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Impact of intra-category food substitutions on the risk of type 2 diabetes: a modelling study on the pizza category

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Running title: Pizza substitutions and risk of type 2 diabetes

Abbreviations:

ANSES: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (French Agency for Food, Environmental and Occupational Health Safety)

BMI: Body mass index

CIQUAL: Centre d'Information sur la Qualité des Aliments (Food Quality Information Center)

CNIL: Commission Nationale de l'Informatique et des Libertés (French National Commission for Computed Data and Individual Freedom)

FP: Food Pattern

HAC: Hierarchical Ascending Classification

IDF: International Diabetes Federation

IE substitution: Isoenergetic substitution

INCA2: Etude Individuelle Nationale des Consommations Alimentaires 2 (second Individual and National Food consumption survey)

MEDI-LITE: Literature-Based Adherence Score to the Mediterranean Diet

mPNNS-GS: version modifiée du Programme National Nutrition Santé Guideline Score (modified version of the French National Nutrition Health Program)

NCD: Non-Communicable Disease

NIE substitution : Non-isoenergetic substitution

Oqali: Observatoire de la qualité de l'alimentation (French food quality observatory)

PCA: Principal Component Analysis

PRIME: Preventable Risk Integrated ModEl

T2D: Type 2 Diabetes

1 **ABSTRACT**

2 Advice on replacing unhealthy foods with healthier alternatives within the same food category
3 may be more acceptable and might ease the transition towards a healthy diet. Here, we studied
4 the potential impact of substitutions within the pizza category on the risk of type 2 diabetes
5 (T2D). The study sample consisted of 2,510 adults from the INCA2 French national survey.
6 Based on their nutritional characteristics, the 353 pizzas marketed in France were grouped in
7 100 clusters that were used to run various scenarios of pizza substitutions, which were either
8 isoenergetic (IE) or non-isoenergetic (NIE). We then used a model structurally similar to the
9 Preventable Risk Integrated Model (PRIME) to assess the expected rate of change in risk of
10 T2D. Pizzas characterized by a low energy, high vegetable content and whole grain dough
11 were associated with a greater reduction in the risk of T2D. The rates of change in risk of T2D
12 were markedly stronger in men and for NIE substitutions. When the rates of change were
13 estimated in the subsample of pizza consumers, replacing the observed pizzas with the best
14 pizza resulted in a T2D risk reduction of -6.7% (-8.4%; -4.9%, IE) and -8.9% (-11.2%; -6.3%,
15 NIE), assuming that this is their usual diets. The greatest risk reduction induced by an IE
16 substitution of the observed pizza with a mixed dish was similar to that observed with the best
17 pizzas. Overall, this modelling study suggests that healthy swaps within a category can
18 effectively supplement broader dietary changes toward a healthier diet.

19 **Keywords:** Food substitutions: Pizza categories: Type 2 diabetes: Public health

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28 INTRODUCTION

29 Diabetes is one of the most challenging public health issues, with a prevalence that is steadily
30 increasing worldwide (1). According to the International Diabetes Federation (IDF), the
31 number of people with diabetes is expected to rise from 425 million in 2017 to 629 million in
32 2045 (2). Diabetes can lead to long-term complications, including coronary heart disease,
33 kidney disease, stroke, eye disease and neurological damage, and increase the overall risk of
34 premature death. It has a considerable health-care cost and significantly impacts quality of life
35 (1,3–5).

36 Type 2 diabetes (T2D) is the most common type of diabetes. Epidemiological studies suggest
37 that a combination of non-modifiable risk factors (such as age, ethnicity and genetics) and
38 modifiable risk factors (including physical inactivity, unhealthy diet, excess body weight and
39 tobacco use) are contributors to the development of T2D (6,7). According to current scientific
40 evidence, eating a healthy diet, having a high level of physical activity and avoiding smoking
41 could prevent up to 80% of type 2 diabetes cases (8,9). Regarding the T2D risk, several
42 epidemiological studies have shown negative associations for healthy diets (characterized by a
43 high consumption of plant-based foods, whole grain products, fish and olive oil) ensuring an
44 adequate intake of various vitamins and minerals, and positive associations for unhealthy diets
45 (characterized by a high consumption of red and processed meats, refined grains, and foods
46 high in sugars, saturated fats or trans fats) (10–12). Mediterranean and vegetarian diets have
47 been shown to be particularly beneficial (13–15).

48 An overall healthy dietary pattern is the core objective for populations in public health
49 nutrition, but because changing overall dietary patterns is an overwhelming task, guidelines
50 have increasingly focused on making healthy choices within the different food groups as a
51 practical method for implementation (16). More specifically, choosing a healthier alternative
52 within a food category may be more readily achievable than substituting foods between
53 different categories. However, to our knowledge, the efficiency of within-category
54 substitutions on reducing the risk of T2D has not been evaluated to date.

55 The aim of this study was therefore to evaluate the potential impact of pizza substitutions on
56 the risk of T2D as compared to substitutions by foods from the different category of mixed
57 dishes, and to identify the characteristics of pizzas related to a stronger reduction in the risk of
58 T2D. We also wanted to examine whether the impact of tailored substitutions, i.e.
59 implementing a substitution based on an individual dietary risk assessment differed from that

60 of generic substitution, i.e. the same substitution for all individuals. The pizza category
61 (generally classified as unhealthy) was selected for the present study because of the
62 considerable nutritional variability in this category and its relatively high consumption (17).

63 **MATERIALS AND METHODS**

64 **Study Population**

65 Our analyses were based on the second Individual and National Food consumption survey
66 (INCA2) conducted in 2006-2007 by the French Agency for Food, Environmental and
67 Occupational Health Safety (agence nationale de sécurité sanitaire de l'alimentation, de
68 l'environnement et du travail, ANSES) to assess dietary intake and associated behaviors in a
69 nationally representative sample of the French population (18,19). The survey included two
70 home visits by trained investigators. The INCA2 survey has been approved by the French
71 National Commission for Computed Data and Individual Freedom (Commission Nationale de
72 l'Informatique et des Libertés, CNIL) (18).

73 In the present study, participants aged 3-17 years (n=1,455) were excluded from the initial
74 INCA2 sample (n = 4,079). Under-reporters defined as participants who reported a daily
75 energy intake of less than 1000 Kcal (n=114) were also excluded. The final sample therefore
76 included 2,510 participants (57.1% women) aged 18-79 years (**Supplemental Figure 1**).

77 **Data collection**

78 Socioeconomic, demographic and physical activity data were collected during face-to-face
79 interviews. Regarding physical activity, the short form of the French version of the
80 International Physical Activity Questionnaire (20) was used to estimate energy expenditure in
81 metabolic equivalents, expressed in MET-min per week. Trained investigators also collected
82 weight and height data and body mass index (BMI) was calculated as the ratio of weight to
83 squared height (kg/m²).

84 **Dietary data**

85 Dietary intake was assessed using 7-day food records (18). During the survey week, the
86 participants were asked to report all foods and beverages consumed at each meal. Portion
87 sizes were estimated using validated photographs (21), household measurements or by
88 specifying the exact amount consumed.

89 In order to obtain a precise estimate of the consumption of each food group identified as
90 having an impact on the risk of T2D (whole grains, refined grains, fruits, green leafy

91 vegetables, other vegetables, nuts, potatoes, dairy products, red meats, fish, eggs, processed
92 meats, butter, olive oil, tea, coffee, chocolate, sugar-sweetened beverages, alcoholic
93 beverages) (12,22–29), each item reported by the participants was broken down into its
94 ingredients (expressed as a quantity). The daily intake of energy and certain nutrients
95 (carbohydrates, dietary fibers and magnesium) associated with the risk of T2D (30–32) were
96 also estimated for each participant using CIQUAL (Centre d’Information sur la Qualité des
97 Aliments) food composition tables. Other nutrients associated with the risk of T2D, such as
98 polyphenols (33) were not considered in our study because the data were not available.

99 ***Pizza composition and classification***

100 We used the database from the “Observatoire de la qualité de l’alimentation” (Oqali), which
101 collects labelling information on foods marketed in France, to estimate the nutrient
102 composition and proportions of ingredients in the 353 pizza recipes (data collected in 2011)
103 sold by medium and large supermarkets and frozen food stores. These 353 pizzas presented
104 considerable diversity in terms of their nutritional quality, which was dependent on numerous
105 criteria, such as the pizza family (cheese, vegetarian, ham-cheese, etc.), ratio of animal/plant
106 ingredients or the quantity of dough.

107 These pizzas were grouped into 100 clusters based on their recipes and nutritional
108 composition using a hierarchical ascending classification (HAC). First, a principal component
109 analysis (PCA) was performed using the quantities of the main ingredients and the nutritional
110 composition of the pizzas as input variables. The HAC using Ward’s step method was then
111 performed for the first 4 factors resulting from the PCA (54% of the total variance explained).
112 In order to keep a good picture of the large variability in the composition of the pizza
113 category, the number of clusters at the end of the HAC was set at 100. For each cluster, the
114 mean recipe and nutritional composition were determined and an “average” pizza
115 (**Supplemental Table 1**) was therefore used for the pizza substitutions.

116 **Statistical analysis**

117 Baseline characteristics are presented separately for pizza consumers (participants who
118 reported pizza consumption at least once during the 7-day food records) and non-consumers
119 using means and standard deviation for continuous variables and percentages for categorical
120 variables. Pizza consumers were compared to non-consumers using chi2 tests or t-tests as
121 appropriate.

122

123 *Estimation of the rate of change in the risk of type 2 diabetes*

124 The rate of change in the risk of T2D was estimated using a model structurally similar to the
125 Preventable Risk Integrated Model (PRIME). PRIME is a scenario model that estimates the
126 impact of lifestyle changes in the population (diet, alcohol / tobacco consumption, BMI and
127 physical activity) on non-communicable disease (NCD) mortality (34,35). Briefly, the PRIME
128 estimates the change in the annual number of NCD deaths between the baseline and
129 counterfactual scenarios that depends on changes in the distribution of one or more behavioral
130 risk factors in the study population. The model is parameterized using meta-analyses of
131 epidemiological studies providing estimates of relative risks (RR) linking diet and lifestyle
132 variables and disease outcomes.

133 Using comparative risk assessment to estimate the rate of changes in T2D risk consists in
134 estimating $(x'-x)/x$, where x is the observed baseline incidence resulting from the initial
135 distribution of risk factors and x' the counterfactual situation resulting from changes in risk
136 factors. Here, we set $x=1$, resulting in a rate of change in risk being equal to $x'-1$, which is
137 thus the relative change (expressed as %) in risk.

138 If referring to the classical framework of the Comparative Risk Assessment on which the
139 PRIME model is based (35), this rate of change in risk for each factor (i.e. nutritional
140 variable) is the final Population Attributable Fraction (PAF) ascribed to this factor. The PAF
141 for the different risk factors 1 to n for the same disease are then combined multiplicatively in
142 the PRIME model (PAF_{tot}).

143
$$PAF = \left[\int RR(q) P(q) dq - \int RR(q) P'(q) dq \right] / \int RR(q) P(q) dq$$

144 and

145
$$PAF_{tot} = 1 - \prod_{i=1}^n (1 - PAF_i)$$

146 where $RR(q)$ is the relative risk of disease for risk factor level q (i.e. the level of intake for the
147 nutritional variable), $P(q)$ is the number of people in the population with risk factor level q in
148 the baseline scenario, and $P'(q)$ is the number of people in the population with risk factor
149 level q in the counterfactual scenario.

150 With this background, the rate of change in risk as estimated in the present study therefore
151 refer to $-PAF_{tot}$.

152 In this study, we estimated the rate of change in the risk of T2D that would result from pizza
153 substitutions (i.e. how much the risk of T2D varies when varying the intake of dietary factors
154 (food groups and nutrients in the diet as affected by the pizza substitution). The model
155 parameterization does not require data regarding the mortality nor the diabetes incidence in
156 the population, and the latter was anyway not reliably available for France. Model
157 parameterization was achieved using recently published RR data on the dose-response
158 associations between diet (food groups and nutrients previously mentioned) and the risk of
159 T2D (12,22–28,30–32) as shown in **Supplemental figure 2**. The macrosimulation model also
160 requires the baseline distributions of the various nutritional variables that are risk factors (sex-
161 specific distributions for each food group and nutrient in the study population before pizza
162 substitution) and the counterfactual distributions (sex-specific distributions for each food
163 group and nutrient after pizza substitution).

164 Monte Carlo simulations (10,000 iterations) were performed to estimate 95% credible
165 intervals around the estimates (2.5th percentile; 97.5th percentile).

166 Given the strong association between BMI (and therefore energy intake) and the risk of T2D,
167 both isoenergetic (IE) and non-isoenergetic (NIE) substitutions were considered. The IE
168 substitution consisted in replacing the observed pizza with the same weight of another pizza,
169 while maintaining energy intake constant, by homogeneously adjusting the weight of all the
170 other solid foods consumed. The NIE substitution only consisted in replacing the observed
171 pizza with the same weight of another pizza without maintaining energy intake.

172 The macrosimulation model algorithm was implemented in R. All other statistical analyses
173 were conducted using SAS (version 9.4; SAS institute Inc., Cary, NC, USA) with a
174 significance level of 0.05 for two-sided tests.

175 *Pizza substitutions*

176 The substitutions were first performed at the individual level in order to identify for each
177 participant the best/worst pizzas. To do this, each individual was artificially over-represented
178 (so that it represents half of the overall population) so as to achieve sufficient precision in the
179 estimate and thereby enabling easy individual ranking of the pizzas. The rates of change in the
180 risk of T2D attributable to the various pizza substitutions were then ranked in ascending order
181 to identify the pizzas leading to the highest relative increase (worst pizzas) or decrease (best
182 pizzas) in the risk of T2D.

183 Second, we made three different types of pizza substitutions in pizza consumers in the overall
184 sample. These substitutions consisted in simultaneously replacing the observed pizza by: 1)
185 each of the five best/worst pizzas specific to the individual (tailored substitution); 2) the
186 pizzas most frequently identified as the best or worst by all consumers (generic substitution)
187 and 3) all the 68 mixed dishes identified in the INCA food database (generic substitution;
188 **Supplemental Table 2**). Generic substitutions were analyzed by considering either the
189 overall sample study (i.e. pizza consumers and non-consumers) or the subsample of pizza
190 consumers (all pizza consumers, as well as consumer sub-groups created according to their
191 observed pizza consumption level), or other subgroups based on age, fruit and vegetable
192 consumption, BMI and the overall diet quality.

193 Diet quality was measured using three dietary scores, namely the Literature-Based Adherence
194 Score to the Mediterranean Diet (MEDI-LITE), the provegetarian food pattern (FP) and the
195 modified version of the French National Nutrition Health Program (Programme National
196 Nutrition Santé Guideline Score, mPNNS-GS). The mPNNS-GS, MEDI-LITE and
197 provegetarian FP had respectively been developed to measure adherence to French nutritional
198 guidelines, adherence to the Mediterranean diet and preferences for plant-derived foods (36–
199 39). The description and scoring systems for these dietary scores are presented in
200 **Supplemental Figure 3**.

