Supplementary information

Title: Economic Evaluation of a Personalized Nutrition Plan based on Omic Sciences versus a General Nutrition Plan in Adults with Overweight and Obesity: A Modelling Study based on Trial Data in Denmark

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Supplement 1: The type and number of behavioral messages delivered by ONMI to the participants in the personalized and control groups, as presented by Aldubayan et al. 2022[1]

Type of messages	Quantity	Description	Example	PP	C
Starter Do	1	Easy start of the programme on behavioural questionnaire completion at V2	SWITCH SEATS DAY! Move some seating around today. Sit somewhere different at meals/ when working/when watching TV. Get a new view!—Shaking up old habits is good for you and puts you back in charge of your life. Try something new regularly. Make every day count! --	✓	✓
General Do	5	Apply to everyone, relatively easy, to get user hooked to the programme	NEW WAY DAY. Take a detour today, go the prettiest route not the shortest. Allow more time, smile at people. Spot 3 beautiful things along the way.—Wakey Wakey. Regularly challenging our brain keep us alert and interesting. When we take notice of our surroundings we start to live life to the fullest.	✓	
Personalised Do	10	Based on behavioural questionnaire	WHAT ARE YOU EATING FOR? Back off from boredom, address your stress. Get busy, unwind, release your emotions so you only eat when you're hungry today.	✓	
System Message	3	Encouragements, tips, manage expectations	HEALTH TIP. Regular contact with friends and family is key to good mental and physical health. Connections give meaning and purpose to our lives, even when it is digitally.	✓	
Expander Do	3	Prompt user to explore new parts of personality, based on behavioural questionnaire	EXPANDER: It's NO Day today. Don't say yes when you really want to say no. Give no reason or excuse. Just say, 'Sorry, but the answer's no'.	✓	
Preventomics Messages	6	Template messages that use inputs from the nutritional recommendations of food to increase	PREVENTOMICS: Are you getting the right amount of {{.R1}} and {{.R2}} in your diet? Go online and find some interesting recipes to try at home. Do it now.	✓	
General Messages	24	Recommendations from the NHS and WHO on eating, eating out, exercise, check-ups, help and support, balanced diet	Eating a healthy, balanced diet is an important part of maintaining good health, and can help you feel your best. This means eating a wide variety of foods in the right proportions, and consuming the right amount of food and drink to achieve and maintain a healthy body weight.		✓

C, control; NHS, The National Health Service; PP, personalised plan; PREVENTOMICS, Empowering consumers to PREVENT diet-related diseases through OMICS sciences; WHO, World Health Organization.

Supplement 2: Productivity costs calculation

This supplement provides more information on the cost calculation of productivity loss. This explanation is based on information provided by Hoogendoorn et al.[2]

The costs of productivity loss were estimated based on SHARE data [3] for central European countries since the employment status in Denmark is comparable with those in central European countries [4,5].

Costs for long-term work loss were calculated using data on the percentage of people with a paid job (Table S1), the mean number of working hours per week (Table S1) and the probability of becoming unemployed (Table S2). The friction costs method, with additional input provided in Table S3, was applied in this process.

Table S1: Coefficient for the equation prediction probability to be employed at baseline†.

	Coefficients
Country	Central-European countries
Intercept	-14.6526***
Sex (female vs. male)	0.7523***
Age	-0.00861***
Age^2	-0.3354***
Working hours per week	Males: 38, Females: 30

*** p<0.001; †Prob=exp(outcome_equation)/(1+exp(outcome_equation)).

Table S2: Coefficients for regression equation predicting the probability to become unemployed ‡

Coefficient	**Coefficients**
Country	Central-European countries
Intercept	-2.7395***
Sex (Female=1)	0.09195**
Age (years, scaled) †	0.7042***
BMI (continuous)	0.01681***
Diabetes incidence (Yes=1)	-0.1404
Stroke incidence (Yes=1)	0.2981*
Heart attack incidence (Yes=1)	0.01624

† Age_scaled = as (age-mean[age])/std; where mean= =57.67046; std=6.064744
‡ Probability = exp(outcome_equation)/(1+exp(outcome_equation))
* significant at <0.05; **significant at <0.01; ***significant at <0.0001

The productivity costs for short-term working hours lost were calculated by multiplying the estimated annual number of working days lost (Central-European countries: without disease = 10 days, with disease = 15 days) with the reference price (see Table S3).

