- rnorm(nunc,1.46,0.29)
1165 yld_25_29_w <- rnorm(nunc,1.56,0.35)
1166 yll_25_29_m <- rnorm(nunc,20.95,3.25)
1167 yll_25_29_w <- rnorm(nunc,22.42,3.91)
1168
1169 yldcase_25_29_m <- yld_25_29_m/inc_25_29_m

```

```

1170 yldcase_25_29_w <- yld_25_29_w/inc_25_29_w
1171 yllcase_25_29_m <- yll_25_29_m/inc_25_29_m
1172 yllcase_25_29_w <- yll_25_29_w/inc_25_29_w
1173
1174
1175 #30 - 34 years
1176 inc_30_34_m <- rnorm(nunc,3.83,0.61)
1177 inc_30_34_w <- rnorm(nunc,4.17,0.66)
1178 yld_30_34_m <- rnorm(nunc,2.58,0.62)
1179 yld_30_34_w <- rnorm(nunc,2.77,0.68)
1180 yll_30_34_m <- rnorm(nunc,37.91,5.31)
1181 yll_30_34_w <- rnorm(nunc,39.75,6.46)
1182
1183 yldcase_30_34_m <- yld_30_34_m/inc_30_34_m
1184 yldcase_30_34_w <- yld_30_34_w/inc_30_34_w
1185 yllcase_30_34_m <- yll_30_34_m/inc_30_34_m
1186 yllcase_30_34_w <- yll_30_34_w/inc_30_34_w
1187
1188 #35 - 39 years
1189 inc_35_39_m <- rnorm(nunc,6.96,1.12)
1190 inc_35_39_w <- rnorm(nunc,7.71,1.21)
1191 yld_35_39_m <- rnorm(nunc,4.55,1.17)
1192 yld_35_39_w <- rnorm(nunc,4.93,1.13)
1193 yll_35_39_m <- rnorm(nunc,68.97,9.99)
1194 yll_35_39_w <- rnorm(nunc,73.41,10.23)
1195
1196 yldcase_35_39_m <- yld_35_39_m/inc_35_39_m
1197 yldcase_35_39_w <- yld_35_39_w/inc_35_39_w
1198 yllcase_35_39_m <- yll_35_39_m/inc_35_39_m
1199 yllcase_35_39_w <- yll_35_39_w/inc_35_39_w
1200
1201 #40 - 44 years
1202 inc_40_44_m <- rnorm(nunc,12.54,1.80)
1203 inc_40_44_w <- rnorm(nunc,13.12,1.93)
1204 yld_40_44_m <- rnorm(nunc,7.87,2.04)
1205 yld_40_44_w <- rnorm(nunc,8.10,1.97)
1206 yll_40_44_m <- rnorm(nunc,123.90,16.62)
1207 yll_40_44_w <- rnorm(nunc,125.68,16.25)
1208
1209 yldcase_40_44_m <- yld_40_44_m/inc_40_44_m
1210 yldcase_40_44_w <- yld_40_44_w/inc_40_44_w
1211 yllcase_40_44_m <- yll_40_44_m/inc_40_44_m
1212 yllcase_40_44_w <- yll_40_44_w/inc_40_44_w
1213
1214 #45 - 49 years
1215 inc_45_49_m <- rnorm(nunc,26.89,3.22)
1216 inc_45_49_w <- rnorm(nunc,24.63,3.20)
1217 yld_45_49_m <- rnorm(nunc,16.17,3.42)
1218 yld_45_49_w <- rnorm(nunc,14.55,2.99)
1219 yll_45_49_m <- rnorm(nunc,274.46,29.53)
1220 yll_45_49_w <- rnorm(nunc,246.59,29.53)
1221
1222 yldcase_45_49_m <- yld_45_49_m/inc_45_49_m
1223 yldcase_45_49_w <- yld_45_49_w/inc_45_49_w
1224 yllcase_45_49_m <- yll_45_49_m/inc_45_49_m
1225 yllcase_45_49_w <- yll_45_49_w/inc_45_49_w
1226
1227 #50 - 54 years
1228 inc_50_54_m <- rnorm(nunc,52.45,6.12)
1229 inc_50_54_w <- rnorm(nunc,49.50,5.81)
1230 yld_50_54_m <- rnorm(nunc,29.78,6.68)
1231 yld_50_54_w <- rnorm(nunc,28.17,6.45)
1232 yll_50_54_m <- rnorm(nunc,539.41,55.45)

```

