Promoting healthy lifestyle habits among participants in cancer screening programs: Results of the randomized controlled Sti.Vi study

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Abstract

Background: Unhealthy diets, physical inactivity, alcohol and tobacco consumption are among the leading risk factors for non-communicable diseases. It is estimated that around 40% of cancers could be prevented by adopting healthy lifestyles.

Design and methods: The Stili di Vita (Sti.Vi) study was a randomized study for assessing the impact of healthy lifestyle interventions on anthropometric measures, metabolic parameters, and health outcomes among participants of cancer screening programs in Turin (Italy). Eligible women aged 50–54 years, invited to biennial mammography screening, and 58-years-old men and women, invited to a once-only sigmoidoscopy for colorectal cancer (CRC) screening were randomly allocated to Diet group (DG), Physical Activity group (PAG), Physical Activity plus Diet group (PADG), or control group (CG). Physical and eating habits, metabolic and anthropometric measurements, repeatedly collected, were the study outcomes. The active intervention, offered to participants assigned to the DG, PAG, and PADG arms, consisted of a basic module and an advanced module. The effect of the interventions was estimated through logistic regression or a difference in differences approach. A multiple imputation procedure was implemented to deal with missing values and *q*-values have been calculated in the presence of multiple hypothesis testing.

Results: Out of the 8442 screened attendees, 1270 signed informed consent, while 1125 participants accomplished the baseline visit. Participants were equally distributed across the four treatments as following: 273 (24.3%) in DG, 288 (25.6%) in the PAG, 283 (25.1%) in PADG, and 281 (25%) in the CG. Participants assigned to DG or PADG increased their consumption of whole grains (OR = 1.77, 95% CI: 1.20–2.60 and OR = 1.55, 95% CI: 1.06–2.27, respectively) and legumes (OR = 1.77, 95% CI: 1.12–2.79 and OR = 2.24, 95% CI: 1.41–3.57, respectively), with respect to CG. The participants randomized to DG reduced processed meat and increased fruit consumption (OR = 2.57, 95% CI: 1.76–3.76 and OR = 2.38, 95% CI: 1.12–5.06, respectively). The effects were more evident in the CRC screening subgroup. No relevant difference was observed between PAG and CG. No impact was observed on physical activity habits.

Conclusions: Our findings suggest that active interventions can increase awareness and induce diet changes. However, participation rate and compliance to the courses was quite low, innovative strategies to enhance participants' retention are needed, with the ultimate goal of increasing awareness and inducing positive lifestyle changes.

Introduction

The World Health Organization (WHO) states that non-communicable diseases (NCDs), including cardiovascular diseases, cancers, and diabetes, are the leading cause of deaths in the world, being collectively responsible for almost 70% of all deaths worldwide.[1] Unhealthy diets, physical inactivity, alcohol and tobacco consumption are among the leading risk factors for these diseases. Thus, the socioeconomic costs associated with NCDs make prevention and control of these diseases a priority for the 21st century.[1]

Among the European population of 743.8 million inhabitants, there were 4.23 million new cancer cases and 1.94 million deaths from cancer in 2018.[2] Excluding non-melanoma skin cancer, the top five most frequent cancers were breast, colorectal, lung, prostate, and bladder.[2] It is estimated that around 40% of cancer cases could be prevented by eating a healthy diet, being more active each day and maintaining a healthy weight.[3–5]

Parkin et al.[6] estimated the fraction of cancers occurring in the UK in 2010 that can be attributed to tobacco, alcohol, consumption of meat, fruit and vegetables, fiber, and salt, overweight, lack of physical exercise. These results highlighted that tobacco smoking, dietary factors, alcohol drinking, and bodyweight accounted for 34% of the cancers that occurred in 2010.[6]

In 2018, in accordance with this evidence, the World Cancer Research Fund (WCRF)[7] updated the review on the balance between cancer and lifestyles and the main recommendations for cancer prevention.

The European Code against Cancer[8] is a set of recommendations for cancer prevention. In its fourth edition, published in 2015,[8] twelve recommendations concern the adoption of healthier lifestyles.

Interventions aimed at improving lifestyle may positively affect not only cancer risk, but also other chronic diseases. Adults with common chronic conditions participating in lifestyle modification programs experience significant and sustainable improvements in biometric, laboratory, and psychosocial outcomes.[9,10] Introducing a combination of healthy habits can further prevent and handle several current and future cases of chronic diseases.[11]

The rhythms of society have progressively induced a reduction of physical activity in the population. In addition to a lack of sports facilities or protected routes for walking or cycling, and environments which discourage physical exercise in favor of sedentary behaviors. Regarding eating habits, the difficulty of finding healthy and economically accessible food and the lack of time to cook are barriers to overcome in order to achieve a balanced diet. Thus, interventionist approaches, which are not necessarily just educational, are needed to attenuate the burden of NCDs. Successful prevention requires a combination of individual preventive and population-based actions, to eliminate or reduce the risk exposure at both individual and population level.