Table S3. Friction period [6] and reference price [7]

Friction period in days	Productivity cost per hour 2020
91.25	338 DKK

Supplement 3: Method used to calculate unrelated medical costs.

Unrelated medical costs were calculated by subtracting the related costs per capita for diabetes, IHD and stroke from the annual health care spending per capita by sex and age. This annual health care spending per capita by sex and age was calculated following several steps.

1. Information from the DYNAMO-HIA project [8,9] about the percentage of people with disability per age group, divided by sex (in year 2014), was used as a proxy for a certain distribution of the total health care costs over the Danish population.
2. The total health care expenditure of Denmark, in 2014 [10], which was 201,522 DKK in millions of units, was divided over de different age groups by sex, based on the defined distribution in step 1, In this way, we got a total expenditure per age group divided by sex.
3. The total health care expenditure per capita was calculated by dividing the total expenditure per age group divided by sex that was found in the second step, by the number of people in that certain age group divided by sex [8,9].
4. The total health care expenditure per capita was divided by 'last year of life' and 'other years of life' with the following formula in R, using R studio:

   ```
   sc     <-  as,matrix(R_file_data_female$ac,tot)/(1 + (as,matrix(R_file_data_female$r,i)-
   1)*R_file_data_female$mr)
   dc     <-  as,matrix(R_file_data_female$r,i)*sc

   sc     <-  as,matrix(R_file_data_male$ac,tot)/(1 + (as,matrix(R_file_data_male$r,i)-
   1)*R_file_data_male$mr)
   dc     <-  as,matrix(R_file_data_male$r,i)*sc
   ```

   Hereby, 'ac,tot' is the same as total health care expenditure per capita as found in the third step, 'r,i' is the ratio of decedent/survivor as found in an article written by Kalseth et al. [11]. It was assumed that this ratio could be applied in the Danish setting. 'Mr' is the overall mortality rate that was used from the DYNAMO_HIA study [8,9].

   This resulted in a total health care expenditure per capita divided by last year of life and other years of life.

5. Prevalence data of diabetes, IHD and stroke were obtained from the DYNAMO-HIA study [8,9], as well as incidence data of MI and stroke, all divided by age and sex.
6. The prevalence/incidence data together with the disease related costs per capita, were used to calculate the related costs. These costs were subtracted from the total health care expenditure costs per capita, to finally get the total unrelated health care costs per capita per age group divided by sex.
7. These costs were converted to 2020 DKK using the Consumer price index [12].

Supplement 4: Non-medical costs calculation

Mokri et al.[13] applied a method that utilized the methodologies of van Baal et al.[14] and Kellerborg et al.[15] as a starting point to calculate non-medical costs. Due to constraints in data availability, adjustments were made by Mokri et al.[13] to the cost derivation. In our study, we adopted this methodology applied by Mokri et al.[13] to calculate the non-medical costs for Denmark. A summary of this approach will be presented in this supplement.

The costs were determined based on non-medical consumption per household equivalent [13]. This involved adjusting household consumption to account for economies of scale within households in terms of consumption. In other words, as the household size grows, the marginal consumption by each additional member decreases, leading to a reduction in the costs of consumption per person in larger households [16]. When applying the economies of scale concept to future non-medical costs, it implies that preventing a death in a single-person household would contribute to more future non-medical consumption compared to preventing a death in a multi-person household [17].

The following equation was used to estimate the average annual non-medical consumption by age, when a death in an average household is prevented:

$$nmc(a) = [hh\ equiv(a) \times h(a) \times w] + [hh\ equiv(a) \times (1 - h(a))]$$

'h' is the probability of a household having more than one adult

'hh equiv' is the annual non-medical consumption per household equivalent

'w' is the consumption share of a household member: 0.5 for an adult and 0.3 for a child

For this, we utilized aggregate-level data from Eurostat's Household Budget Surveys [18], focusing on the average household consumption corresponding to distinct age groups of the main breadwinner—categorized as less than 30 years, 30-44 years, 45-59 years, and 60 years or over. Components that were included in these data were all household purchases such as rent, food, clothing, and transport.

We estimated the average non-medical costs per household equivalent based on the age category of the breadwinner. These costs were adjusted for both the average household size and economies of scale within households, accounting for the first and second adults. To determine the likelihood of having more than one adult per household, we incorporated data from UK sources [13]. A smoothing function was applied to interpolate the age profiles.