201 **RESULTS**

202 The analyses included 1,076 men and 1,434 women aged 46.6 ± 15.5 and 45.2 ± 15.2 years
203 respectively. Among the 880 pizza consumers, 78.2% reported pizza consumption once
204 during the food data collection week and 16% twice. Compared to non-consumers, pizza
205 consumers were more likely to be men, younger people, living alone, smokers, students or
206 people in employment. They were also more likely to have a higher level of education (high
207 school diploma or university level), a normal BMI and a low consumption of fruits and
208 vegetables ($<400\text{g/day}$) (**Table 1**).

209 We used the pizza ranking results specific to each individual to identify the best pizzas to be
210 used for generic substitutions. Only four pizzas resulted in the highest risk reduction in at
211 least one consumer. In IE substitutions, pizza clusters #88, #99, #22 and #100 were identified
212 as the best pizzas for 96.6%, 1.6%, 0.9% and 0.9% of pizza consumers, respectively
213 (**Supplemental Table 1**). These four clusters were characterized by a high proportion of
214 vegetables (including green leafy vegetables for cluster #100) and a whole grain dough

215 (except the cluster #100). Clusters #88 and #100 were also identified as the best pizzas in NIE
216 substitutions for 99.9% and 0.1% of pizza consumers, respectively (**Supplemental Table 1**).
217 Regarding the worst pizzas, the clusters identified (clusters #78 and #84 for both IE
218 substitutions and NIE substitutions) were characterized by a low proportion of vegetables and
219 a high proportion of processed meat (**Supplemental Table 1**).

220 Tailored and generic pizza substitutions in the whole population resulted in rates of change in
221 the risk of T2D in the range of -3.6%; +5.2% (**Figure 1**). Overall, the rates of change were
222 stronger in men and for NIE substitutions. For IE substitutions, replacing each consumer's
223 pizza with one of his/her five best pizzas (tailored substitution) led to a population-wide
224 reduction in the risk of T2D that ranged from -2.6% (-3.3%; -1.9%) to -2.0% (-2.5%; -1.4%)
225 in men, and -1.4% (-1.8%; -1.0%) to -1.1% (-1.4%; -0.7%) in women. Symmetrically,
226 changing for one of the five worst pizzas led to an increased risk of T2D that ranged from
227 2.6% (1.8%; 3.4%) to 1.1% (0.7%; 1.5%) among men and 1.3% (0.9%; 1.7%) to 0.6% (0.4%;
228 0.8%) among women. The beneficial/detrimental estimated impacts of tailored substitutions
229 decreased significantly between the first and third best/worst pizzas and only slightly
230 thereafter.

231 For generic substitutions (using the pizzas most frequently identified as the best/worst), only
232 pizzas identified as such for both IE and NIE substitutions (clusters #88 and #100 for the best
233 pizzas and clusters #78 and #84 for the worst pizzas) were considered. The IE substitution of
234 the observed pizzas for one of these four pizzas resulted in rates of change in the risk of T2D
235 that ranged from -2.6% (-3.3%; -1.9%) to +2.6% (1.8%; 3.4%) in men (**Figure 1**). Overall,
236 the greatest reduction was achieved with cluster #88 for both IE and NIE substitutions. In
237 addition, generic substitutions (**Figure 1**, lower panel) showed similar rates of change in the
238 risk of T2D that were similar to those observed for tailored substitutions (**Figure 1**, upper
239 panel).

240 For both IE and NIE substitutions, the rates of change in the risk of T2D were more
241 pronounced when estimated in the pizza consumers sub-sample, with a rate of change that
242 increased in line with the frequency of pizza consumption (**Table 2**). Regarding the rates of
243 change in the risk of T2D among other population subgroups, the most important changes
244 were generally observed among younger participants (**Supplemental Table 3**).

245 Inter-category substitutions resulted in rates of change in the risk of T2D for the whole
246 population that ranged from -5.4% to +9.5% (**Figure 2**). We identified one best mixed dish
247 (pan bagnat for IE substitutions and spaghetti with tomato sauce for NIE substitutions) and
248 one worst mixed dish (hotdog, for both IE and NIE substitutions). For IE substitutions, no
249 replacement with a mixed dish led to a greater reduction in T2D than that observed when
250 replacing with the best pizza, unlike NIE substitutions where a few mixed dishes allowed
251 greater risk reductions than those observed with the best pizzas. For both IE and NIE
252 substitutions, we found that some mixed dishes had a markedly stronger rates of change in the
253 risk of T2D than the worst pizzas identified in this study. The best / worst mixed dishes were
254 the same in the different population subgroups, except in the case of NIE substitutions where
255 the best mixed dish was spaghetti with tomato sauce for some subgroups and spring rolls for
256 others (**Supplemental Table 4**).

257 **DISCUSSION**

258 To our knowledge, this is the first study to have investigated the potential impact of food
259 substitutions within the same category on the risk of T2D. In this modeling study based on
260 food records collected on a large representative sample of the French population, we found
261 that substitutions within the pizza category showed high rates of change in the risk of T2D
262 when the recipe included several ingredients with a documented impact on T2D.

263 The best pizzas identified in this study contained high levels of plant-based ingredients and
264 had a whole grain dough. Most of them had a low energy density and contain large quantities
265 of fiber and magnesium. Despite the large number of pizzas containing a high proportion of
266 vegetables, only four were identified as the first best for IE substitutions. These findings could
267 be explained by the fact that all vegetables have a low and borderline beneficial impact on the
268 risk of T2D (RR=0.98; 95% CI=0.96-1.00) (12). Overall, the food groups included in PRIME
269 that are considered to have a strong impact on the risk of T2D are: whole grains (RR=0.87;
270 95% CI=0.82-0.93), green leafy vegetables (RR=0.87; 95% CI=0.76-0.99) and olive oil
271 (RR=0.91; 95% CI=0.87-0.95) (12,29). Indeed, whole grains are an important source of
272 phytochemicals and other nutrients such as vitamins B and E, cereal fiber, zinc and
273 magnesium (40–42). The regular consumption of whole grains (particularly high-fiber
274 cereals) has been associated with greater insulin sensitivity and lower fasting insulin levels.
275 Eating plenty of whole grains may also reduce the risk of T2D by lowering levels of
276 inflammatory markers, including C reactive protein and Interleukin-6 (43). As for green leafy
277 vegetables, their beneficial impacts have been attributed to their low carbohydrate content and

278 antioxidant and anti-inflammatory properties (29). Our modeling study could provide final
279 risk estimates regarding the potential impact of modulating these ingredients in the recipe of a
280 food item found to be consumed by the population.

281 For both pizzas and the other dishes, NIE substitutions showed higher rates of change in the
282 risk of T2D than IE substitutions. Indeed, based on data from meta-analyses (12,22–28,30–
283 32), our model was parameterized so that an increase in energy intake resulted in an increased
284 T2D risk, as a function of the BMI and level of physical activity of the subjects. Under this
285 model, a change in energy intake is an important factor for risk estimates, in line with the
286 importance of energy imbalances in being overweight and of being overweight in the T2D
287 risk, as highlighted in the literature (44). However, although energy density and portion size
288 are key drivers of a long-term energy imbalance, mechanisms for adjustment to subsequent
289 energy intake should partly buffer the impact of a difference in energy content between two
290 dishes on long-term energy intake. Therefore, the final impact of a substitution is expected to
291 be somewhere between the impacts of IE and NIE substitutions.

292 More specifically, we found that the rates of change in the risk for IE and NIE pizza
293 substitutions were more pronounced when the substitution resulted in an increase in risk, and
294 very small when it resulted in a decrease. This could be explained by the fact that when pizzas
295 contain a highly adverse pattern of ingredients they are also higher in energy. Conversely,
296 only two of the four best pizzas identified for IE substitutions remained the best when used
297 for NIE substitutions, apparently because their energy content is not particularly high.
298 Differences in energy content could also explain the switch in the order of the two worst
299 pizzas, depending on whether they were used for IE or NIE substitutions.

300 In this study, the rates of change in the risk of T2D attributable to the various pizza
301 substitutions observed in the whole population may appear to be small. In contrast, rates of
302 change in the risk of T2D were higher for NIE substitutions and when estimated in the pizza
303 consumers sub-sample, with a rate of change that increased in line with the frequency of pizza
304 consumption. The small range observed for the rates of change in the risk of T2D could first
305 be explained by the fact that only one food category was replaced, while a diet consists of
306 several meals and therefore several food categories. Secondly, not all participants in this study
307 consumed pizza during the food data collection period. In addition, pizza was consumed in
308 relatively small portions (particularly among women, with an average portion size of 187 g
309 for women compared to 262 g for men) and approximately 78% of pizza consumers ate it

310 only once during the food record week. Intra-category substitutions applied simultaneously to
311 several food categories would lead to much greater reductions in the T2D risk. We had
312 previously reported that extended and repeated intra-category substitutions can drive very
313 marked healthy changes in nutrient intakes in the whole population (45). Here, we once again
314 showed that rates of change in risk for NIE substitutions in the population of men consuming
315 pizzas more than twice per week could reach -18% and $+32\%$.

316 The findings of this study show that tailored substitutions do not have a greater impact than
317 generic substitutions with pizzas that have been identified as the best. This was explained by
318 the fact that the first best pizza (cluster #88) was the same for almost all pizza consumers
319 (96.5%). Cluster #88 differed from the other clusters by its low energy content and high
320 whole grain content. Interestingly, substitutions at the individual level showed that if cluster
321 #88 were set aside, the second best pizza (cluster #100) was the same for a large majority
322 (76%) of pizza consumers. This second best pizza enabled a reduction in the T2D risk close
323 that obtained with cluster #88, with a different recipe, as it included green leafy vegetables but
324 not whole grains. Taken together these results of intra-category substitutions showed that the
325 dietary levers for reducing the T2D risk proved to be the same for the vast majority of the
326 population, which makes tailored advice useless. Although pizzas present a broad diversity of
327 composition, we cannot generalize this finding to all food categories.

328 Quite unexpectedly, we failed to identify a mixed dish that induced a greater reduction in the
329 risk of T2D than the best pizza in IE substitution. This may have been due to the fact that
330 although we considered a broad range of dishes ($n=68$), their recipes included no or only a
331 tiny proportion of ingredients from the food groups with the most favorable expected impacts
332 on the risk of diabetes. The best mixed dish identified for IE substitutions had nutritional
333 characteristics similar to those of the best pizza, i.e. high in fiber and magnesium. Regarding
334 NIE substitutions, the greatest estimated T2D risk reduction achieved with mixed dishes such
335 as spaghetti or spring rolls compared to the best pizza was not due to their higher proportion
336 of healthy ingredient, but to their lower energy density. Overall, these results showed that
337 substitutions within a category can have a considerable impact on the T2D risk since it was
338 comparable to substitutions between categories.

339 In this study, our estimates were not translated into numbers of avoided incident cases of
340 T2D, because we do not have valid direct estimates of diabetes incidence in France in the
341 entire adult population (46). However, based on available data, we may consider that T2D

342 incidence might be in the order of 500 per 100,000 person year in men and 350 per 100.000
343 person in women. If using data from table 2 showing rates of changes in risk of diabetes in
344 men and women for substitution with the best and worst pizzas, and if considering that the
345 effect would lie in between that of iso-energetic substitution and non-isoenergetic
346 substitutions, the substitutions might result in between 6700 and 9400 new cases of diabetes
347 avoided each year in France.

348 This modelling study has some potential limitations that should be mentioned. First,
349 parametrization of our model is limited by the availability of robust meta-analyses estimating
350 RR values for associations between lifestyle indicators and health outcomes. Indeed, most of
351 the available RR have been estimated for the general population, while for some factors, the
352 estimated risks may vary as a function of socio-demographic and health characteristics. In
353 addition, in the absence of reliable information, we considered that the initial risk of T2D was
354 the same for all the population subgroups examined in our study. Further, some nutritional
355 factors such as polyphenols, cholesterol and zinc, among others, could not be included in the
356 model, either because their relation to T2D risk has not been sufficiently characterized or due
357 to lack of detailed data on their contents in different foods. Another limitation of this study is
358 that it cannot be excluded that the relative risks used in the parameterization of the model may
359 vary slightly according to the population groups considered and this may have added some
360 uncertainty on the estimates of risk changes drawn on this population.

361 In this study, some participants had missing data on some variables, but BMI is the only one
362 that is used in the risk assessment model. The missing values that could have an impact on the
363 model are limited to 2 missing BMI values among the 878 pizza consumers for whom non-
364 isoenergetic substitutions were run.

365 Some important strengths of this study include its large sample size (with approximately 35%
366 of pizza consumers), the quality of the dietary data based on 7-day food records that reflected
367 the actual dietary habits of the participants as well as that of anthropometric data because they
368 were taken by trained investigators. Another strength is the availability of a large database
369 including recipes of more than 300 pizzas marketed in France, which was useful to exploring
370 all possibilities in a realistic way.

371 In conclusion, the results of this study suggest that substitutions within the pizza category are
372 associated with modest reduction in T2D risk, with a rate of change that increased in line with
373 the frequency of pizza consumption, justifying the promotion of a healthier swap, as it is

374 increasingly advocated in dietary guidelines. Our results also suggest that substitutions within
375 the same category might be particularly effective inasmuch as in principle they are easier to
376 implement than the total exclusion of a food category and could play a role in achieving a
377 generally better dietary pattern. For these theoretical results to work in practice, the messages
378 would of course need to be accompanied by a radical transformation of the food offer that
379 takes account of sensory acceptability. The results of this article remain theoretical and are
380 based on comparative risk assessment on modelled diets. They would need to be corroborated
381 in long-term interventional studies, assessing the effects of limited and well-defined dietary
382 changes on endpoints related to diabetes risk.

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386 and A.S.-E. supplied the databases essential for the research; G.F. and P.L. provided
387 methodological support; M.A. and P.L. analyzed the data. M.A., F.M., P.L. and J.-F.H.
388 interpreted the results; M.A. wrote the first draft of the manuscript; F.M. and J.-F.H.
389 contributed to writing the manuscript; all authors provided critical comments on the
390 manuscript. All authors read and approved the final manuscript.