In order to be successful at improving lifestyle habits, behavioral interventions should be accepted by participants.[12] Whereas, among people who are at risk, reducing unhealthy behaviors can be easier, it is more difficult to introduce the same changes among healthy subjects.[13] Cancer screening programs, in addition to providing a unique opportunity to communicate health education messages to a wide audience, have the advantage of reaching people repeatedly over the years and can be the ideal place to propose models capable of promoting healthy lifestyles.[14–22] On the one hand, with individuals being the exposed simultaneously to exogenous (related to the external environment) and endogenous (linked to individual lifestyles) risk factors, the idea is that prevention should be implemented in a unique context where individual, collective, and environmental prevention interventions are closely linked.

Aim

The Stili di Vita (Sti.Vi) randomized controlled trial (RCT) aimed to firstly determine the acceptability among screening participants of healthy lifestyle interventions, and secondly to assess the impact of such interventions on anthropometric measures, metabolic parameters, and health outcomes such as diet and physical activity.

In this article we reported the results of the second aim, namely the impact of healthy lifestyle interventions on anthropometric measures, metabolic parameters, and compliance to lifestyle recommendations.

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Material and methods

Trial setting

The randomized controlled trial (RCT) was performed in Turin, Piedmont, Italy. The recruitment of eligible participants, residing in Turin, started in May 2010 and lasted 2.5 years.

In the screening setting, women aged 50–54 years, invited to biennial mammography screening, and 58-years-old men and women, invited to a once-only sigmoidoscopy for colorectal cancer (CRC) screening, were eligible for participation. Eligible participants received a leaflet on how to participate. Along with screening invitation, eligible subjects received a leaflet, presenting the study.

The same exclusion criteria applied to screening invitation were adopted (recent breast cancer (BC) or CRC tests, terminal diseases, psychiatric diseases, presence of neoplastic pathology), with the addition of exclusion criteria related to psycho-physical conditions which could negatively affect the participation: presence of psychiatric disorders, disabling disease, eating or deambulation disorders, being in physiotherapy at the time of recruitment. Compliance to screening was not considered a prerequisite for participation.

At the screening center, after signing informed consent, participants were randomly allocated (ratio 1:1:1:1) through a permuted block design, with block size of 12, 16, and 20 units width, into four groups: Diet group (DG), Physical Activity group (PAG), Physical Activity plus Diet group (PADG), and Usual Care control group (CG). This method allowed an almost complete uniform distribution of the randomization groups in every moment of the study, which his was necessary in order to simplify the subsequent courses management. Enrollment was carried out by a group of researchers (a dietician, a biostatistician, and two biologists) specifically trained for this task. At this stage only the enrollment staff was aware of the group allocation, while participants were blinded.

Randomized people were invited to undergo a baseline visit. The group he/she was assigned to was communicated only after have completed the baseline visit, in order to avoid immediately losing whoever had ended up in a group not of his interest.

Interventions

All participants, independently from group allocation, received a lifestyle booklet (see Supplemental Material), specifically developed for this study and based on WCRF,[7] including information on healthy diet and physical activity.

A basic course (one theoretical lesson) and advanced module (practical lessons) were offered to participants belonging to the three active intervention groups (DG, PAG, PADG). Details of intervention are provided as Supplemental Material.

Briefly, for participants randomized to the DG intervention, the basic course consisted of one theoretical lesson of 1.5 h held by a nutritionist, aimed to enhance knowledge on healthy diet, disease prevention, nutritional value of food and energy balance. During the advanced module, participants assigned to the DG arm were invited to attend 3 cooking classes (4 h each) held by a professional cook and a dietician, where examples of recipes and daily and weekly menus were also provided.

For participants randomized to the PAG intervention, the basic course (1.5 h), held by a physical education expert, provided information about the benefits of physical activity and its relation to weight and energy intake, explained how to increase it, how to breath properly during exercise and how to measure the intensity of training. The advanced module consisted in three gym classes (2 h each) held by a physical education expert, aimed to increase physical strength and to improve postural balance, control and coordination, aerobic capacity, and breathing control.

For participants randomized to the PADG intervention, the basic course, a 2 h theoretical lesson, held by a nutritionist and physical education expert, provided general information on both diet and physical exercise. After having completed the basic course, participants in the PADG arm were invited to both dietary and physical activity interventions: specifically, to attend two cooking classes (4 h each) and two gym sessions (2 h each).

Measurements

Physical and eating habits questionnaire. The physical and eating habits questionnaire was a self-reported tool aimed at assessing each individuals physical and eating behavior, derived from EPIC semi-quantitative questionnaire, already validated in Italy.[21] The questionnaire was divided into different sections. In section 1, participants were asked to indicate both the frequency and duration of different physical activities, for example: walking, gardening, or gym work done during the previous year. In section 2, participants were asked to report the frequency of consumption of several foods and beverages during the last year.

Blood samples. Two types of fasting blood samples were drawn, one to be cryo-preserved and another for immediate biochemical analyses (insulin, glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides for all participants).