```

1233 yll_50_54_w <- rnorm(nunc,477.55,49.32)
1234
1235 yldcase_50_54_m <- yld_50_54_m/inc_50_54_m
1236 yldcase_50_54_w <- yld_50_54_w/inc_50_54_w
1237 yllcase_50_54_m <- yll_50_54_m/inc_50_54_m
1238 yllcase_50_54_w <- yll_50_54_w/inc_50_54_w
1239
1240 #55 - 59 years
1241 inc_55_59_m <- rnorm(nunc,105.30,11.88)
1242 inc_55_59_w <- rnorm(nunc,80.44,9.49)
1243 yld_55_59_m <- rnorm(nunc,58.96,11.27)
1244 yld_55_59_w <- rnorm(nunc,44.80,9.41)
1245 yll_55_59_m <- rnorm(nunc,1013.21,100.00)
1246 yll_55_59_w <- rnorm(nunc,747.13,74.93)
1247
1248 yldcase_55_59_m <- yld_55_59_m/inc_55_59_m
1249 yldcase_55_59_w <- yld_55_59_w/inc_55_59_w
1250 yllcase_55_59_m <- yll_55_59_m/inc_55_59_m
1251 yllcase_55_59_w <- yll_55_59_w/inc_55_59_w
1252
1253 #60 - 64 years
1254 inc_60_64_m <- rnorm(nunc,181.19,18.72)
1255 inc_60_64_w <- rnorm(nunc,137.06,14.96)
1256 yld_60_64_m <- rnorm(nunc,98.03,17.92)
1257 yld_60_64_w <- rnorm(nunc,74.37,14.34)
1258 yll_60_64_m <- rnorm(nunc,1607.14,143.84)
1259 yll_60_64_w <- rnorm(nunc,1182.11,110.86)
1260
1261 yldcase_60_64_m <- yld_60_64_m/inc_60_64_m
1262 yldcase_60_64_w <- yld_60_64_w/inc_60_64_w
1263 yllcase_60_64_m <- yll_60_64_m/inc_60_64_m
1264 yllcase_60_64_w <- yll_60_64_w/inc_60_64_w
1265
1266 #65 - 69 years
1267 inc_65_69_m <- rnorm(nunc,257.88,24.84)
1268 inc_65_69_w <- rnorm(nunc,178.24,19.15)
1269 yld_65_69_m <- rnorm(nunc,136.92,24.79)
1270 yld_65_69_w <- rnorm(nunc,95.58,18.95)
1271 yll_65_69_m <- rnorm(nunc,1989.12,182.38)
1272 yll_65_69_w <- rnorm(nunc,1368.77,130.28)
1273
1274 yldcase_65_69_m <- yld_65_69_m/inc_65_69_m
1275 yldcase_65_69_w <- yld_65_69_w/inc_65_69_w
1276 yllcase_65_69_m <- yll_65_69_m/inc_65_69_m
1277 yllcase_65_69_w <- yll_65_69_w/inc_65_69_w
1278
1279 #70 - 74 years
1280 inc_70_74_m <- rnorm(nunc,397.21,39.56)
1281 inc_70_74_w <- rnorm(nunc,260.66,28.25)
1282 yld_70_74_m <- rnorm(nunc,202.73,34.91)
1283 yld_70_74_w <- rnorm(nunc,134.13,25.09)
1284 yll_70_74_m <- rnorm(nunc,2807.38,248.05)
1285 yll_70_74_w <- rnorm(nunc,1807.14,165.89)
1286
1287 yldcase_70_74_m <- yld_70_74_m/inc_70_74_m
1288 yldcase_70_74_w <- yld_70_74_w/inc_70_74_w
1289 yllcase_70_74_m <- yll_70_74_m/inc_70_74_m
1290 yllcase_70_74_w <- yll_70_74_w/inc_70_74_w
1291
1292 #75 - 79 years
1293 inc_75_79_m <- rnorm(nunc,508.23,52.67)
1294 inc_75_79_w <- rnorm(nunc,353.31,36.79)
1295 yld_75_79_m <- rnorm(nunc,250.56,45.68)

```