391 None of the other authors declare any conflicts of interest.

References

1. World Health Organization. *Global report on diabetes*. WHO: France (2016).
2. International Diabetes Federation. *IDF Diabetes Atlas*, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017. Available at: <http://www.diabetesatlas.org> (Accessed Oct 29, 2019)
3. Zhang P, Zhang X, Brown J, Vistisen D, Sicree R, Shaw J, Nichols G. Global healthcare expenditure on diabetes for 2010 and 2030. *Diabetes Res Clin Pract* (2010) **87**:293–301. doi:10.1016/j.diabres.2010.01.026
4. Chevreur K, Berg Brigham K, Bouché C. The burden and treatment of diabetes in France. *Glob Health* (2014) **10**:6. doi:10.1186/1744-8603-10-6
5. da Rocha Fernandes J, Ogurtsova K, Linnenkamp U, Guariguata L, Seuring T, Zhang P, Cavan D, Makaroff LE. IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. *Diabetes Res Clin Pract* (2016) **117**:48–54. doi:10.1016/j.diabres.2016.04.016
6. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol* (2018) **14**:88–98. doi:10.1038/nrendo.2017.151
7. Sami W, Ansari T, Butt NS, Hamid MRA. Effect of diet on type 2 diabetes mellitus: A review. *Int J Health Sci* (2017) **11**:65–71.
8. World Health Organization. *2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases*. Geneva (2008).
9. Steinbrecher A, Morimoto Y, Heak S, Ollberding NJ, Geller KS, Grandinetti A, Kolonel LN, Maskarinec G. The preventable proportion of type 2 diabetes by ethnicity: the multiethnic cohort. *Ann Epidemiol* (2011) **21**:526–535. doi:10.1016/j.annepidem.2011.03.009
10. Jannasch F, Kröger J, Schulze MB. Dietary Patterns and Type 2 Diabetes: A Systematic Literature Review and Meta-Analysis of Prospective Studies. *J Nutr* (2017) **147**:1174–1182. doi:10.3945/jn.116.242552
11. Qian F, Liu G, Hu FB, Bhupathiraju SN, Sun Q. Association Between Plant-Based Dietary Patterns and Risk of Type 2 Diabetes: A Systematic Review and Meta-analysis. *JAMA Intern Med* (2019) doi:10.1001/jamainternmed.2019.2195
12. Schwingshackl L, Hoffmann G, Lampousi A-M, Knüppel S, Iqbal K, Schwedhelm C, Bechthold A, Schlesinger S, Boeing H. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* (2017) **32**:363–375. doi:10.1007/s10654-017-0246-y
13. Olfert MD, Wattick RA. Vegetarian Diets and the Risk of Diabetes. *Curr Diab Rep* (2018) **18**:101. doi:10.1007/s11892-018-1070-9

14. Schwingshackl L, Missbach B, König J, Hoffmann G. Adherence to a Mediterranean diet and risk of diabetes: a systematic review and meta-analysis. *Public Health Nutr* (2015) **18**:1292–1299. doi:10.1017/S1368980014001542
15. Lee Y, Park K. Adherence to a Vegetarian Diet and Diabetes Risk: A Systematic Review and Meta-Analysis of Observational Studies. *Nutrients* (2017) **9**: doi:10.3390/nu9060603
16. U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015 – 2020 Dietary Guidelines for Americans*. (2015)
17. Rhodes DG, Adler ME, Clemens JC, LaComb RP, Moshfegh AJ. Consumption of Pizza: What We Eat in America, NHANES 2007-2010. Food Surveys Research Group Dietary Data Brief No. 11. (2014)
18. Dubuisson C, Lioret S, Touvier M, Dufour A, Calamassi-Tran G, Volatier J-L, Lafay L. Trends in food and nutritional intakes of French adults from 1999 to 2007: results from the INCA surveys. *Br J Nutr* (2010) **103**:1035–1048. doi:10.1017/S0007114509992625
19. Agence française de sécurité sanitaire des aliments (AFSSA). *Etude Individuelle Nationale des Consommations Alimentaires 2 (INCA2) 2006–2007 [Individual National Study of Food Consumption 2006–2007]*. Maisons-Alfort: AFSSA (2009).
20. Hagstromer M, Oja P, Sjostrom M. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. *Public Health Nutr* (2006) **9**:755–762.
21. Le Moullec N, Deheeger M, Preziosi P, et al. Validation du manuel photos utilisé pour l'enquête alimentaire de l'étude SU.VI.MAX [Validation of the photo manual used for the dietary assessment of the SU.VI.MAX study]. *Cah Nutr Diet* (1996) **31**:158–164.
22. Schwingshackl L, Schwedhelm C, Hoffmann G, Boeing H. Potatoes and risk of chronic disease: a systematic review and dose-response meta-analysis. *Eur J Nutr* (2019) **58**:2243–2251. doi:10.1007/s00394-018-1774-2
23. Pimpin L, Wu JHY, Haskelberg H, Del Gobbo L, Mozaffarian D. Is Butter Back? A Systematic Review and Meta-Analysis of Butter Consumption and Risk of Cardiovascular Disease, Diabetes, and Total Mortality. *PloS One* (2016) **11**:e0158118. doi:10.1371/journal.pone.0158118
24. Huang J, Wang X, Zhang Y. Specific types of alcoholic beverage consumption and risk of type 2 diabetes: A systematic review and meta-analysis. *J Diabetes Investig* (2017) **8**:56–68. doi:10.1111/jdi.12537
25. Carlström M, Larsson SC. Coffee consumption and reduced risk of developing type 2 diabetes: a systematic review with meta-analysis. *Nutr Rev* (2018) **76**:395–417. doi:10.1093/nutrit/nuy014
26. Yang W-S, Wang W-Y, Fan W-Y, Deng Q, Wang X. Tea consumption and risk of type 2 diabetes: a dose-response meta-analysis of cohort studies. *Br J Nutr* (2014) **111**:1329–1339. doi:10.1017/S0007114513003887

27. Yuan S, Li X, Jin Y, Lu J. Chocolate Consumption and Risk of Coronary Heart Disease, Stroke, and Diabetes: A Meta-Analysis of Prospective Studies. *Nutrients* (2017) **9**: doi:10.3390/nu9070688
28. Neuenschwander M, Ballon A, Weber KS, Norat T, Aune D, Schwingshackl L, Schlesinger S. Role of diet in type 2 diabetes incidence: umbrella review of meta-analyses of prospective observational studies. *BMJ* (2019) **366**:l2368. doi:10.1136/bmj.l2368
29. Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open* (2014) **4**:e005497. doi:10.1136/bmjopen-2014-005497
30. InterAct Consortium. Dietary fibre and incidence of type 2 diabetes in eight European countries: the EPIC-InterAct Study and a meta-analysis of prospective studies. *Diabetologia* (2015) **58**:1394–1408. doi:10.1007/s00125-015-3585-9
31. Greenwood DC, Threapleton DE, Evans CEL, Cleghorn CL, Nykjaer C, Woodhead C, Burley VJ. Glycemic index, glycemic load, carbohydrates, and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. *Diabetes Care* (2013) **36**:4166–4171. doi:10.2337/dc13-0325
32. Dong J-Y, Xun P, He K, Qin L-Q. Magnesium intake and risk of type 2 diabetes: meta-analysis of prospective cohort studies. *Diabetes Care* (2011) **34**:2116–2122. doi:10.2337/dc11-0518
33. Rienks J, Barbaresko J, Oluwagbemigun K, Schmid M, Nöthlings U. Polyphenol exposure and risk of type 2 diabetes: dose-response meta-analyses and systematic review of prospective cohort studies. *Am J Clin Nutr* (2018) **108**:49–61. doi:10.1093/ajcn/nqy083
34. Scarborough P, Morgan RD, Webster P, Rayner M. Differences in coronary heart disease, stroke and cancer mortality rates between England, Wales, Scotland and Northern Ireland: the role of diet and nutrition. *BMJ Open* (2011) **1**:e000263. doi:10.1136/bmjopen-2011-000263
35. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated ModEl and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. *Scientifica* (2014) **2014**:748750. doi:10.1155/2014/748750
36. Kesse-Guyot E, Amieva H, Castetbon K, Henegar A, Ferry M, Jeandel C, Hercberg S, Galan P, SU.VI.MAX 2 Research Group. Adherence to nutritional recommendations and subsequent cognitive performance: findings from the prospective Supplementation with Antioxidant Vitamins and Minerals 2 (SU.VI.MAX 2) study. *Am J Clin Nutr* (2011) **93**:200–210. doi:10.3945/ajcn.2010.29761
37. Estaquio C, Kesse-Guyot E, Deschamps V, Bertrais S, Dauchet L, Galan P, Hercberg S, Castetbon K. Adherence to the French Programme National Nutrition Sante Guideline Score is associated with better nutrient intake and nutritional status. *JAmDietAssoc* (2009) **109**:1031–1041.

38. Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. *Public Health Nutr* (2014) **17**:2769–2782.
39. Martínez-González MA, Sánchez-Tainta A, Corella D, Salas-Salvadó J, Ros E, Arós F, Gómez-Gracia E, Fiol M, Lamuela-Raventós RM, Schröder H, et al. A provegetarian food pattern and reduction in total mortality in the Prevención con Dieta Mediterránea (PREDIMED) study. *Am J Clin Nutr* (2014) **100 Suppl 1**:320S–8S. doi:10.3945/ajcn.113.071431
40. Aune D, Norat T, Romundstad P, Vatten LJ. Whole grain and refined grain consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Eur J Epidemiol* (2013) **28**:845–858. doi:10.1007/s10654-013-9852-5
41. Venn BJ, Mann JI. Cereal grains, legumes and diabetes. *Eur J Clin Nutr* (2004) **58**:1443–1461. doi:10.1038/sj.ejcn.1601995
42. Steyn NP, Mann J, Bennett PH, Temple N, Zimmet P, Tuomilehto J, Lindström J, Louheranta A. Diet, nutrition and the prevention of type 2 diabetes. *Public Health Nutr* (2004) **7**:147–165. doi:10.1079/phn2003586
43. Xu Y, Wan Q, Feng J, Du L, Li K, Zhou Y. Whole grain diet reduces systemic inflammation. *Medicine (Baltimore)* (2018) **97**: doi:10.1097/MD.00000000000012995
44. Toplak H, Leitner DR, Harreiter J, Hoppichler F, Wascher TC, Schindler K, Ludvik B. ["Diabesity"-Obesity and type 2 diabetes (Update 2019)]. *Wien Klin Wochenschr* (2019) **131**:71–76. doi:10.1007/s00508-018-1418-9
45. Verger EO, Holmes BA, Huneau JF, Mariotti F. Simple changes within dietary subgroups can rapidly improve the nutrient adequacy of the diet of French adults. *J Nutr* (2014) **144**:929–936. doi:10.3945/jn.113.188284
46. Fuentes S, Mandereau-Bruno L, Regnault N, Bernillon P, Bonaldi C, Cosson E, Fosse-Edorh S. Is the type 2 diabetes epidemic plateauing in France? A nationwide population-based study. *Diabetes Metab* (2020) **46**:472–479. doi:10.1016/j.diabet.2019.12.006

Table 1 Characteristics of the study population, INCA2 study †

Characteristics	Pizza consumers (n=880)		Non pizza consumers (n=1,630)		P ‡
	Men	Women	Men	Women	
n	426	454	650	980	
Age, years	41.2 ± 14.3	39.2 ± 14.3	50.1 ± 15.2	48.0 ± 14.9	<0.0001
Marital status, n (%)					<0.0001
Living alone	103 (24.2)	110 (24.2)	121 (18.6)	147 (15.0)	
Married/Cohabiting	286 (67.1)	275 (60.6)	456 (70.2)	606 (61.8)	
Divorced/Widowed	37 (8.7)	69 (15.2)	73 (11.2)	225 (23.0)	
Missing values	0	0	0	2 (0.2)	
Educational level, n (%)					0.0002
< High school diploma	210 (49.3)	200 (44.0)	356 (54.8)	517 (52.8)	
High school diploma	84 (19.7)	97 (21.4)	86 (13.2)	167 (17.0)	
University level	132 (31.0)	156 (34.4)	207 (31.9)	295 (30.1)	
Missing values	0	1 (0.2)	1 (0.1)	1 (0.1)	
Employment status, n (%)					<0.0001
Employed/Self-employed	304 (71.4)	269 (59.3)	383 (58.9)	535 (54.6)	
Unemployed	33 (7.7)	90 (19.8)	43 (6.6)	205 (20.9)	
Students	38 (8.9)	52 (11.4)	21 (3.2)	29 (3.0)	
Retired/Early-retired	51 (12.0)	43 (9.5)	203 (31.3)	211 (21.5)	
Smoking, n (%)					0.002
Non smokers	133 (31.2)	203 (44.7)	190 (29.2)	487 (49.7)	
Former smokers	132 (31.0)	94 (20.7)	247 (38.0)	220 (22.5)	
Current smokers	158 (37.1)	146 (32.2)	202 (31.1)	247 (25.2)	
Missing values	3 (0.7)	11 (2.4)	11 (1.7)	26 (2.6)	
Body mass index, n (%)					0.0002
Underweight/Normal weight	243 (57.0)	321 (70.7)	290 (44.6)	608 (62.0)	
Overweight	132 (31.0)	88 (19.4)	282 (43.4)	228 (23.3)	
Obesity	51 (12.0)	43 (9.5)	75 (11.5)	127 (13.0)	
Missing values	0	2 (0.4)	3 (0.5)	17 (1.7)	
Number of recording days	6.9 ± 0.4	6.9 ± 0.4	6.9 ± 0.6	6.9 ± 0.5	0.02
Total energy intake, Kcal/days	2347 ± 613	1830 ± 452	2382 ± 677	1834 ± 466	0.27
Energy intake without alcohol, Kcal/d	2213 ± 582	1787 ± 438	2223 ± 640	1784 ± 452	0.15
Carbohydrates, % energy §	44.6 ± 5.8	43.5 ± 5.9	43.5 ± 6.6	42.9 ± 5.9	0.0003
Plant proteins, % energy §	4.9 ± 0.8	4.6 ± 0.8	4.9 ± 1.0	4.6 ± 0.9	0.25
Animal proteins, % energy §	11.7 ± 2.8	11.2 ± 2.9	12.3 ± 3.4	11.8 ± 3.2	<0.0001
Lipids, % energy §	37.6 ± 5.2	38.9 ± 5.5	38.0 ± 6.1	38.6 ± 5.7	0.81
Fruit and vegetables consumption, n (%)					<0.0001
< 400 g/days	337 (79.1)	355 (78.2)	434 (66.8)	638 (65.1)	
≥ 400 g/days	89 (20.9)	99 (21.8)	216 (33.2)	342 (34.9)	
Diet quality scores					
mPNNS-GS	7.9 ± 1.4	8.2 ± 1.4	8.0 ± 1.5	8.4 ± 1.5	0.001
MEDI-LITE	7.2 ± 2.4	7.2 ± 2.4	7.7 ± 2.7	7.7 ± 2.6	<0.0001
Provegetarian FP	35.7 ± 4.8	35.6 ± 4.8	36.1 ± 5.1	35.9 ± 5.0	0.11
Pizza consumption, n (%) ¶					
1	316 (74.2)	372 (82.0)			
2	74 (17.4)	66 (14.5)			
≥ 3	36 (8.4)	16 (3.5)			
Average pizza portion size, g	262.0 ± 153.9	187.3 ± 132.0			

INCA2 second Individual and National Food consumption survey; **MEDI-LITE** Literature-based adherence score to the Mediterranean diet; **mPNNS-GS** modified Programme National Nutrition Santé Guideline Score; **Provegetarian FP** Provegetarian food pattern

† Values are means ± standard deviation or numbers (percentages) as appropriate

‡ P-values are based on the T-test or chi-square test, and refer to the comparison between consumers and non-consumers of pizza