Anthropometric measures. Anthropometric measures as height, weight, body mass index (BMI), and blood pressure were collected (measured by the dietician).

At baseline, randomized participants were invited to undergo blood samples, anthropometric measurements, and fill out the physical and eating habits questionnaire.

Follow-up

Two follow-ups were planned:

- Intermediate: 8 months after biological sampling/anthropometric measurements all participants were invited by letter and/or telephone call to contact the study secretariat in order to fix an appointment for repeating anthropometric measurements and the questionnaire.
- Final: 6 months after the intermediate follow-up, all participants were invited by letter and/or telephone call to contact the study secretariat in order to fix an appointment for repeating anthropometric measurements, the questionnaire, and biological sampling.

Participants that expressed their intention to withdraw from the study, by mail or telephone, were considered withdrawn participants.

Ethical aspect

The trial was approved by the local Ethics Committee and registered in ClinicalTrials.gov (NCT03118882). All the participants signed an informed consent form. To ensure privacy, participants were assigned a unique identification code and their information was stored in locked archives. All archives complied with the Italian Privacy legislation.

Sample size

Assuming a small treatment effect (Cohen's $f = 0.15$),[22] 290 individuals per group ensured a power of 90% of refusing the null hypothesis of no effect, fixing $\alpha = 0.001$ according to a Bonferroni's adjustment which accounted for multiple tests. We then enrolled a total of 320 subjects per treatment arm in order to account for possible dropouts.

Statistical analysis

We analyzed data according to the intention-to-treat (ITT) approach, which provides an unbiased estimate of the effectiveness of treatment assignment.

Since this study was of longitudinal nature, with measurements at different points in time, one of the main problems was the presence of missing values, arising from the loss of follow-up, non-response to single items of questionnaire or incomplete metabolic and anthropometric measurements. In order to deal with missing data,[22] we applied a multiple imputation by chained equations (MICE) procedure[23] separately for each intervention arm and screening program, under the missing at random (MAR) assumption. In the MICE algorithm,[23] we used classification and regression trees (CART)[24] as conditional models for imputation. We generated $M = 30$ complete data

sets, and we conducted on each of them the planned analyses. Then, for each parameter of interest, the M estimated effects and their standard errors were combined by using the Rubin's rule,[25] obtaining a summary result which accounted for the additional uncertainty due to the presence of missing values.

The impact of the intervention models was evaluated on the following outcomes:

- Compliance to lifestyle recommendations, derived from the World Cancer Research Fund (WCRF)[7] and European Code against Cancer 4th edition,[8] and their maintenance:
  - Whole grains: daily consumption of cereals and products that derive from their processing, favoring whole grains
  - Legumes: fresh or dried legumes at least 2–3 times a week
  - Raw vegetables and cooked vegetables: at least three servings of vegetables a day, better fresh and in season
  - Fruits: two fresh and seasonal fruit servings a day
  - Fish: increase the consumption
  - Red and processed meats: decrease the consumption
  - Cheese: consume with extreme moderation, favoring seasoned cheeses
  - Vegetable oil: in order to limit daily fat intake, preferably use oil at raw or at the end of cooking
  - Sugary drinks: limit the consumption of carbonated and/or soft sugary drinks to the occasions
  - Alcohol and spirits: do not exceed two glasses per day (man) and one glass per day (woman)
  - Be physical active: 30 min of physical activity of moderate intensity for 5 days a week (or 20 min of physical activity of vigorous intensity three times a week) plus tonifying and flexibility exercises twice a week
- Changes in anthropometric measurements, measured at baseline and at the final follow-up:
  - Weight
  - BMI class
- Changes in metabolic parameters measured at baseline and at the final follow-up:
  - Glucose
  - Total cholesterol
  - Low-density lipoprotein (LDL)
  - High-density lipoprotein (HDL)
  - Triglycerides

Regarding diet recommendations, we considered a subject as "improved" if, between baseline and the end of the study, he/she increased/decreased the consumption of the

specific food/drink considered. Those who already followed the recommendation at baseline and who maintained it even at the end of the study were also considered improved. For example, for the first recommendations *"Daily consumption of cereals and products that derive from their processing, favoring whole grains"* a participant was considered as improved if, at the end of the study, he/she increased the consumption of whole grains or he/she already ate daily whole grains at the baseline and maintained this healthy habit even at the end of the study. For "*Decrease the consumption of red meat and processed meats*" recommendation, we considered a participant as improved if, at the end of the study, he/she decreased the consumption of red meat or he/she already ate red meat 1–3 times a week at the baseline and maintained this healthy habit even at the end of the study.

For the analysis of anthropometric measurements, we followed the guidelines for management of obesity,[26] which consider a weight loss program as successful when there is a decrease in weight by 5%–10% minimum, compared to the initial body weight. Therefore, for the BMI and weight outcomes, we considered the subjects as improved if, between baseline and the end of the study, they decreased their BMI class or had at least 5% of reduction of the initial weight. Those who were normal BMI at baseline visit and maintained the weight also at the end of the study were considered as improved. We considered those that were underweight as improved if they gained weight.