Supplement 5: Details on probabilistic sensitivity analyses from Hoogendoorn et al. 2023[2]

To incorporate the inherent uncertainty in input parameters and its impact on model outcomes, a probabilistic sensitivity analysis (PSA) was conducted. The PSA encompassed uncertainty surrounding relative risks (RRs) associated with body mass index (BMI) and its relationship with all-cause mortality and obesity-related diseases, as well as cost uncertainties. Other parameters were held constant during the analysis, which was because of several reasons. First and foremost, it was anticipated that the results would predominantly depend on relative risks, making them the primary focus of the PSA. Second, introducing uncertainty for parameters such as prevalence, incidence, BMI in the population, mortality, etc., proved challenging due to their interdependence. Altering one of these parameters, like observed BMI, inherently affects others, such as disease prevalence and mortality. Consequently, separate adjustments become impractical. Third, incorporating uncertainties for utilities posed additional challenges, as they are age- and sex-dependent, requiring percentage adjustments for each age and sex. Finally, while uncertainties for utility decrements could have been added, the lack of data on the magnitude of uncertainty led us to forgo this inclusion. Additionally, it was expected that including uncertainty around these decrements would have impacted the results minimally.

For the RRs associated with BMI and all-cause mortality, uncertainty intervals of 11 different BMI values from Aune et al. [19] were used. Ten random values were drawn from the intervals around the relative risks for each reported value of BMI, assuming a normal distribution. Using second-degree polynomial regression, a model was estimated with RR as the outcome and BMI as the predictor, based on the mean RRs and surrounding uncertainty. In the PSA, uncertainty was derived from the uncertainty around the coefficients in the estimated model and random draws for all coefficients were made by considering their covariance. Results were estimated separately for males and females.

A similar approach was used for RRs reflecting the association between BMI and obesity-related diseases. The Global Burden of Disease Study [20] provided RRs for 12 age groups including their uncertainty intervals. Random draws (10 per observation) around each reported RR were taken and were assumed to follow a normal distribution. Subsequently, a linear model was estimated based on the reported RRs and surrounded uncertainty, using age as the predictor and RR as outcome. For the PSA, random draws for the coefficients were made while considering covariance.

Due to the absence of available data on cost uncertainty, a standard error of 20% of the mean value was assumed for all cost estimates. A gamma distribution was applied for cost uncertainty. The effectiveness estimates from the trial and intervention costs were assumed to follow a normal distribution.

Supplement 6: Results of the scenario analysis

Table S4: QALYs and costs of a scenario analysis in which non-medical costs and unrelated medical costs were excluded.

	Discounted at 4%			Undiscounted		
	PP	**Control**	**Difference**	**PP**	**Control**	**Difference**
			Effects			
QALYs	15.117	15.106	0.011	28.483	28.464	0.019
			Costs (in 2020 € (DKK))			
Diabetes	18,118 (135,305)	18,193 (135,864)	-75 (-559)	46,769 (349,272)	46,926 (350,445)	-157 (-1,173)
IHD	2,910 (21,732)	2,916 (21,774)	-6 (-43)	7,219 (53,915)	7,230 (53,997)	-11 (-82)
Stroke	3,642 (27,199)	3,649 (27,252)	-7 (-53)	10,775 (80,465)	10,791 (80,586)	-16 (-121)
Unrelated	-	-	-	-	-	-
Non-medical	-	-	-	-	-	-
Intervention	7,402 (55,277)	5,653 (42,215)	1,749 (13,062)	7,402 (55,277)	5,653 (42,215)	1,749 (13,062)
Informal care	5,581 (41,680)	5,582 (41,683)	0 (-3)	16,169 (120,753)	16,164 (120,713)	5 (41)
Productivity	17,234 (128,703)	17,236 (128,772)	-3 (-19)	24,668 (184,221)	24,670 (184,240)	-2 (-18)
TOTAL	55,558 (414,908)	53,904 (402,560)	1,658 (12,385)	113,996 (851,329)	112,433 (839,657)	1,568 (11,708)
ICUR	***156,173 (1,166,309)***			***84,076 (627,880)***		

DKK Danish Krone, *ICUR* incremental cost-utility ratio, *IHD* Ischemic heart disease, *PP* Personalized Plan, *QALYs*, quality-adjusted life years.

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