§ Values are percentages of total daily energy intake without alcohol

|| 12 missing data among pizza consumers and 35 among non-pizza consumers

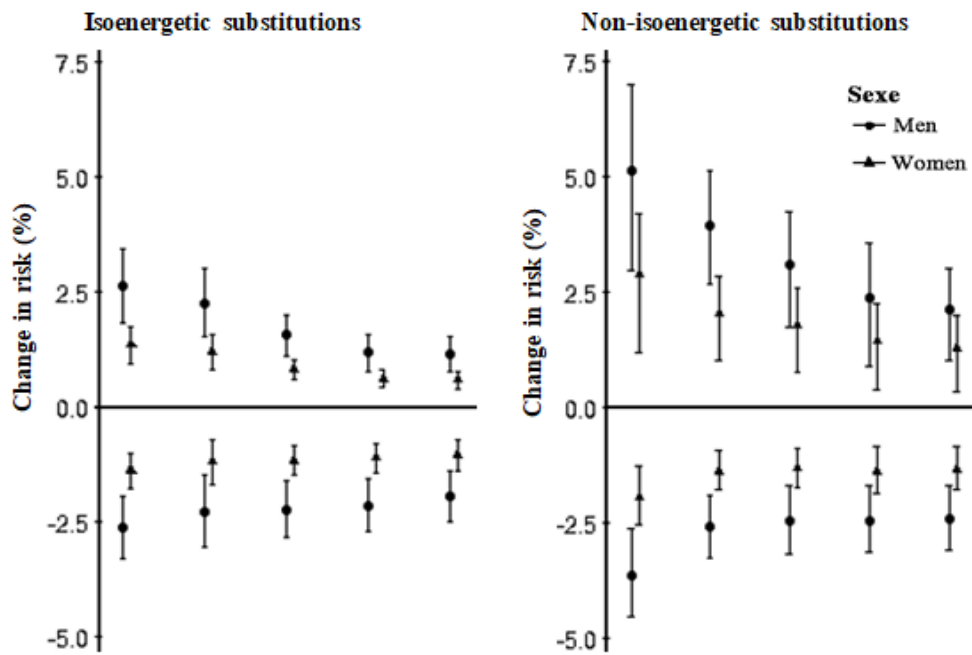
¶ Number of times during the food data collection period

Table 2 Rates of change in risk of type 2 diabetes (percentage) for substitutions with the best and worst pizzas †

Population	Isoenergetic substitution		Non-Isoenergetic substitution	
	Men	Women	Men	Women
1st Best pizza (#88)				
Whole population	-2.6 (-3.3; -1.9)	-1.4 (-1.7; -1.0)	-3.6 (-4.5; -2.6)	-2.0 (-2.5; -1.3)
Pizza consumers	-6.7 (-8.4; -4.9)	-4.5 (-5.6; -3.3)	-8.9 (-11.2; -6.3)	-6.0 (-7.9; -3.9)
Participants who consumed pizza once	-5.1 (-6.4; -3.8)	-3.9 (-4.9; -2.8)	-6.8 (-8.6; -4.91)	-5.3 (-6.8; -3.5)
Participants who consumed pizza twice	-9.9 (-12.4; -7.3)	-6.4 (-8.0; -4.7)	-12.7 (-16.1; -8.9)	-7.8 (-10.7; -4.6)
Participants who consumed pizza more than twice	-13.9 (-17.2; -10.4)	-10.3 (-12.8; -7.6)	-18.3 (-23.2; -12.6)	-14.6 (-18.5; -9.7)
2nd Best pizza (#100)				
Whole population	-2.3 (-3.4; -1.1)	-1.2 (-1.8; -0.6)	-2.3 (-3.4; -1.1)	-1.2 (-1.8; -0.6)
Pizza consumers	-5.7 (-8.5; -2.8)	-3.8 (-5.6; -1.9)	-5.7 (-8.5; -2.8)	-3.7 (-5.6; -1.8)
Participants who consumed pizza once	-4.4 (-6.5; -2.2)	-3.3 (-4.9; -1.6)	-4.4 (-6.5; -2.1)	-3.2 (-4.8; -1.5)
Participants who consumed pizza twice	-8.4 (-12.3; -4.2)	-5.5 (-8.1; -2.8)	-8.4 (-12.3; -4.2)	-5.4 (-8.1; -2.7)
Participants who consumed pizza more than twice	-11.9 (-17.4; -5.8)	-8.7 (-12.9; -4.2)	-12.3 (-17.8; -6.2)	-8.9 (-13.1; -4.5)
1st Worst pizza (#78)				
Whole population	2.6 (1.8; 3.4)	1.3 (0.9; 1.7)	3.9 (2.7; 5.0)	2.1 (1.2; 2.8)
Pizza consumers	6.6 (4.5; 8.6)	4.2 (2.9; 5.4)	9.7 (6.5; 12.8)	6.5 (3.7; 8.9)
Participants who consumed pizza once	4.8 (3.3; 6.2)	3.5 (2.5; 4.6)	7.2 (4.8; 9.4)	5.6 (3.3; 7.6)
Participants who consumed pizza twice	9.8 (6.8; 12.8)	6.0 (4.2; 7.8)	14.4 (9.5; 19.2)	8.3 (4.0; 12.4)
Participants who consumed pizza more than twice	16.0 (10.7; 21.4)	10.8 (7.5; 14.2)	23.0 (15.0; 30.9)	17.2 (10.7; 23.0)
2nd Worst pizza (#84)				
Whole population	2.3 (1.5; 3.0)	1.2 (0.8; 1.6)	5.2 (2.9; 7.0)	2.8 (1.2; 4.2)
Pizza consumers	5.6 (3.8; 7.5)	3.7 (2.6; 4.9)	13.1 (7.1; 18.3)	9.0 (3.5; 13.5)
Participants who consumed pizza once	4.1 (2.8; 5.4)	3.2 (2.2; 4.1)	9.6 (5.2; 13.4)	7.8 (3.2; 11.6)
Participants who consumed pizza twice	8.4 (5.5; 11.2)	5.3 (3.6; 6.9)	19.6 (10.8; 27.8)	10.7 (2.1; 18.7)
Participants who consumed pizza more than twice	14.0 (9.1; 19.0)	9.7 (6.6; 12.9)	32.4 (17.9; 46.1)	25.7 (12.3; 36.9)

† Substituted pizzas are those identified as the first best/worst at individual level substitutions. “Pizza” here stands for a cluster of pizzas ($n=100$, out of 353 pizzas).

Tailored substitutions



Generic substitutions

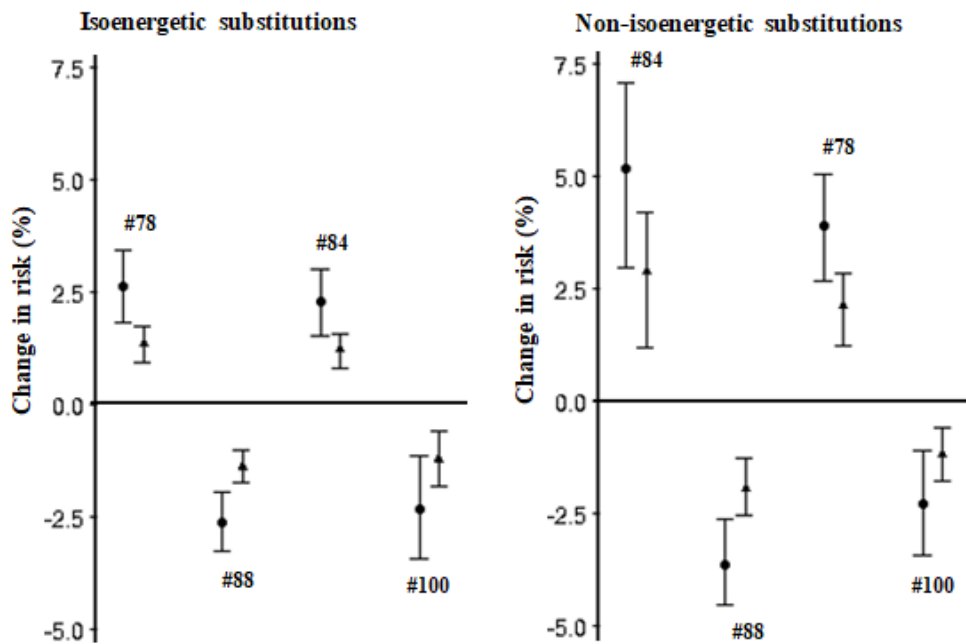


Figure 1. Rates of change in risk of type 2 diabetes in the overall sample population when simulating substitutions with the five best and five worst pizzas (out of 100) specific to each of 2,510 individuals (“tailored substitution”). Upper panels: according to isoenergetic substitutions (upper left) or non-isoenergetic substitutions (upper right); and substitutions with the four pizzas most frequently identified as the best/worst (“generic substitution”), according to isoenergetic substitutions (lower left) or non-isoenergetic substitutions (lower right). The numbers below the estimates are the ID of the pizza. “Pizza” here stands for a cluster of pizzas ($n=100$, out of 353 pizzas).

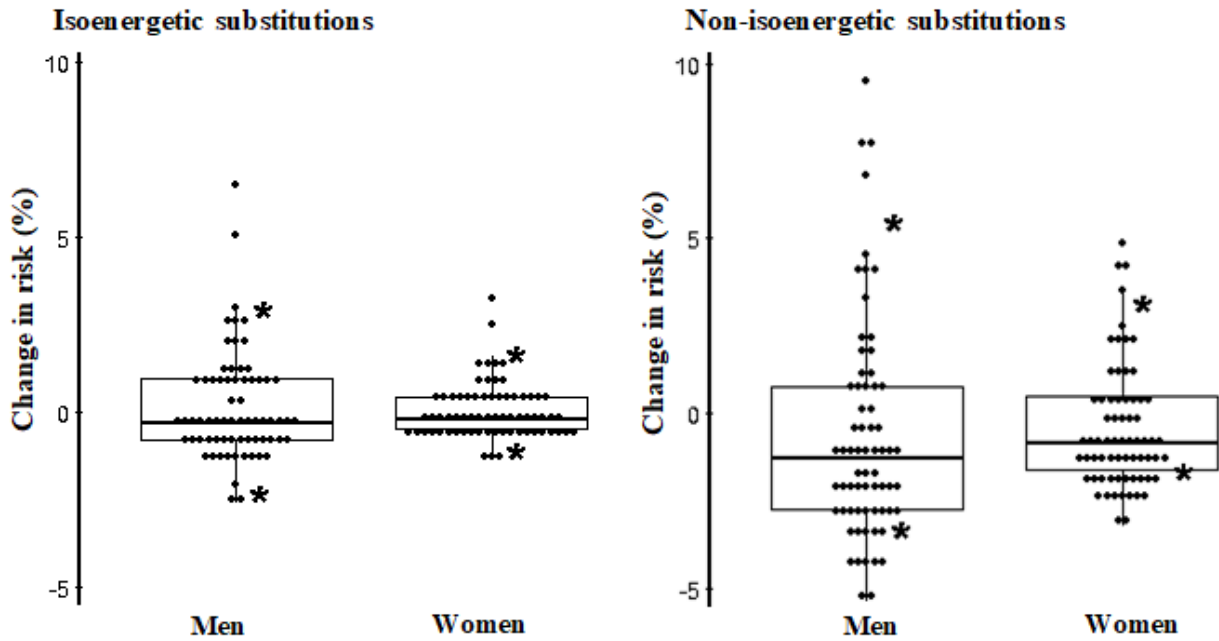
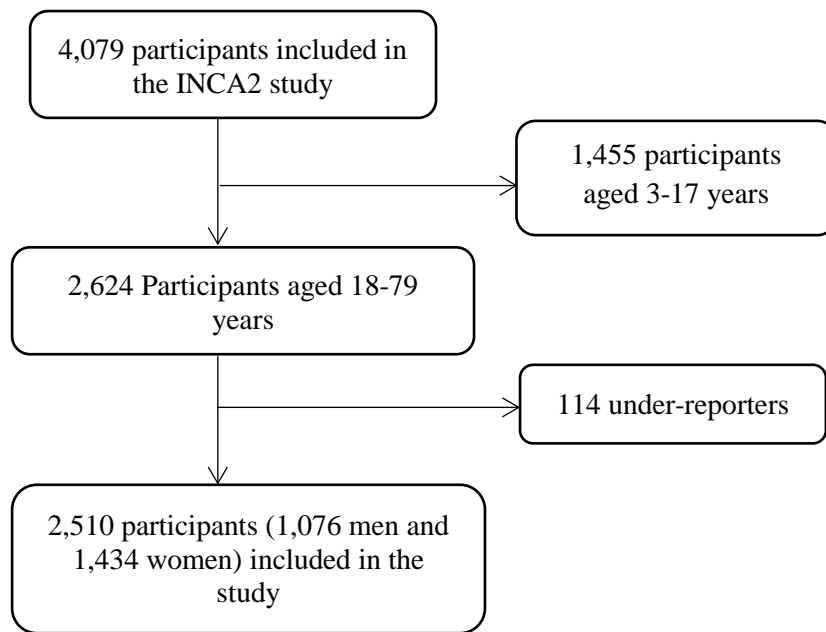
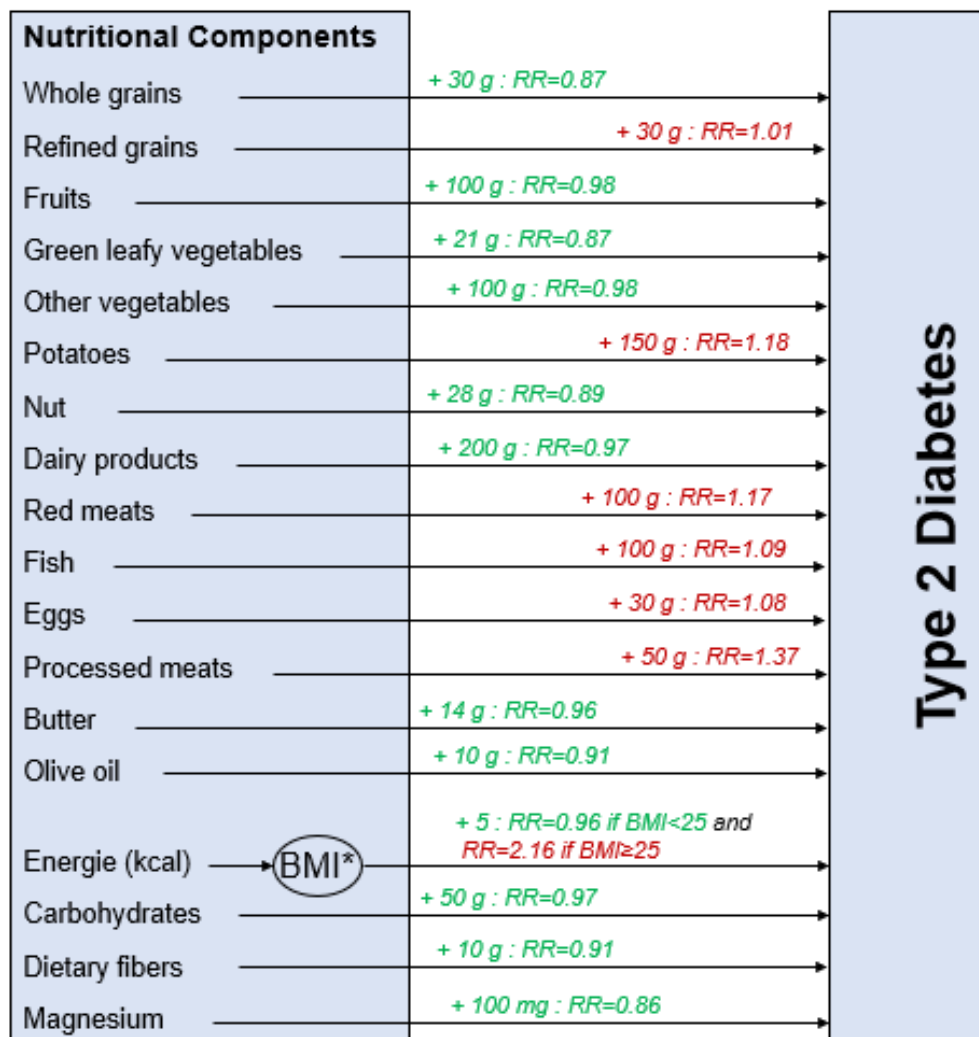


Figure 2. Rates of change in risk of type 2 diabetes in the overall sample when simulating substitutions in each pizza consumer with the mixed dishes ($n=68$). * **reports** the estimates found for generic substitutions with the best and worst pizzas (see Figure 1), for the comparison purposes. “Pizza” here stands for a cluster of pizzas ($n=100$, out of 353 pizzas).