For these categorical outcomes, we estimated the effect of the intervention through logistic regressions, adjusting for age and sex.

For metabolic parameters and for questions related to the physical activity (minutes of walking, bicycle, gardening, and gym), we adopted a difference in differences (DID) approach[27] by using linear regressions, adjusting for age and sex.

DID requires data measured from a treatment group and a CG at two or more different time periods, specifically at least one time period before "treatment" and at least one time period after "treatment."[27] It calculates the effect of a treatment on an outcome by comparing the average change over time in the outcome variable for the treatment group with the average change over time for the CG.[27]

In all the analyses, we evaluated the impact of being assigned to each of the three intervention groups (PAG, DG, and PADG) toward the CG.

Stratified analyses by type of screening, breast and colorectal cancer screening, were performed.

The results have been reported in terms of point estimates and 95% confidence intervals. However, being in the presence of multiple tests, we applied also the Benjamini-Hochberg procedure[28] to correct the proportion of false positives, or false discovery rate (FDR),[28] calculating the *q*-values. Each *q*-value should be interpreted as the proportion of false positives over all the rejected hypotheses.

The statistical analyses were performed using R software, version 3.5.1.[29] The package "mice"[23] was used to implement multiple imputation and the function "p.adjust" to control for multiple tests.

Results

Out of the 8442 screened attendees (3873 from breast cancer program and 4569 from the colorectal screening program), 1270 signed informed consent to the trial: 667 enrolled through breast cancer screening and 603 through colorectal cancer screening (369 females and 234 males). Of those who agreed to participate, 12% did not show up for the baseline visit, therefore out of 1270 enrolled participants, just 1125 completed the initial visit. Therefore resulting in a total of 602 (53.5%) enrolled through breast cancer screening and 523 through colorectal cancer screening (208 males and 315 females).

The total participation rate in this study was 13% out of screened attendees, in details 15% through the breast cancer screening and 11% through the colorectal cancer screening. The mean age was 55.4 years (±3.5 years). Figure 1 outlines the study flow. Follow-up lasted 1.24 years (±0.19 years).

The number of participants randomized to the four groups was the following: 273 (24.3%) in DG, 288 (25.6%) in the PAG, 283 (25.1%) in PADG, and 281 (25%) in the Usual Care CG.

Due to randomization, groups were well-balanced at baseline on socio-demographic and health status characteristics (Table 1). The compliance to practical courses, defined as less than an absence to the courses, was different between groups (*p* = 0.021, Table 1), with the largest compliance in the DG arm and the lowest in the PAG arm.

Figure 2 summarizes the frequency of the missing data at baseline and follow-up visits for each variable collected.

Due to the large amount of missing data (1%–80% at baseline, 24%–85% at intermediate visit, and 27%–85%, at the final visit), we set *M*, the number of imputed data sets, to 30[30].

Overall, taking the CG as reference, a positive impact of being assigned to the intervention groups was observed in the healthy eating outcomes (Table 2). With respect to being assigned to the CG, being assigned to the DG improved the healthy habits regarding the consumption of whole grains (OR = 1.77, 95% CI: 1.20–2.60), legumes (OR = 1.77, 95% CI: 1.12–2.79), fruits (OR = 2.38, 95% CI: 1.12–5.06), and processed meats 2.57 (95% CI: 1.76–3.76).