```

1296 yld_75_79_w <- rnorm(nunc,172.39,45.68)
1297 yll_75_79_m <- rnorm(nunc,3236.40,303.33)
1298 yll_75_79_w <- rnorm(nunc,2230.57,197.09)
1299
1300 yldcase_75_79_m <- yld_75_79_m/inc_75_79_m
1301 yldcase_75_79_w <- yld_75_79_w/inc_75_79_w
1302 yllcase_75_79_m <- yll_75_79_m/inc_75_79_m
1303 yllcase_75_79_w <- yll_75_79_w/inc_75_79_w
1304
1305
1306
1307
1308 yldcase <- matrix(nrow=nvar,ncol=nunc) # defining empty variable with number of rows equal to the
1309 variability dimension and columns equal to the uncertainty dimension
1310
1311 for (i in 1:nrow(cons_total)) {
1312   for(j in 1:ncol(yldcase)) {
1313     if(cons_total$sex[i] == 1){ #male
1314       if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1315         yldcase[i,j] <- yldcase_20_24_m[j]
1316       }
1317       if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1318         yldcase[i,j] <- yldcase_25_29_m[j]
1319       }
1320       if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1321         yldcase[i,j] <- yldcase_30_34_m[j]
1322       }
1323       if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1324         yldcase[i,j] <- yldcase_35_39_m[j]
1325       }
1326       if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1327         yldcase[i,j] <- yldcase_40_44_m[j]
1328       }
1329       if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1330         yldcase[i,j] <- yldcase_45_49_m[j]
1331       }
1332       if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1333         yldcase[i,j] <- yldcase_50_54_m[j]
1334       }
1335       if(cons_total$age[i] > 54 & cons_total$age[i] < 60){
1336         yldcase[i,j] <- yldcase_55_59_m[j]
1337       }
1338       if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1339         yldcase[i,j] <- yldcase_60_64_m[j]
1340       }
1341       if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1342         yldcase[i,j] <- yldcase_65_69_m[j]
1343       }
1344       if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1345         yldcase[i,j] <- yldcase_70_74_m[j]
1346       }
1347       if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1348         yldcase[i,j] <- yldcase_75_79_m[j]
1349       }
1350     }
1351   }
1352   if(cons_total$sex[i] == 2){ #female
1353     if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1354       yldcase[i,j] <- yldcase_20_24_m[j]
1355     }
1356     if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1357       yldcase[i,j] <- yldcase_25_29_w[j]
1358     }
1359   }

```

```

1359   if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1360     yldcase[i,j] <- yldcase_30_34_w[j]
1361   }
1362   if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1363     yldcase[i,j] <- yldcase_35_39_w[j]
1364   }
1365   if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1366     yldcase[i,j] <- yldcase_40_44_w[j]
1367   }
1368   if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1369     yldcase[i,j] <- yldcase_45_49_w[j]
1370   }
1371   if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1372     yldcase[i,j] <- yldcase_50_54_w[j]
1373   }
1374   if(cons_total$age[i] > 54 & cons_total$age[i] < 60){
1375     yldcase[i,j] <- yldcase_55_59_w[j]
1376   }
1377   if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1378     yldcase[i,j] <- yldcase_60_64_w[j]
1379   }
1380   if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1381     yldcase[i,j] <- yldcase_65_69_w[j]
1382   }
1383   if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1384     yldcase[i,j] <- yldcase_70_74_w[j]
1385   }
1386   if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1387     yldcase[i,j] <- yldcase_75_79_w[j]
1388   }
1389 }
1390 }
1391 }
1392
1393
1394
1395 yllcase <- matrix(nrow=nvar,ncol=nunc)
1396
1397 for (i in 1:nrow(cons_total)) {
1398   for(j in 1:ncol(yllcase)) {
1399     if(cons_total$sex[i] == 1){ #male
1400       if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1401         yllcase[i,j] <- yllcase_20_24_m[j]
1402       }
1403       if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1404         yllcase[i,j] <- yllcase_25_29_m[j]
1405       }
1406       if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1407         yllcase[i,j] <- yllcase_30_34_m[j]
1408       }
1409       if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1410         yllcase[i,j] <- yllcase_35_39_m[j]
1411       }
1412       if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1413         yllcase[i,j] <- yllcase_40_44_m[j]
1414       }
1415       if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1416         yllcase[i,j] <- yllcase_45_49_m[j]
1417       }
1418       if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1419         yllcase[i,j] <- yllcase_50_54_m[j]
1420       }
1421       if(cons_total$age[i] > 54 & cons_total$age[i] < 60){

```