Supplemental Figure 1 Flow chart of participant selection



Supplemental Figure 2 Structure and parameters of the macrosimulation model

*The change in BMI was calculated as indicated by Scarborough et al., but at constant physical activity.

References

Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated Model and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. *Scientifica* (2014) **2014**:748750. doi:10.1155/2014/748750

Schwingshackl L, Hoffmann G, Lampousi A-M, Knüppel S, Iqbal K, Schwedhelm C, Bechthold A, Schlesinger S, Boeing H. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* (2017) **32**:363–375. doi:10.1007/s10654-017-0246-y

Schwingshackl L, Schwedhelm C, Hoffmann G, Boeing H. Potatoes and risk of chronic disease: a systematic review and dose-response meta-analysis. *Eur J Nutr* (2019) **58**:2243–2251. doi:10.1007/s00394-018-1774-2

Pimpin L, Wu JHY, Haskelberg H, Del Gobbo L, Mozaffarian D. Is Butter Back? A Systematic Review and Meta-Analysis of Butter Consumption and Risk of Cardiovascular Disease, Diabetes, and Total Mortality. *PloS One* (2016) **11**:e0158118. doi:10.1371/journal.pone.0158118

Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open* (2014) **4**:e005497. doi:10.1136/bmjopen-2014-005497

InterAct Consortium. Dietary fibre and incidence of type 2 diabetes in eight European countries: the EPIC-InterAct Study and a meta-analysis of prospective studies. *Diabetologia* (2015) **58**:1394–1408. doi:10.1007/s00125-015-3585-9

Greenwood DC, Threapleton DE, Evans CEL, Cleghorn CL, Nykjaer C, Woodhead C, Burley VJ. Glycemic index, glycemic load, carbohydrates, and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. *Diabetes Care* (2013) **36**:4166–4171. doi:10.2337/dc13-0325

Dong J-Y, Xun P, He K, Qin L-Q. Magnesium intake and risk of type 2 diabetes: meta-analysis of prospective cohort studies. *Diabetes Care* (2011) **34**:2116–2122. doi:10.2337/dc11-0518

mPNNS-GS (Kesse-Guyot et al., 2011a ; Estaquio C. et al, 2009) †

Food intake recommendations	Moderation in consumption	Penalty
Fruit and vegetables without potatoes (0-2), starchy foods (0-1), whole grain products (0-1), milk and dairy products (0-1), meat, poultry, fish, eggs, and seafood (0-1), seafood (0-1), vegetable fat (0-1), water vs soda (0-1)	Sweetened foods (-0.5-1), salt (-0.5-1.5), added fats (0-2), alcohol (0-1)	Deduction of points if energy intake exceeded energy needs by 5%
The mPNNS-GS score is the sum of components minus penalty (range: 0-13.5 points)		

MEDI-LITE (Sofi F. et al, 2013) ‡

Desirable components (0-2 points for each component)	Undesirable components (0-2 points for each component)
Fruit, vegetables without potatoes, grains, legumes, fish, olive oil, moderate alcohol consumption	Meat/meat products, dairy products
The MEDI-LITE score is the sum of components (range: 0-18 points)	

Provegetarian food pattern (Martínez-González. et al, 2014) §

Vegetable food groups (1-5 points for each food group)	Animal food groups (1-5 points for each food group)
Fruit, vegetables, legumes, cereals, potatoes, nuts, olive oil	Meats/meat products, eggs, animal fats for cooking or as a spread, Fish and other seafood, dairy products
The Provegetarian FP is the sum of the sex-specific quintile values of the 12 food groups (range: 12-60 points)	

MEDI-LITE Literature-Based Adherence Score to the Mediterranean Diet; mPNNS-GS modified Programme National Nutrition Santé Guideline Score.

† Values were assigned by using fixed portion numbers for each food group, with a maximum of points attributed for high consumption of “desirable” components

‡ Values were assigned to food groups by using fixed cut-off points (portion sizes multiplied by the number of servings per day/week) determined from an extensive published review of the literature. A maximum of points is attributed for high consumption of “desirable” components and the scoring was reversed for the “undesirable” components.

§ Consumption (g/d) of each food group was energy-adjusted using the residual method and divided into sex-specific quintiles. A value between 1 and 5 was assigned to each quintile, with a maximum of points attributed for high consumption of “vegetable food groups”. The scoring was reversed for the “animal food groups”.

Supplemental Figure 3 Computation of diet quality scores

Supplemental table 1 Nutritional characteristics of the 100 pizza clusters

Cluster	Number of pizzas	Average composition per 100g										Isoenergetic substitution †		Non-Isoenergetic substitution ‡	
		Energy (Kcal)	Whole grains (g)	Refined grains (g)	Dairy products (g)	Green leafy vegetables (g)	Other vegetables (g)	Fish (g)	Red meat (g)	Processed meat (g)	Olive oil (g)	1 st best or worst (n)	2 nd best or worst (n)	1 st best or worst (n)	2 nd best or worst (n)
#1	4	200.6 ± 6.5	0	28.5 ± 0.3	12.7 ± 4.1	0	4.6 ± 1.9	0	0	11.6 ± 1.5	0				
#2	6	200.5 ± 7.7	0	30.0 ± 0.7	10.7 ± 3.5	0	19.5 ± 3.0	0	0	12.8 ± 0.7	0				
#3	14	241.9 ± 11.6	0	29.8 ± 1.1	24.7 ± 2.2	0	23.0 ± 2.2	0	0	0	0				
#4	8	229.9 ± 12.0	0	28.1 ± 0.6	13.5 ± 2.5	0	24.2 ± 2.3	0	0	13.2 ± 0.5	0				
#5	4	186.8 ± 2.9	0	27.8 ± 0.6	8.5 ± 0.7	0	32.1 ± 2.5	0	0	8.9 ± 0.2	0				
#6	7	243.4 ± 9.7	0	27.1 ± 0.9	19.7 ± 2.3	0	22.7 ± 2.0	0	0	9.8 ± 0.8	0				
#7	7	208.6 ± 6.3	0	27.6 ± 1.3	18.8 ± 1.9	0	33.1 ± 2.5	0	0	0	0				
#8	2	219.3 ± 1.0	0	36.7 ± 0.0	4.5 ± 0.0	0	17.4 ± 0.0	0	0	14.8 ± 0.0	0				
#9	9	213.9 ± 10.6	0	23.1 ± 0.8	16.2 ± 1.4	0	29.4 ± 3.0	0	0	12.3 ± 1.6	0				
#10	12	202.3 ± 7.4	0	24.3 ± 1.3	16.0 ± 1.8	0	21.5 ± 1.4	0	0	18.1 ± 2.3	0		2 ^w		
#11	5	258.0 ± 13.4	0	25.0 ± 0.9	18.4 ± 0.9	0	19.5 ± 2.2	0	0	16.5 ± 1.0	0				
#12	13	198.8 ± 7.7	0	25.2 ± 1.0	12.1 ± 1.3	0	31.3 ± 2.2	0	0	11.2 ± 0.8	0				
#13	8	236.4 ± 12.1	0	22.4 ± 0.6	36.4 ± 2.7	0	23.0 ± 4.8	0	0	0	0				
#14	13	257.6 ± 10.8	0	25.7 ± 0.8	31.6 ± 2.0	0	23.6 ± 3.0	0	0	0	0				
#15	6	209.7 ± 5.0	0	25.8 ± 0.9	11.0 ± 4.1	0	31.1 ± 2.7	0	0	6.9 ± 1.1	0				
#16	6	230.5 ± 8.3	0	32.2 ± 2.6	10.6 ± 2.9	0	22.1 ± 3.1	0	0	9.5 ± 0.9	0				
#17	10	193.3 ± 5.5	0	27.0 ± 0.7	16.8 ± 2.1	0	26.3 ± 1.5	0	0	9.2 ± 1.9	0				
#18	4	186.5 ± 5.4	0	25.4 ± 0.8	4.0 ± 3.3	0	40.9 ± 2.5	0	0	2.2 ± 4.5	0				
#19	12	224.4 ± 6.4	0	27.7 ± 1.2	28.6 ± 3.2	0.04 ± 0.1	20.4 ± 3.2	0	0	0.6 ± 2.0	0				
#20	6	269.2 ± 8.0	0	25.5 ± 1.3	12.2 ± 4.4	0	26.9 ± 2.4	0	0	14.1 ± 1.0	0				
#21	4	227.3 ± 8.4	0	30.8 ± 1.2	15.2 ± 1.0	0	24.6 ± 1.7	0	0	8.2 ± 1.6	0				
#22	3	259.3 ± 3.1	12.5 ± 0.2	12.5 ± 0.2	36.6 ± 1.6	0	19.6 ± 1.1	0	0	0	0	8 ^b	146 ^b		
#23	2	195.0 ± 5.7	0	32.9 ± 0.2	0	0	33.7 ± 0.3	0	0	0	0				

† Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for isoenergetic substitutions

‡ Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for non-isoenergetic substitutions

Cluster	Number of pizzas	Average composition per 100g										Isoenergetic substitution †		Non-Isoenergetic substitution ‡	
		Energy (Kcal)	Whole grains (g)	Refined grains (g)	Dairy products (g)	Green leafy vegetables (g)	Other vegetables (g)	Fish (g)	Red meat (g)	Processed meat (g)	Olive oil (g)	1 st best or worst (n)	2 nd best or worst (n)	1 st best or worst (n)	2 nd best or worst (n)
#24	4	258.5 ± 5.3	0	30.0 ± 0.4	31.4 ± 1.4	0	16.9 ± 1.7	0	0	0	0				
#25	7	248.7 ± 8.5	0	25.1 ± 0.3	23.5 ± 4.5	0	21.7 ± 2.7	0	0	4.1 ± 2.0	0				
#26	4	216.1 ± 5.5	0	32.3 ± 0.8	16.6 ± 0.5	0	12.4 ± 4.7	0	0	16.6 ± 3.6	0				
#27	4	239.0 ± 6.6	0	22.5 ± 0.5	28.4 ± 2.1	0	18.0 ± 6.3	0	0	8.2 ± 1.2	0				
#28	5	237.0 ± 4.1	0	22.5 ± 1.0	19.2 ± 2.8	0	22.1 ± 2.2	0	0	17.4 ± 1.4	0				
#29	2	262.0 ± 0.0	0	23.3 ± 1.1	14.0 ± 0.0	0	30.9 ± 0.2	8.9 ± 0.1	0	0	0				
#30	2	238.5 ± 3.5	0	27.0 ± 0.8	27.1 ± 1.2	0	0	0	0	0	0				
#31	4	169.0 ± 1.4	0	24.3 ± 1.8	8.7 ± 3.3	0	34.8 ± 2.7	0	0	14.7 ± 2.2	0				
#32	5	230.0 ± 15.5	0	31.6 ± 3.2	11.8 ± 1.9	0	26.8 ± 2.9	0	0	0	0				
#33	4	191.7 ± 8.0	0	25.2 ± 1.1	8.7 ± 2.2	0	36.1 ± 2.1	0	9.7 ± 0.4	0	0				
#34	2	199.2 ± 7.3	0	33.0 ± 0.0	17.2 ± 0.2	0	26.1 ± 1.9	0	0	0	0				
#35	6	220.3 ± 14.7	0	26.1 ± 0.8	19.4 ± 3.6	0	22.1 ± 1.8	0	0	0	0				
#36	5	268.6 ± 9.7	0	27.2 ± 1.7	27.5 ± 1.5	0	12.4 ± 2.3	0	0	12.8 ± 1.4	0				
#37	4	209.3 ± 7.0	0	29.5 ± 0.6	9.7 ± 2.6	0	29.6 ± 3.3	0	0	7.9 ± 1.5	0				
#38	3	272.0 ± 7.2	0	23.3 ± 2.0	39.2 ± 1.8	0	18.1 ± 2.9	0	0	0	0				
#39	4	196.5 ± 5.1	0	23.6 ± 0.7	11.5 ± 4.0	0	38.2 ± 3.3	0	0	0	0				
#40	3	225.5 ± 12.6	0	27.0 ± 0.0	17.8 ± 2.7	0	20.9 ± 3.3	12.1 ± 1.0	0	0	0				
#41	3	224.0 ± 4.6	0	29.0 ± 0.9	34.8 ± 2.4	0	11.2 ± 2.8	0	0	0	0				
#42	3	226.7 ± 5.8	0	24.6 ± 1.6	9.1 ± 2.9	0	28.4 ± 2.8	0	0	17.7 ± 0.8	0				
#43	4	200.4 ± 14.7	0	26.6 ± 1.0	4.4 ± 3.3	0	26.5 ± 4.2	0	0	14.2 ± 3.2	0				
#44	3	248.0 ± 10.5	0	31.3 ± 0.4	19.3 ± 2.8	0	14.8 ± 2.0	0	0	12.7 ± 2.2	0				
#45	4	204.3 ± 3.4	0	28.6 ± 0.9	9.2 ± 3.6	0	22.0 ± 3.7	0	0	0	0				
#46	4	213.3 ± 5.4	0	26.1 ± 2.4	9.7 ± 0.9	0	32.5 ± 2.2	0	8.0 ± 0.7	0	0				
#47	3	226.7 ± 7.1	0	27.8 ± 1.6	26.6 ± 2.8	0	0	0	0	0	0				
#48	3	201.9 ± 9.1	0	31.0 ± 3.5	9.2 ± 3.0	0	22.8 ± 4.5	0	0	9.8 ± 0.3	0				
#49	4	205.8 ± 14.8	0	28.4 ± 0.9	12.4 ± 0.9	0	2.7 ± 3.1	0	0	11.0 ± 1.1	0				

† Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for isoenergetic substitutions

‡ Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for non-isoenergetic substitutions

Cluster	Number of pizzas	Average composition per 100g										Isoenergetic substitution †		Non-Isoenergetic substitution ‡	
		Energy (Kcal)	Whole grains (g)	Refined grains (g)	Dairy products (g)	Green leafy vegetables (g)	Other vegetables (g)	Fish (g)	Red meat (g)	Processed meat (g)	Olive oil (g)	1 st best or worst (n)	2 nd best or worst (n)	1 st best or worst (n)	2 nd best or worst (n)
#50	2	210.5 ± 4.9	0	24.6 ± 1.7	8.2 ± 1.7	0	37.0 ± 0.5	12.4 ± 0.6	0	0	0				
#51	3	284.3 ± 15.8	0	29.0 ± 1.4	37.7 ± 4.7	0	11.9 ± 1.1	0	0	0	0				
#52	3	200.0 ± 11.5	13.1 ± 0.9	13.1 ± 0.9	11.2 ± 1.9	0	26.6 ± 4.5	0	0	15.4 ± 3.5	0				
#53	3	181.3 ± 11.0	0	26.9 ± 1.2	18.9 ± 4.7	0	19.2 ± 0.7	0	0	11.5 ± 2.8	0				
#54	2	202.5 ± 16.3	0	27.3 ± 0.5	15.4 ± 0.1	3.4 ± 0.1	19.7 ± 0.6	0	0	14.2 ± 0.1	0				
#55	6	226.7 ± 11.0	0	25.3 ± 1.2	21.4 ± 2.1	0.2 ± 0.3	15.7 ± 2.8	0	0	14.1 ± 3.4	0				
#56	2	210 ± 0.0	0	27.8 ± 2.2	19.0 ± 0.0	0	16.3 ± 3.2	17.0 ± 0.0	0	0	0				
#57	5	215.2 ± 19.1	0	31.2 ± 2.9	12.8 ± 1.2	0	10.4 ± 5.0	0	0	1.3 ± 1.8	0				
#58	3	229.0 ± 21.2	11.1 ± 0.8	11.1 ± 0.8	13.8 ± 2.6	0	36.8 ± 0.8	0	0	9.1 ± 0.5	0				
#59	3	226.0 ± 13.5	0	25.6 ± 0.3	12.8 ± 6.1	0	38.9 ± 5.3	0	0	0	0				
#60	2	193.0 ± 9.9	0	32.1 ± 0.4	7.4 ± 0.6	0	15.0 ± 2.1	8.3 ± 1.9	0	0	0				
#61	2	184.6 ± 6.5	0	29.1 ± 1.3	9.3 ± 0.3	0	34.3 ± 6.6	0	0	0	0				
#62	4	231.0 ± 12.4	13.9 ± 1.1	13.9 ± 1.1	13.5 ± 1.9	0	24.9 ± 3.0	0	0	12.6 ± 4.1	0				
#63	2	266.1 ± 2.6	0	31.8 ± 5.1	25.7 ± 3.3	0	5.0 ± 7.0	0	0	0	0				
#64	2	259.8 ± 9.5	0	31.2 ± 2.5	10.0 ± 4.4	0	20.8 ± 2.4	0	0	8.6 ± 1.1	0				
#65	2	244.0 ± 0.0	0	37.7 ± 3.3	19.5 ± 2.1	0	15.8 ± 3.2	0	0	0	0				
#66	2	260.5 ± 9.2	0	28.3 ± 0.6	24.7 ± 4.5	0	11.4 ± 0.2	0	11.8 ± 0.8	3.5 ± 4.9	0				
#67	2	245.5 ± 12.0	0	29.1 ± 0.4	24.6 ± 1.2	0	21.4 ± 1.3	0	0	1.5 ± 2.2	1.9 ± 0.2				
#68	2	214.0 ± 2.8	0	28.2 ± 1.7	17.8 ± 0.4	0	12.4 ± 0.4	0	14.5 ± 1.7	0	0				
#69	2	202.0 ± 8.5	0	25.9 ± 3.3	10.4 ± 0.4	0	13.8 ± 10.5	0	10.6 ± 0.0	1.3 ± 1.9	0				
#70	2	235.5 ± 0.7	0	30.3 ± 0.4	18.6 ± 2.0	0	25.4 ± 5.2	0	0	4.9 ± 6.9	0.4 ± 0.1				
#71	2	241.0 ± 15.6	13.8 ± 0.4	13.8 ± 0.4	27.0 ± 2.3	0	19.6 ± 3.3	0	0	5.2 ± 7.4	0				
#72	2	221.0 ± 18.4	7.8 ± 0.4	7.8 ± 0.4	22.5 ± 10.1	0	35.8 ± 1.4	0	0	0	0				
#73	2	227.5 ± 3.5	10.4 ± 0.2	10.4 ± 0.2	21.9 ± 6.7	0	26.1 ± 3.3	0	0	12.0 ± 7.3	0				
#74	1	217.0	0	30.0	4.0	0	21.5	15.5	0	0	0				

Cluster	Number of pizzas	Average composition per 100g										Isoenergetic substitution †		Non-Isoenergetic substitution ‡	
		Energy (Kcal)	Whole grains (g)	Refined grains (g)	Dairy products (g)	Green leafy vegetables (g)	Other vegetables (g)	Fish (g)	Red meat (g)	Processed meat (g)	Olive oil (g)	1 st best or worst (n)	2 nd best or worst (n)	1 st best or worst (n)	2 nd best or worst (n)
#75	1	221.0	0	24.6	10.9	0	31.3	16.8	0	0	0				
#76	1	201.0	9.0	9.0	14.0	0	37.1	0	0	11.9	0				
#77	1	196.0	0	27.6	25.1	0	11.6	11.3	0	0	0				
#78	1	269.0	0	25.1	32.3	0	0.7	0	0	25.1	0	820 ^w	60 ^w	19 ^w	789 ^w
#79	1	280.0	0	27.0	16.0	0	0	0	0	18.7	0				
#80	1	220.0	0	22.2	13.9	0	12.0	0	0	0	0				
#81	1	231.0	0	30.0	6.5	0	35.5	0	0	7.5	0.5				
#82	1	178.0	0	25.4	13.8	0	25.1	9.2	0	0	0				5 ^b
#83	1	210.0	0	25.8	9.1	0	17.7	4.6	0	0	0				
#84	1	320.0	0	19.8	29.0	0	12.2	0	0	24.5	0	60 ^w	818 ^w	861 ^w	19 ^w
#85	1	290.0	0	21.6	27.6	0	20.4	0	0	12.2	0				
#86	1	220.0	0	28.2	23.3	0	28.6	0	0	0	1.1				
#87	1	251.0	0	27.0	33.3	0	18.7	0	0	0	1.3				
#88	1	190.0	14.1	14.1	11.7	0	27.6	0	0	0	0	850 ^b	9 ^b	879 ^b	1 ^b
#89	1	210.0	12.3	12.3	14.2	0	7.1	0	0	0	0		44 ^b		253 ^b
#90	1	210.0	0	28.8	3.2	0	25.5	0	15.5	0	0				
#91	1	252.0	8.4	8.4	40.0	0	28.8	0	0	0	0				
#92	1	211.0	0	25.8	13.1	0	33.2	0	0	6.8	1.7				
#93	1	255.0	0	31.7	17.0	0	22.3	0	6.7	0	0				
#94	1	293.0	12.6	12.6	21.2	0	3.5	0	0	10.7	0				
#95	1	191.0	0	28.2	4.9	2.4	37.1	0	0	0	0				390 ^b
#96	1	235.0	0	27.0	35.2	3.3	6.6	0	0	0	0				
#97	1	250.0	0	29.4	36.2	0	0	10.7	0	0	0				
#98	1	203.0	0	23.4	10.4	5.2	45.4	0	0	0	0				21 ^b
#99	1	354.0	12.3	12.3	15.9	0	25.7	0	11.5	0	0	14 ^b	5 ^b		72 ^w
#100	1	227.0	0	31.2	15.0	9.0	24.0	0	0	0	0	8 ^b	676 ^b	1 ^b	210 ^b

† Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for isoenergetic substitutions

‡ Number of participants for whom the cluster was identified as the first or second best (b) / worst (w) pizza for non-isoenergetic substitutions

Supplemental table 2 Nutritional characteristics of mixed dishes used for inter-categories substitutions

Mixed dish name	Proportion per 100 g												
	Energy (Kcal)	Refined grains (g)	Green leafy vegetables (g)	Other vegetables (g)	Fruit (g)	Dairy products (g)	Fish (g)	Eggs (g)	Red meat (g)	Processed meat (g)	Potatoes (g)	Butter (g)	Olive oil (g)
Canned cassoulet	136	1	0	5	0	0	0	0	6	20	0	0	0
Canned sauerkraut	110	0	0	27.5	0	0	0	0	7.5	14	10	0	0
Shepherd's pie	145	2.3	0	19	0	26	0	0	13	0	8	7.5	0
Sausages with lentils	131	0.5	0	4	0	0	0	0	13	13	0	0	0
Pot-au-feu	72.3	0	0	36.3	0	0	0	0	52.5	0	10.6	0	0
Meat ravioli with tomato sauce (canned product)	97.4	54.5	0	26.7	0	0	0	0	10	0	0	0	0.3
Garnished mutton couscous	148	30.5	0	26.5	0	0	0	0	30	0	0	0	1.5
Paella	169	50.5	0	14	0	0	6	0	0	3	0	0	0
Potato gratin	110	0	0	0	0	26.9	0	7.5	0	0	62	3.1	0
Milanese "osso bucco"	102	3.1	0	23.2	0	0	0	0	37	0	0	0	2.8
Hotpot from Auvergne (pork, sausages and vegetable)	88.4	0	0	40	0	0	0	0	20	8	23	0	0
Cannelloni with meat	154	22.8	0	25.3	0	12.7	0	0	25	0	1.5	0.3	0.3
Lasagne with bolognese sauce	140	44.0	0	14.6	0	11.8	0	0	13.5	0	0	0.2	0.1
Pasta bolognese	137	57	0	25.4	0	0	0	0	10	0	0	0	0
Fried rice	141	61	0	15	0	0	0	10	0	9	0	0	0
Basque chicken with rice	101	1	0	28.4	0	0	0	0	0	0	0	0	0
Basque chicken with pasta	96.6	9.4	0	21.6	0	0	0	0	0	0	0	0	0
Spaghetti with tomato sauce	67.4	47.5	0	13	0	0	0	0	0	0	0	0	0
Baked pasta	150	56.2	0	0	0	21.5	0	15	0	7	0	0	0
Moussaka	138	3.4	0	47	0	22.2	0	0	17	0	0	0.5	0
Lamb stew	139	1.5	0	41.4	0	0	0	0	47	0	0	0	0
Royal couscous with meat	149	31	0	28	0	0	0	0	10	5	0	0	1.5
Endive gratin with ham	90.9	1.4	0	31.6	0	41.7	0	0	0	23.5	0	1	0
Pasta carbonara	166	74.9	0	0	0	12	0	5	0	8	0	0	0
Tartiflette	144	0	0	4	0	31	0	0	0	3	61	0	0
Chicken couscous	158	31	0	29	0	0	0	0	0	0	0	0	1.5
Cheese ravioli	209	21.5	0	0	0	32.5	0	9	0	0	2	0	0
Vegetable gratin	107	1.9	0	81.7	0	5.3	0	3.2	0	0	0	1.07	0
Croque-monsieur (toasted ham and cheese sandwich)	290	25.6	0	0	0	28.7	0	0	0	24	0	0.2	0
Hot-dog	318	32.6	0	3	0	0	0	0	0	50	0	0	0
French quiche Lorraine	292	21	0	0	0	48.4	0	10	0	11	0	3	0

Hamburger	216	26.1	3.5	10.5	0	2.1	0	0	39.5	0	0	0	0
Cheeseburger	262	28.8	2.5	4.5	0	22.3	0	0	23	0	0	0	0
Double cheeseburger	297	24.6	5.5	7.5	0	24	0	0	25	0	0	0	0
Vegetable pie	237	22.1	7.5	30	0	28	0	8	0	0	0	4.3	0
Spring rolls	116	20.4	9	41	0	0	0	0	0	0	0	0	0
Kebab and raw vegetable	233	17.7	7	26.2	0	0	0	0	43	0	0	0	0
Tuna and raw vegetable sandwich	274	43.9	2.7	12.6	0	0	19.3	0.9	0	0	0	0	0
Ham panini with mozzarella and tomatoes	243	28.9	5	16	0	20.9	0	0	0	16.5	0	0	0
Cheese pie or quiche	263	22.4	0	0	0	48.5	0	16	0	0	0	8.8	0
Ham sandwich with boiled egg and raw vegetable	222	42.5	4.7	14.2	0	0	0	6.7	0	21	0	4.3	0
Chicken and raw vegetable sandwich	258	41.5	4	13	0	0	0	0.8	0	0	0	0	0
Smoked salmon, and butter sandwich	265	57.2	0	0	5.2	0	19.5	0	0	0	0	3.3	0
Chicken vol-au-vent with fish and seafood	208	7.9	0	17	0	37.2	16	0	0	0	0	2.7	0
Chicken nugget	188	9.2	0	0	0	0	0	19.4	0	0	0	0	0
Pan bagnat	245	32.7	0	30	0	0	8.7	5	0	0	0	0	10.2
Ham and butter sandwich	283	47.7	0	0	0	0	0	0	0	30	0	10	0
Cheese and butter sandwich	339	47.7	0	0	0	30	0	0	0	0	0	10	0
Pâté and pickle sandwich	299	41.3	0	0	0	0	0	0.9	9.4	0	0.4	0	0
Butter and dry sausage sandwich	375	47.7	0	0	0	0	0	0	0	30	0	10	0
Ham sandwich with emmental and butter	309	42.1	0	0	0	13	0	0	0	25	0	9	0
Sandwich with raw vegetable and mayonnaise	221	39.9	0	37	0	0	0	0.9	0	0	0	0	0
Turkey sandwich with raw vegetable	255	43.1	2	11	0	0	0	1.1	0	0	0	0	0
Egg and raw vegetable sandwich	247	43.9	2.7	12.6	0	0	0	20.2	0	0	0	0	0
Pork and raw vegetable sandwich	267	43.1	2	11	0	0	0	1.1	19	0	0	0	0
Sandwich with merguez, ketchup and mustard	282	39.7	0	0	0	0	0	0	0	42	0	0	0
Salami and butter sandwich	379	47.7	0	0	0	0	0	0	0	30	0	10	0
Croque-madame (toasted ham and cheese sandwich topped with a fried egg)	264	20.3	0	0	0	25.3	0	17.9	0	19	0	0.1	0
Flamenkueche (salted pie with bacon)	263	34	0	16	0	18	0	0.6	17	11.2	0	0	0
Stuffed pancake with bechamel, ham, cheese and mushroom	145	14	0	20	0	48.1	0	7.9	0	7	0	0.8	0
Leek pie	258	24.2	0	18.2	0	43.8	0	0	0	0	0	4.1	0
Tomato pie	218	25.2	0	45.5	0	8	0	4	0	0	0	4.9	0.8
Salmon and sorrel pie	230	21.7	14.5	16	0	33.1	17	0	0	0	0	4.5	0
Tuna salad with vegetable (canned product)	123	0.3	0	57.6	0	0	24.92	0	0	0	0	0	1.3
Potato salad	127	0.4	0	22	0	0	2.7	4.7	0	2	54.5	0	0