Being assigned to the PADG appeared to have an effect on whole grains and legumes consumption (OR = 1.55, 95% CI: 1.06–2.27 and OR = 2.24, 95% CI: 1.41–3.57, respectively), and on alcohol use (OR = 2.99, 95% CI: 1.26–7.07). No clear evidence was noted between PAG
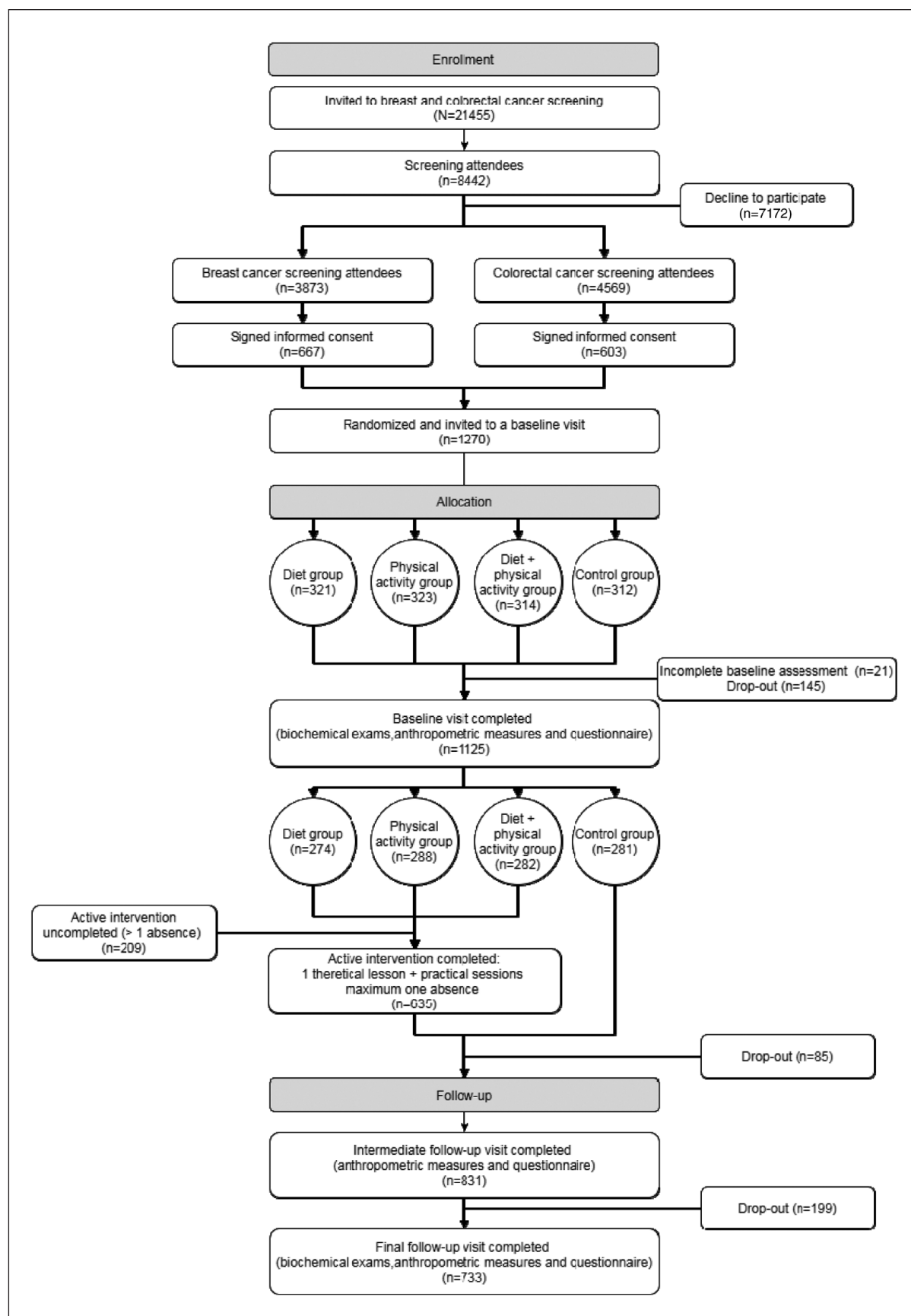
Figure 1. CONSORT flow diagram of Sti.Vi study.

Table 1. Socio-demographic and health status characteristics. Categorical variables are reported in terms of frequency (%), continuous variables in terms of mean and standard deviation (SD).

	Group randomization (Total 1125)*								
	DG (*n*=274)		PAG (*n*=288)		PADG (*n*=282)		CG (*n*=281)		*p***
	n	%	*n*	%	*n*	%	*n*	%	
Sex									
Male	37	13.5	55	19.1	57	20.2	59	21	0.1
Screening									
Breast cancer	154	50.2	149	51.7	151	53.5	148	52.7	0.7
Job									
Unemployed	82	29.9	91	31.6	73	25.9	87	31	0.9
Office worker	77	28.1	79	27.4	94	33.4	81	28.8	
Technical professions	53	19.3	51	17.7	54	19.1	50	17.8	
Academic	56	20.5	59	20.5	54	19.1	57	20.3	
Manager	6	2.2	8	2.8	7	2.5	6	2.1	
Compliance to the intervention									
>1 absence to the courses	52	19.0	82	28.5	75	26.6	—	—	0.021
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	55.4	3.5	55.5	3.5	55.4	3.6	55.3	3.4	0.9
Weight (kg)	66.6	12.6	69.5	15.2	68.7	14.1	68.3	13.9	0.1
Height (cm)	159.9	7.8	161.8	7.9	161	8.3	161.3	7.8	0.05
BMI (kg/m^2)	26	4.7	26.5	5.2	26.5	5	26.2	4.8	0.7
Glucose (mg/dl)	87.5	17.2	86.6	14.4	86.5	14.6	85.9	15.5	0.7
Total cholesterol (mg/dl)	220.6	39.1	218.3	40.1	219.2	35	222.1	39.2	0.7
Low-density lipoprotein (mg/dl)	134.3	34.7	132.7	35.1	134.1	32.7	135.4	32.7	0.8
High-density lipoprotein (mg/dl)	66.3	18	65.2	18.9	65.4	15.6	67.2	18	0.5
Triglycerides (mg/dl)	99.2	55.7	105	60.9	96.4	47	100.8	54.4	0.3
Diastolic blood pressure (mmHg)	79.8	10.8	80.1	9.8	80.7	11.6	79.4	10.3	0.5
Systolic blood pressure (mmHg)	121.3	18	121.9	17.1	121.8	18.5	119.3	18.6	0.3

*Group randomization: CG: control group; D: diet group; PADG: physical activity + diet group; PAG: physical activity group.
**p Value were extracted from χ^2 test for categorical variables or ANOVA for continuous variables.

and the CG, even if most of the point estimates of the ORs were larger than 1.