```

1422     yllcase[i,j] <- yllcase_55_59_m[j]
1423   }
1424   if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1425     yllcase[i,j] <- yllcase_60_64_m[j]
1426   }
1427   if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1428     yllcase[i,j] <- yllcase_65_69_m[j]
1429   }
1430   if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1431     yllcase[i,j] <- yllcase_70_74_m[j]
1432   }
1433   if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1434     yllcase[i,j] <- yllcase_75_79_m[j]
1435   }
1436 }
1437
1438 if(cons_total$sex[i] == 2){ #female
1439   if(cons_total$age[i] > 19 & cons_total$age[i] < 25){
1440     yllcase[i,j] <- yllcase_20_24_m[j]
1441   }
1442   if(cons_total$age[i] > 24 & cons_total$age[i] < 30){
1443     yllcase[i,j] <- yllcase_25_29_w[j]
1444   }
1445   if(cons_total$age[i] > 29 & cons_total$age[i] < 35){
1446     yllcase[i,j] <- yllcase_30_34_w[j]
1447   }
1448   if(cons_total$age[i] > 34 & cons_total$age[i] < 40){
1449     yllcase[i,j] <- yllcase_35_39_w[j]
1450   }
1451   if(cons_total$age[i] > 39 & cons_total$age[i] < 45){
1452     yllcase[i,j] <- yllcase_40_44_w[j]
1453   }
1454   if(cons_total$age[i] > 44 & cons_total$age[i] < 50){
1455     yllcase[i,j] <- yllcase_45_49_w[j]
1456   }
1457   if(cons_total$age[i] > 49 & cons_total$age[i] < 55){
1458     yllcase[i,j] <- yllcase_50_54_w[j]
1459   }
1460   if(cons_total$age[i] > 54 & cons_total$age[i] < 60){
1461     yllcase[i,j] <- yllcase_55_59_w[j]
1462   }
1463   if(cons_total$age[i] > 59 & cons_total$age[i] < 65){
1464     yllcase[i,j] <- yllcase_60_64_w[j]
1465   }
1466   if(cons_total$age[i] > 64 & cons_total$age[i] < 70){
1467     yllcase[i,j] <- yllcase_65_69_w[j]
1468   }
1469   if(cons_total$age[i] > 69 & cons_total$age[i] < 75){
1470     yllcase[i,j] <- yllcase_70_74_w[j]
1471   }
1472   if(cons_total$age[i] > 74 & cons_total$age[i] < 80){
1473     yllcase[i,j] <- yllcase_75_79_w[j]
1474   }
1475 }
1476 }
1477 }
1478
1479
1480 #daly/case should be zero for everyone below the age at risk, instead of NA
1481 yldcase[is.na(yldcase)] <- 0
1482 yllcase[is.na(yllcase)] <- 0
1483
1484

```

```

1485
1486
1487 # DALY estimations
1488
1489 yld_rf <- yldcase*cons_total$p_rf
1490 yld_rf_unc <- apply(yld_rf,2,function(x) mean(x)*100000)
1491 mean_median_ci(yld_rf_unc)
1492 yld_100 <- yldcase*p_100
1493 yld_100_unc <- apply(yld_100,2,function(x) mean(x)*100000)
1494 mean_median_ci(yld_100_unc)
1495
1496
1497 yll_rf <- yllcase*cons_total$p_rf
1498 yll_rf_unc <- apply(yll_rf,2,function(x) mean(x)*100000)
1499 mean_median_ci(yll_rf_unc)
1500 yll_100 <- yllcase*p_100
1501 yll_100_unc <- apply(yll_100,2,function(x) mean(x)*100000)
1502 mean_median_ci(yll_100_unc)
1503
1504
1505 DALY_rf <- (yldcase+yllcase)*cons_total$p_rf
1506 DALY_rf_unc <- apply(DALY_rf,2,function(x) mean(x)*100000)
1507 mean_median_ci(DALY_rf_unc)
1508 DALY_100 <- (yldcase+yllcase)*p_100
1509 DALY_100_unc <- apply(DALY_100,2,function(x) mean(x)*100000)
1510 mean_median_ci(DALY_100_unc)
1511
1512
1513 # DALY change
1514 #The delta DALYs per 100,000
1515
1516
1517 # Alternative scenario
1518 yld_change_100 <- yld_100 - yld_rf
1519 yld_change_unc_100 <- apply(yld_change_100, 2, function(x) mean(x)*100000)
1520 mean_median_ci(yld_change_unc_100)
1521
1522 yll_change_100 <- yll_100 - yll_rf
1523 yll_change_unc_100 <- apply(yll_change_100, 2, function(x) mean(x)*100000)
1524 mean_median_ci(yll_change_unc_100)
1525
1526
1527 daly_change_100 <- DALY_100 - DALY_rf
1528 daly_change_unc_100 <- apply(daly_change_100, 2, function(x) mean(x)*100000)
1529 mean_median_ci(daly_change_unc_100)
1530

```