Supplemental table 3 Rates of change in risk of type 2 diabetes (percentage) in population subgroups for substitutions with the best and worst pizzas

Population	Isoenergetic substitution		Non-isoenergetic substitution	
	Men	Women	Men	Women
1st Best pizza (#88)				
Age < 45 years	-4.2 (-5.2; -3.1)	-1.9 (-2.4; -1.4)	-5.4 (-7.0; -3.7)	-2.4 (-3.3; -1.4)
Age ≥ 45 years	-1.4 (-1.7; -1.0)	-0.9 (-1.1; -0.6)	-2.0 (-2.4; -1.5)	-1.3 (-1.6; -0.9)
Body mass index < 25	-3.2 (-4.0; -2.4)	-1.5 (-1.9; -1.1)	-3.2 (-4.7; -1.7)	-1.5 (-2.3; -0.6)
Body mass index ≥ 25	-2.0 (-2.5; -1.5)	-1.2 (-1.5; -0.8)	-3.3 (-3.8; -2.6)	-2.0 (-2.4; -1.6)
Fruit and vegetables consumption < 400g/day	-3.0 (-3.7; -2.2)	-1.6 (-2.0; -1.2)	-4.1 (-5.1; -2.9)	-2.3 (-3.0; -1.5)
Fruit and vegetables consumption ≥ 400g/day	-1.7 (-2.2; -1.3)	-0.9 (-1.1; -0.6)	-2.4 (-3.0; -1.8)	-1.2 (-1.6; -0.8)
Low adherence to the mPNNS-GS	-3.3 (-4.1; -2.4)	-1.5 (-1.8; -1.1)	-4.5 (-5.7; -3.1)	-2.0 (-2.6; -1.3)
Medium adherence to the mPNNS-GS	-2.1 (-2.6; -1.5)	-1.6 (-2.1; -1.2)	-2.9 (-3.6; -2.2)	-2.3 (-3.0; -1.5)
High adherence to the mPNNS-GS	-2.4 (-3.0; -1.8)	-1.2 (-1.5; -0.9)	-3.3 (-4.2; -2.4)	-1.7 (-2.1; -1.1)
Low adherence to the MEDI-LITE	-3.0 (-3.7; -2.2)	-1.5 (-1.9; -1.1)	-4.1 (-5.2; -2.9)	-2.2 (-2.9; -1.5)
Medium adherence to the MEDI-LITE	-2.9 (-3.6; -2.1)	-1.5 (-1.9; -1.1)	-4.0 (-5.0; -2.9)	-2.0 (-2.7; -1.3)
High adherence to the MEDI-LITE	-2.0 (-2.5; -1.5)	-1.2 (-1.5; -0.9)	-2.8 (-3.5; -2.0)	-1.6 (-2.1; -1.0)
Low adherence to the provegetarian FP	-2.8 (-3.6; -2.1)	-1.4 (-1.8; -1.1)	-4.0 (-5.0; -2.9)	-2.1 (-2.8; -1.4)
Medium adherence to the provegetarian FP	-2.6 (-3.3; -1.9)	-1.3 (-1.6; -1.0)	-3.7 (-4.6; -2.7)	-1.9 (-2.4; -1.3)
High adherence to the provegetarian FP	-2.3 (-2.9; -1.7)	-1.4 (-1.8; -1.1)	-3.2 (-4.0; -2.3)	-1.9 (-2.4; -1.2)
2nd Best pizza (#100)				
Age < 45 years	-3.6 (-5.3; -1.8)	-1.7 (-2.5; -0.8)	-3.6 (-5.3; -1.8)	-1.6 (-2.5; -0.8)
Age ≥ 45 years	-1.2 (-1.8; -0.6)	-0.8 (-1.1; -0.4)	-1.2 (-1.8; -0.6)	-0.7 (-1.1; -0.3)
Body mass index < 25	-2.8 (-4.2; -1.4)	-1.3 (-2.0; -0.7)	-2.8 (-4.2; -1.4)	-1.3 (-2.0; -0.7)
Body mass index ≥ 25	-1.8 (-2.7; -0.9)	-1.0 (-1.5; -0.5)	-1.8 (-2.7; -0.9)	-1.0 (-1.5; -0.5)
Fruit and vegetables consumption < 400g/day	-2.6 (-3.9; -1.3)	-1.4 (-2.2; -0.7)	-2.6 (-3.9; -1.3)	-1.4 (-2.1; -0.7)
Fruit and vegetables consumption ≥ 400g/day	-1.5 (-2.2; -0.7)	-0.7 (-1.1; -0.3)	-1.5 (-2.2; -0.7)	-0.7 (-1.1; -0.3)
Low adherence to the mPNNS-GS	-2.9 (-4.3; -1.4)	-1.3 (-1.9; -0.6)	-2.9 (-4.3; -1.4)	-1.3 (-1.9; -0.6)
Medium adherence to the mPNNS-GS	-1.8 (-2.7; -0.9)	-1.5 (-2.2; -0.7)	-1.8 (-2.7; -0.8)	-1.4 (-2.2; -0.7)
High adherence to the mPNNS-GS	-2.1 (-3.2; -1.0)	-1.0 (-1.5; -0.5)	-2.1 (-3.1; -1.0)	-1.0 (-1.5; -0.5)
Low adherence to the MEDI-LITE	-2.6 (-3.9; -1.3)	-1.4 (-2.0; -0.7)	-2.6 (-3.9; -1.3)	-1.4 (-2.0; -0.7)
Medium adherence to the MEDI-LITE	-2.5 (-3.8; -1.2)	-1.3 (-1.9; -0.6)	-2.5 (-3.7; -1.2)	-1.2 (-1.9; -0.6)
High adherence to the MEDI-LITE	-1.7 (-2.6; -0.8)	-1.0 (-1.5; -0.5)	-1.7 (-2.6; -0.8)	-1.0 (-1.5; -0.5)
Low adherence to the provegetarian FP	-2.5 (-3.8; -1.2)	-1.3 (-2.0; -0.7)	-2.5 (-3.7; -1.2)	-1.3 (-2.0; -0.6)
Medium adherence to the provegetarian FP	-2.3 (-3.5; -1.1)	-1.1 (-1.7; -0.6)	-2.4 (-3.5; -1.2)	-1.1 (-1.7; -0.5)
High adherence to the provegetarian FP	-2.0 (-3.0; -1.0)	-1.2 (-1.8; -0.6)	-2.0 (-3.0; -0.9)	-1.2 (-1.8; -0.6)
1st Worst pizza (#78)				
Age < 45 years	4.1 (2.9; 5.4)	1.9 (1.3; 2.4)	5.7 (3.7; 7.7)	2.6 (1.3; 3.7)
Age ≥ 45 years	1.3 (0.9; 1.7)	0.8 (0.5; 1.0)	2.1 (1.5; 2.7)	1.3 (0.9; 1.7)
Body mass index < 25	3.2 (2.2; 4.2)	1.5 (1.1; 2.0)	3.2 (1.3; 5.0)	1.4 (0.3; 2.5)
Body mass index ≥ 25	2.1 (1.4; 2.7)	1.1 (0.8; 1.4)	3.5 (2.8; 4.3)	2.2 (1.7; 2.6)
Fruit and vegetables consumption < 400g/day	2.9 (2.0; 3.8)	1.5 (1.1; 2.0)	4.3 (2.9; 5.7)	2.4 (1.4; 3.3)
Fruit and vegetables consumption ≥ 400g/day	1.8 (1.2; 2.3)	0.8 (0.6; 1.1)	2.7 (1.9; 3.4)	1.3 (0.8; 1.7)
Low adherence to the mPNNS-GS	3.3 (2.3; 4.2)	1.5 (1.0; 1.9)	4.8 (3.1; 6.3)	2.2 (1.2; 3.0)
Medium adherence to the mPNNS-GS	2.0 (1.4; 2.6)	1.6 (1.1; 2.1)	3.1 (2.2; 3.9)	2.5 (1.5; 3.4)
High adherence to the mPNNS-GS	2.5 (1.7; 3.3)	1.1 (0.8; 1.4)	3.6 (2.5; 4.7)	1.7 (1.1; 2.3)
Low adherence to the MEDI-LITE	2.8 (2.0; 3.7)	1.5 (1.0; 1.9)	4.3 (2.9; 5.6)	2.4 (1.5; 3.2)
Medium adherence to the MEDI-LITE	2.9 (2.0; 3.8)	1.4 (1.0; 1.8)	4.4 (3.0; 5.7)	2.1 (1.2; 2.9)
High adherence to the MEDI-LITE	2.1 (1.5; 2.7)	1.2 (0.8; 1.5)	3.0 (2.1; 3.9)	1.7 (1.0; 2.3)
Low adherence to the provegetarian FP	2.8 (1.9; 3.6)	1.4 (1.0; 1.9)	4.2 (2.9; 5.5)	2.3 (1.4; 3.1)
Medium adherence to the provegetarian FP	2.6 (1.8; 3.5)	1.3 (0.9; 1.6)	4.0 (2.7; 5.1)	2.0 (1.2; 2.6)
High adherence to the provegetarian FP	2.4 (1.6; 3.1)	1.3 (0.9; 1.7)	3.4 (2.3; 4.4)	1.9 (1.1; 2.7)

2nd Worst pizza (#84)

Age < 45 years	3.5 (2.4; 4.7)	1.6 (1.1; 2.2)	7.3 (3.4; 10.6)	3.2 (0.8; 5.4)
Age ≥ 45 years	1.2 (0.8; 1.5)	0.7 (0.5; 0.9)	2.9 (1.9; 3.8)	1.9 (1.0; 2.6)
Body mass index < 25	2.7 (1.8; 3.6)	1.3 (0.9; 1.8)	2.8 (-0.7; 6.4)	1.2 (-1.0; 3.4)
Body mass index ≥ 25	1.8 (1.2; 2.4)	0.9 (0.6; 1.2)	5.1 (4.0; 6.1)	3.3 (2.6; 4.0)
Fruit and vegetables consumption < 400g/day	2.5 (1.7; 3.3)	1.3 (0.9; 1.8)	5.7 (3.1; 7.9)	3.3 (1.3; 4.9)
Fruit and vegetables consumption ≥ 400g/day	1.6 (1.1; 2.1)	0.8 (0.6; 1.0)	3.6 (2.3; 4.8)	1.8 (0.8; 2.6)
Low adherence to the mPNNS-GS	2.7 (1.8; 3.6)	1.3 (0.8; 1.7)	6.2 (3.2; 8.8)	2.8 (1.0; 4.4)
Medium adherence to the mPNNS-GS	1.7 (1.2; 2.3)	1.4 (0.9; 1.8)	4.2 (2.5; 5.6)	3.4 (1.4; 5.0)
High adherence to the mPNNS-GS	2.2 (1.5; 2.9)	1.0 (0.7; 1.3)	4.8 (2.9; 6.5)	2.4 (1.1; 3.4)
Low adherence to the MEDI-LITE	2.4 (1.6; 3.1)	1.2 (0.8; 1.6)	5.7 (3.1; 7.9)	3.3 (1.6; 4.7)
Medium adherence to the MEDI-LITE	2.5 (1.7; 3.4)	1.2 (0.8; 1.6)	5.9 (3.4; 7.9)	2.9 (1.0; 4.4)
High adherence to the MEDI-LITE	1.9 (1.3; 2.5)	1.1 (0.7; 1.4)	4.0 (2.4; 5.5)	2.3 (0.9; 3.4)
Low adherence to the provegetarian FP	2.3 (1.5; 3.1)	1.2 (0.8; 1.6)	5.6 (3.2; 7.7)	3.2 (1.4; 4.6)
Medium adherence to the provegetarian FP	2.3 (1.5; 3.0)	1.1 (0.8; 1.5)	5.3 (3.1; 7.1)	2.7 (1.2; 3.9)
High adherence to the provegetarian FP	2.1 (1.5; 2.8)	1.2 (0.8; 1.6)	4.5 (2.5; 6.2)	2.6 (0.8; 4.0)

MEDI-LITE, Literature-based adherence score to the Mediterranean diet; *mPNNS-GS*, modified Programme National Nutrition Santé Guideline Score; *NIE substitution*, Non-isoenergetic substitution; *Provegetarian FP*, Provegetarian food pattern. “Pizza” here stands for cluster of pizzas ($n=100$, out of 353 pizzas).