For physical activity habits, we did not find any improvement of being assigned to one of the intervention groups compared to the CG. We observed a decrease in the use of a bicycle during winter for the PADG (DID=−29.50 min/week, 95% CI: −58.75 to −0.25 min/week) (Table 2).

For the intervention groups, we did not find clear evidence of weight or BMI improvement in respect to the CG.

Regarding metabolic parameters, we estimated an increase of triglycerides level among the individuals assigned to the PADG at the end of the study (DID=10.75 mg/dl, 95% CI: 3.14–18.36 mg/dl), when compared to the CG.

The results by type of screening are reported in Supplemental Tables 1 and 2. In detail, within the colorectal cancer screening program (Supplemental Table 1), being assigned to the DG improved the healthy habits regarding the consumption of whole grains (OR=2.54,

95% CI: 1.36–4.73), legumes (OR=2.03, 95% CI: 1.05–3.93), processed meats (OR=3.18, 95% CI: 1.76–5.73), extra-virgin oil (OR=2.22, 95% CI: 1.02–4.82), and alcohol (OR=1.82, 95% CI: 1.03–3.19). While being assigned to the PADG improved the healthy habits of eating whole grains (OR=1.83, 95% CI: 1.00–3.35) and legumes (OR=2.91, 95% CI: 1.46–5.79).

Within the breast cancer screening program (Supplemental Table 2), being assigned to the DG improved the healthy habits of reducing processed meats 2.13 (95% CI: 1.28–3.57); being assigned to the PADG improved the healthy habits of eating fruits (OR=3.36, 95% CI: 1.15–9.86). In the PAG, we observed a worsening related to the consumption of cheese and extra-virgin oil.

In Table 3 the *q*-values for all hypotheses with a *p*-value less than 0.20 are reported. Setting the *q*-value threshold to 0.20, seven hypotheses were rejected (the DG improved the healthy habits regarding the consumption of whole grains (*p*=0.004), legumes (*p*= 0.014), and processed meats (*p*<0.0001) and reduced the systolic blood pressure
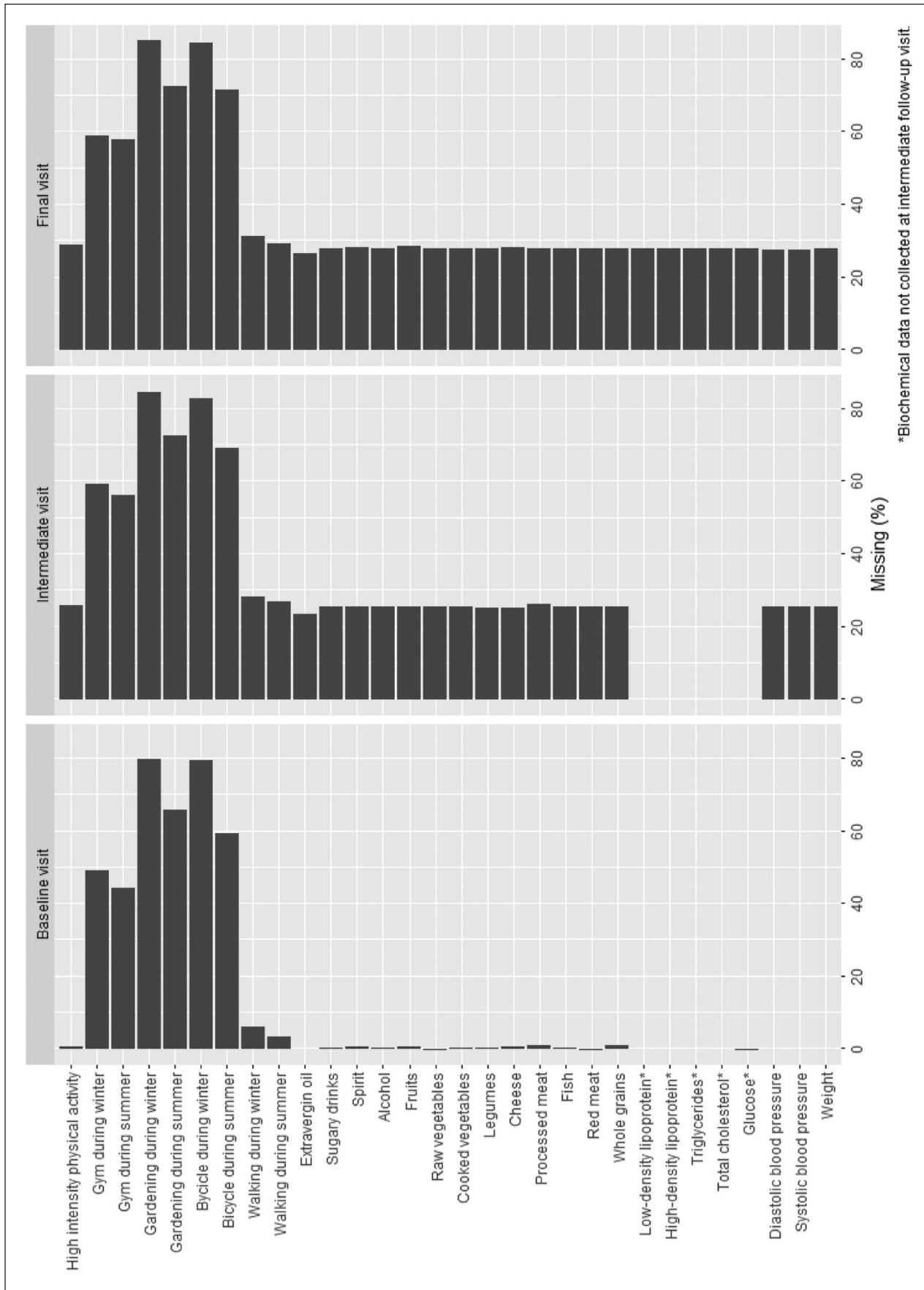
Figure 2. Missing frequency (%) of the outcomes at the baseline and follow-up visits.

Table 2. Estimated impacts of the interventions on lifestyle, physical activity, anthropometric and metabolic parameters.

	CG	PAG*			DG*			PADG*		
		OR	95% CI		OR	95% CI		OR	95% CI	
Whole grains	Ref	1.09	0.74	1.61	1.77	1.20	2.60	1.55	1.06	2.27
Legumes	Ref	1.19	0.79	1.81	1.77	1.12	2.79	2.24	1.41	3.57
Raw vegetables	Ref	1.02	0.68	1.53	1.07	0.70	1.63	1.15	0.77	1.73
Cooked vegetables	Ref	0.80	0.53	1.19	1.13	0.74	1.72	1.22	0.81	1.85
Fruits	Ref	1.18	0.62	2.26	2.38	1.12	5.06	1.85	0.87	3.92
Fish	Ref	0.80	0.45	1.41	0.83	0.47	1.44	0.58	0.34	1.02
Red meat	Ref	1.04	0.71	1.53	1.43	0.98	2.07	1.17	0.80	1.70
Processed meat	Ref	1.22	0.83	1.81	2.57	1.76	3.76	1.37	0.93	2.01
Cheese	Ref	0.76	0.53	1.08	0.91	0.63	1.31	0.91	0.63	1.31
Extravirgin oil	Ref	0.91	0.54	1.54	1.07	0.63	1.79	1.00	0.60	1.67
Sugary drinks	Ref	0.84	0.53	1.32	1.52	0.89	2.62	1.21	0.74	1.97
Alcohol	Ref	0.93	0.63	1.35	1.37	0.93	2.01	0.98	0.67	1.43
Spirits	Ref	1.42	0.69	2.92	2.14	0.94	4.90	2.99	1.26	7.07
High intensity physical activity	Ref	1.19	0.81	1.73	0.82	0.57	1.18	0.92	0.63	1.36
Weight/BMI	Ref	1.23	0.87	1.75	0.96	0.67	1.39	1.10	0.77	1.57
		DID	95% CI		DID	95% CI		DID	95% CI	
Walk during summer (min/week)	Ref	−11.36	−49.49	26.76	8.41	−31.13	47.95	−14.48	−53.66	24.70
Walk during winter (min/week)	Ref	−17.70	−51.08	15.67	0.43	−35.26	36.12	−8.09	−44.16	27.97
Gardening during summer (min/week)	Ref	−10.86	−58.40	36.68	−7.57	−53.03	37.88	10.04	−38.16	58.24
Gardening during winter (min/week)	Ref	−1.65	−19.05	15.74	−10.09	−25.68	5.51	−14.06	−28.91	0.80
Bicycle during summer (min/week)	Ref	−31.00	−78.22	16.22	−26.84	−78.20	24.52	−38.28	−100.89	24.32
Bicycle during winter (min/week)	Ref	−16.26	−40.35	7.84	−8.37	−38.89	22.15	−29.50	−58.75	−0.25
Gym during summer (min/week)	Ref	−23.47	−70.47	23.52	19.32	−28.15	66.79	−17.07	−59.86	25.71
Gym during winter (min/week)	Ref	−31.20	−70.71	8.30	23.49	−15.39	62.37	−16.75	−51.63	18.13
High intensity physical activity (min/week)	Ref	5.40	−7.91	18.72	−2.36	−15.73	11.02	4.06	−9.81	17.94
Glucose (mg/dl)	Ref	−0.16	−2.60	2.28	−1.71	−4.09	0.68	0.73	−1.96	3.43
Total cholesterol (mg/dl)	Ref	−0.91	−6.47	4.65	−1.87	−7.32	3.59	−2.26	−7.84	3.31
Low-density lipoprotein (mg/dl)	Ref	−1.05	−5.59	3.50	−1.95	−6.60	2.71	−2.04	−6.80	2.72
High-density lipoprotein (mg/dl)	Ref	0.58	−1.50	2.67	−0.33	−2.38	1.72	0.57	−1.54	2.69
Triglycerides (mg/dl)	Ref	−0.38	−8.03	7.27	0.04	−7.61	7.70	10.75	3.14	18.36
Diastolic blood pressure (mmHg)	Ref	−0.03	−1.67	1.62	−0.78	−2.48	0.92	−1.33	−2.99	0.32
Systolic blood pressure (mmHg)	Ref	−1.67	−4.41	1.06	−3.86	−6.69	−1.04	−2.24	−4.97	0.50