Supplemental table 4 Rates of change in risk of type 2 diabetes (in percentage) for inter-categories substitutions in the whole population and in population subgroups †

Population	Isoenergetic substitution		Non-isoenergetic substitution	
	Men	Women	Men	Women
Pan bagnat				
Whole population	-2.6 (-3.7; -1.5)	-1.4 (-1.9; -0.8)	-2.1 (-3.2; -1.0)	-1.1 (-1.7; -0.4)
Pizza consumers	-6.5 (-9.1; -3.9)	-4.3 (-6.0; -2.5)	-5.4 (-8.1; -2.6)	-3.4 (-5.3; -1.4)
Participants who consumed pizza once	-5.0 (-7.0; -3.0)	-3.7 (-5.2; -2.2)	-4.1 (-6.2; -1.9)	-2.9 (-4.6; -1.2)
Participants who consumed pizza twice	-9.6 (-13.3; -5.7)	-6.2 (-8.6; -3.7)	-8.0 (-12.0; -3.9)	-5.3 (-8.2; -2.4)
Participants who consumed pizza more than twice	-13.5 (-18.6; -8.0)	-9.7 (-13.4; -5.8)	-11.6 (-17.0; -5.8)	-7.7 (-11.9; -3.4)
Age < 45 years	-4.1 (-5.7; -2.4)	-1.9 (-2.6; -1.1)	-3.5 (-5.2; -1.7)	-1.6 (-2.5; -0.7)
Age ≥ 45 years	-1.4 (-1.9; -0.8)	-0.9 (-1.2; -0.5)	-1.0 (-1.6; -0.4)	-0.6 (-1.0; -0.2)
Body mass index < 25	-3.2 (-4.5; -1.9)	-1.5 (-2.1; -0.9)	-3.2 (-4.6; -1.7)	-1.6 (-2.3; -0.8)
Body mass index ≥ 25	-2.1 (-2.9; -1.2)	-1.2 (-1.6; -0.7)	-1.5 (-2.3; -0.6)	-0.7 (-1.1; -0.2)
Fruit and vegetables consumption < 400g/day	-3.0 (-4.2; -1.8)	-1.6 (-2.3; -1.0)	-2.4 (-3.7; -1.1)	-1.3 (-2.0; -0.5)
Fruit and vegetables consumption ≥ 400g/day	-1.7 (-2.4; -1.0)	-0.8 (-1.1; -0.5)	-1.3 (-2.0; -0.5)	-0.6 (-1.0; -0.2)
Low adherence to the mPNNS-GS	-3.3 (-4.6; -2.0)	-1.5 (-2.1; -0.9)	-2.7 (-4.1; -1.3)	-1.2 (-1.8; -0.5)
Medium adherence to the mPNNS-GS	-2.0 (-2.9; -1.2)	-1.7 (-2.3; -1.0)	-1.6 (-2.5; -0.7)	-1.3 (-2.0; -0.5)
High adherence to the mPNNS-GS	-2.4 (-3.3; -1.4)	-1.1 (-1.5; -0.7)	-1.9 (-2.9; -0.9)	-0.8 (-1.3; -0.3)
Low adherence to the MEDI-LITE	-3.0 (-4.2; -1.8)	-1.5 (-2.2; -0.9)	-2.4 (-3.7; -1.2)	-1.2 (-1.9; -0.5)
Medium adherence to the MEDI-LITE	-2.9 (-4.0; -1.7)	-1.4 (-2.0; -0.9)	-2.3 (-3.5; -1.0)	-1.1 (-1.8; -0.4)
High adherence to the MEDI-LITE	-1.9 (-2.8; -1.1)	-1.1 (-1.6; -0.6)	-1.6 (-2.4; -0.7)	-0.9 (-1.4; -0.4)
Low adherence to the provegetarian FP	-2.9 (-4.0; -1.7)	-1.5 (-2.1; -0.9)	-2.3 (-3.5; -1.1)	-1.1 (-1.8; -0.5)
Medium adherence to the provegetarian FP	-2.6 (-3.7; -1.6)	-1.3 (-1.8; -0.7)	-2.1 (-3.2; -1.0)	-1.0 (-1.6; -0.4)
High adherence to the provegetarian FP	-2.3 (-3.2; -1.3)	-1.4 (-1.9; -0.8)	-1.8 (-2.8; -0.8)	-1.1 (-1.7; -0.4)
Spring rolls				
Whole population	-2.1 (-3.3; -0.8)	-1.2 (-1.8; -0.5)	-5.1 (-7.3; -2.4)	-2.9 (-4.5; -1.0)
Pizza consumers	-5.2 (-8.1; -2.1)	-3.6 (-5.6; -1.6)	-11.4 (-16.9; -4.6)	-8.3 (-12.9; -2.4)
Participants who consumed pizza once	-4.0 (-6.2; -1.6)	-3.1 (-4.8; -1.4)	-8.9 (-13.1; -3.9)	-7.4 (-11.3; -2.4)
Participants who consumed pizza twice	-7.6 (-11.7; -3.1)	-5.1 (-7.9; -2.2)	-15.0 (-23.1; -4.8)	-8.9 (-16.6; 0.2)
Participants who consumed pizza more than twice	-11.0 (-16.8; -4.5)	-8.4 (-12.9; -3.7)	-21.6 (-32.9; -6.0)	-19.5 (-29.0; -6.3)
Age < 45 years	-3.2 (-5.0; -1.3)	-1.6 (-2.4; -0.7)	-6.8 (-10.6; -2.2)	-3.1 (-5.6; -0.3)
Age ≥ 45 years	-1.1 (-1.8; -0.5)	-0.7 (-1.1; -0.3)	-3.0 (-4.0; -1.7)	-2.0 (-2.8; -1.0)
Body mass index < 25	-2.6 (-4.0; -1.0)	-1.3 (-2.0; -0.6)	-2.4 (-6.4; 1.9)	-1.1 (-3.5; 1.5)
Body mass index ≥ 25	-1.7 (-2.6; -0.7)	-0.9 (-1.5; -0.4)	-5.2 (-6.5; -3.9)	-3.6 (-4.3; -2.7)
Fruit and vegetables consumption < 400g/day	-2.3 (-3.7; -0.9)	-1.3 (-2.1; -0.6)	-5.6 (-8.2; -2.5)	-3.4 (-5.2; -1.1)
Fruit and vegetables consumption ≥ 400g/day	-1.5 (-2.3; -0.6)	-0.8 (-1.1; -0.3)	-3.6 (-5.0; -2.0)	-1.8 (-2.8; -0.7)
Low adherence to the mPNNS-GS	-2.6 (-4.0; -1.0)	-1.2 (-1.8; -0.5)	-6.0 (-8.9; -2.4)	-2.8 (-4.5; -0.7)
Medium adherence to the mPNNS-GS	-1.7 (-2.6; -0.7)	-1.4 (-2.1; -0.6)	-4.2 (-5.9; -2.2)	-3.4 (-5.3; -1.1)
High adherence to the mPNNS-GS	-2.0 (-3.1; -0.8)	-1.0 (-1.6; -0.5)	-4.7 (-6.7; -2.3)	-2.6 (-3.7; -1.1)
Low adherence to the MEDI-LITE	-2.3 (-3.6; -0.9)	-1.2 (-1.9; -0.5)	-5.6 (-8.2; -2.5)	-3.5 (-5.0; -1.4)
Medium adherence to the MEDI-LITE	-2.4 (-3.7; -1.0)	-1.3 (-2.0; -0.6)	-5.7 (-8.1; -2.9)	-2.9 (-4.6; -0.9)
High adherence to the MEDI-LITE	-1.7 (-2.6; -0.7)	-1.1 (-1.6; -0.5)	-4.0 (-5.7; -2.0)	-2.3 (-3.6; -0.7)
Low adherence to the provegetarian FP	-2.2 (-3.5; -0.8)	-1.2 (-1.9; -0.5)	-5.5 (-8.0; -2.6)	-3.2 (-4.9; -1.1)
Medium adherence to the provegetarian FP	-2.1 (-3.3; -0.8)	-1.1 (-1.7; -0.5)	-5.3 (-7.5; -2.6)	-2.8 (-4.2; -1.1)
High adherence to the provegetarian FP	-2.0 (-3.1; -0.9)	-1.3 (-1.9; -0.6)	-4.4 (-6.4; -2.1)	-2.6 (-4.2; -0.7)
Spaghetti with tomato sauce				
Whole population	-1.1 (-1.5; -0.6)	-0.7 (-0.9; -0.4)	-5.4 (-8.1; -1.8)	-3.2 (-5.3; -0.6)
Pizza consumers	-2.7 (-3.9; -1.4)	-2.2 (-2.9; -1.4)	-11.4 (-18.4; -2.0)	-8.7 (-15.0; -0.6)
Participants who consumed pizza once	-2.1 (-3.0; -1.1)	-1.9 (-2.5; -1.2)	-9.1 (-14.3; -2.2)	-7.9 (-13.1; -1.0)
Participants who consumed pizza twice	-3.9 (-5.7; -2.0)	-2.9 (-4.0; -1.8)	-13.9 (-24.6; 0.6)	-8.1 (-18.6; 4.7)
Participants who consumed pizza more than twice	-5.7 (-8.2; -3.1)	-4.9 (-6.8; -3.0)	-19.7 (-34.9; 2.4)	-20.0 (-32.4; -1.7)
Age < 45 years	-1.6 (-2.3; -0.8)	-0.9 (-1.2; -0.6)	-6.7 (-11.6; -0.5)	-3.2 (-6.5; 0.8)
Age ≥ 45 years	-0.6 (-0.9; -0.4)	-0.5 (-0.7; -0.3)	-3.3 (-4.6; -1.7)	-2.3 (-3.3; -0.9)
Body mass index < 25	-1.3 (-1.9; -0.7)	-0.8 (-1.1; -0.5)	-1.0 (-6.5; 5.0)	-0.5 (-3.9; 3.2)

Body mass index ≥ 25	-0.9 (-1.4; -0.5)	-0.6 (-0.8; -0.4)	-6.0 (-7.4; -4.5)	-4.3 (-5.2; -3.3)
Fruit and vegetables consumption < 400g/day	-1.2 (-1.7; -0.6)	-0.8 (-1.0; -0.5)	-5.8 (-9.0; -1.7)	-3.7 (-6.1; -0.5)
Fruit and vegetables consumption ≥ 400g/day	-0.9 (-1.2; -0.5)	-0.5 (-0.7; -0.4)	-4.0 (-5.6; -1.9)	-2.1 (-3.3; -0.5)
Low adherence to the mPNNS-GS	-1.2 (-1.8; -0.6)	-0.6 (-0.9; -0.4)	-6.1 (-9.9; -1.2)	-3.0 (-5.3; -0.1)
Medium adherence to the mPNNS-GS	-0.9 (-1.2; -0.5)	-0.8 (-1.1; -0.5)	-4.6 (-6.6; -1.9)	-3.8 (-6.2; -0.6)
High adherence to the mPNNS-GS	-1.1 (-1.6; -0.7)	-0.7 (-0.9; -0.5)	-5.0 (-7.5; -1.9)	-2.9 (-4.5; -0.8)
Low adherence to the MEDI-LITE	-1.1 (-1.5; -0.6)	-0.6 (-0.9; -0.4)	-5.9 (-9.1; -1.7)	-3.9 (-5.9; -1.1)
Medium adherence to the MEDI-LITE	-1.3 (-1.8; -0.7)	-0.8 (-1.0; -0.5)	-6.1 (-9.0; -2.3)	-3.2 (-5.5; -0.3)
High adherence to the MEDI-LITE	-1.0 (-1.4; -0.6)	-0.7 (-0.9; -0.5)	-4.2 (-6.4; -1.6)	-2.5 (-4.3; -0.3)
Low adherence to the provegetarian FP	-1.0 (-1.5; -0.5)	-0.6 (-0.9; -0.4)	-5.8 (-8.9; -1.9)	-3.6 (-5.8; -0.7)
Medium adherence to the provegetarian FP	-1.1 (-1.5; -0.6)	-0.6 (-0.9; -0.4)	-5.6 (-8.3; -2.1)	-3.2 (-5.0; -0.8)
High adherence to the provegetarian FP	-1.2 (-1.6; -0.7)	-0.9 (-1.1; -0.6)	-4.6 (-7.1; -1.5)	-2.8 (-5.0; -0.1)
Hot-dog				
Whole population	6.5 (4.2; 9.1)	3.2 (2.1; 4.4)	9.5 (6.3; 12.8)	4.9 (2.9; 6.7)
Pizza consumers	16.2 (10.5; 22.4)	10.1 (6.7; 13.6)	24.2 (15.6; 32.9)	15.5 (9.0; 21.6)
Participants who consumed pizza once	11.6 (7.6; 15.7)	8.5 (5.7; 11.5)	17.3 (11.3; 23.2)	13.2 (7.81; 18.2)
Participants who consumed pizza twice	24.5 (15.7; 34.2)	14.7 (9.6; 20.0)	37.1 (23.8; 51.3)	20.5 (10.2; 30.8)
Participants who consumed pizza more than twice	42.1 (25.8; 61.8)	26.9 (17.3; 37.4)	64.5 (39.9; 93.0)	44.8 (27.1; 62.5)
Age < 45 years	10.4 (6.6; 14.6)	4.5 (2.9; 6.1)	14.3 (8.9; 19.9)	6.1 (3.2; 8.8)
Age ≥ 45 years	3.3 (2.1; 4.5)	1.9 (1.2; 2.6)	5.0 (3.5; 6.6)	3.1 (2.0; 4.1)
Body mass index < 25	7.9 (5.1; 11.1)	3.6 (2.4; 4.9)	8.1 (3.5; 12.9)	3.5 (1.0; 6.0)
Body mass index ≥ 25	5.1 (3.3; 7.2)	2.6 (1.7; 3.6)	8.5 (6.3; 10.9)	5.0 (3.9; 6.3)
Fruit and vegetables consumption < 400g/day	7.3 (4.7; 10.2)	3.7 (2.5; 5.2)	10.6 (6.9; 14.4)	5.7 (3.4; 7.9)
Fruit and vegetables consumption ≥ 400g/day	4.4 (2.8; 6.2)	2.0 (1.3; 2.7)	6.5 (4.4; 8.7)	3.0 (1.8; 4.0)
Low adherence to the mPNNS-GS	8.3 (5.3; 11.6)	3.5 (2.3; 4.8)	11.8 (7.6; 16.3)	5.1 (2.9; 7.2)
Medium adherence to the mPNNS-GS	4.9 (3.2; 6.7)	3.8 (2.5; 5.2)	7.4 (5.0; 9.6)	5.8 (3.4; 8.0)
High adherence to the mPNNS-GS	6.1 (3.9; 8.5)	2.6 (1.7; 3.6)	8.7 (5.8; 11.8)	4.0 (2.5; 5.4)
Low adherence to the MEDI-LITE	7.2 (4.6; 10.0)	3.5 (2.3; 4.8)	10.6 (6.9; 14.4)	5.6 (3.5; 7.6)
Medium adherence to the MEDI-LITE	7.3 (4.7; 10.3)	3.3 (2.2; 4.5)	10.7 (7.1; 14.5)	5.0 (2.9; 7.0)
High adherence to the MEDI-LITE	5.1 (3.3; 7.0)	2.8 (1.8; 3.9)	7.2 (4.9; 9.7)	4.0 (2.3; 5.6)
Low adherence to the provegetarian FP	7.0 (4.5; 9.7)	3.5 (2.3; 4.8)	10.4 (6.8; 13.9)	5.4 (3.3; 7.4)
Medium adherence to the provegetarian FP	6.6 (4.2; 9.4)	3.0 (2.0; 4.1)	9.7 (6.4; 13.2)	4.6 (2.8; 6.3)
High adherence to the provegetarian FP	5.8 (3.8; 8.0)	3.2 (2.1; 4.4)	8.2 (5.4; 11.0)	4.6 (2.6; 6.4)

MEDI-LITE, Literature-based adherence score to the Mediterranean diet; *mPNNS-GS*, modified Programme National Nutrition Santé Guideline Score; *NIE substitution*, Non-isoenergetic substitution; *Provegetarian FP*, Provegetarian food pattern

† Results are the observed risk variations for the best and worst mixed dishes identified for isoenergetic and non-isoenergetic substitutions.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page number
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1, 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9; eFigures 3, eTables 1-2
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5-6; eFigures 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-9; eFigures 2
		(b) Describe any methods used to examine subgroups and interactions	6-9
		(c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	eFigures 1
		(e) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5; eFigures 1
		(b) Give reasons for non-participation at each stage	5; eFigures 1
		(c) Consider use of a flow diagram	eFigures 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9; Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10; Table 2; Figure 1
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11; Table 2; eTables 3-4; Figure 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Manuscript: Impact of intra-category food substitutions on the risk of type 2 diabetes: a modelling study on the pizza category