*CG was set as reference group. DG: diet group; DID: difference in differences; OR: odds ratio; PADG: physical activity and diet group; PAG: physical activity group.

($p=0.0074$); the PADG appeared to have an effect on legumes consumption and on alcohol use ($p=0.0007$ and $p=0.0127$, respectively), while triglycerides levels increased ($p=0.0057$)), 20% of which (1–2) were expected to be false positive.

Discussion

The Sti.Vi study was a randomized controlled trial designed to promote healthy lifestyle habits and consequently improve the anthropometric and metabolic profile

Table 3. *Q*-value for the comparisons with *p*-value lower than 0.2.

Outcome	Intervention*	*p***	*Q*-value (%)
Processed meat	DG	<0.0001	0.00
Legumes	PADG	0.0007	3.26
Whole grains	DG	0.004	12.40
Triglycerides (mg/dl)	PADG	0.0057	13.25
Systolic blood pressure (mmHg)	DG	0.0074	13.76
Spirits	PADG	0.0127	18.60
Legumes	DG	0.014	18.60
Whole grains	PADG	0.0231	25.73
Fruits	DG	0.0249	25.73
Bicycle during winter (min/week)	PADG	0.0481	44.73
Fish	PADG	0.0569	45.43
Red meat	DG	0.0627	45.43
Gardening during winter (min/week)	PADG	0.0635	45.43
Spirits	DG	0.0701	46.57
Alcohol	DG	0.1078	54.83
Systolic blood pressure (mmHg)	PADG	0.1084	54.83
Fruits	PADG	0.1101	54.83
Processed meat	PADG	0.1146	54.83
Diastolic blood pressure (mmHg)	PADG	0.1148	54.83
Gym during winter (min/week)	PAG	0.1206	54.83
Sugary drinks	DG	0.1275	54.83
Cheese	PAG	0.1297	54.83
Glucose (mg/dl)	DG	0.1608	65.02
Gardening during winter (min/week)	PAG	0.1852	71.77
Gardening during summer (min/week)	PAG	0.1956	72.65

*CG was set as reference group. DG: diet group; PADG: physical activity and diet group; PAG: physical activity group.
**We reported only hypothesis with a *p*-value ≤0.20.

of the participants in two cancer screening programs. We found that the active interventions had a positive effect on some healthy eating recommendations. No effect was observed on the participants' physical activity, anthropometric, and cardio-metabolic outcomes.

In detail, our findings suggest that the active interventions involving healthy diet promotion (DG and PADG), as compared to the CG, that consisted of an information booklet about diet and physical exercise, improved the healthy habits of the participants, inducing a larger consumption of whole grains, legumes, and fruits and a lower consumption of processed meats and spirits. These findings are similar to results observed in some previous studies.[31,32] In Simpson et al. work,[31] where healthy volunteers were invited to participate in a pre-post intervention study, the median of red and processed meat consumption decreased from 1.3 portions to 0.7 portions a day.

Considering BMI and weight, we did not observe a positive effect of being assigned to the intervention groups in respect to the CG. This result differs slightly from Mouodi et al.,[32] who documented an average weight loss of 8.9 kg (95% CI: 7.7–10.2) and a reduction of 2.8 kg/m in BMI in subjects with high grade of obesity, after an intensive lifestyle intervention. However, having used a composite outcome (see the Method section), it makes it

difficult to compare studies where weight and BMI have been evaluated separately.

We did not find any difference between the three intervention groups and the CG regarding the increase of physical activity, and, more importantly, no difference was observed between the PAG and the CG. Likely, this result is in part due to the high proportion of non-compliance among the participants assigned to the PAG, which lead to diluted ITT effect. Additionally, in interpreting our results regarding physical activity outcomes and interventions, we should consider that 70% of the participants in the study declared to be employed. The amount of time that employees spend in their worksites and the lack of work-based sports facilities or protected routes for walking, running, or cycling can act as barriers to practicing more physical activity. As a consequence, changing physical activity levels may be more challenging than changing diet. Moreover, there is probably less awareness of the association between physical activity and cancer than between diet and cancer. Thus, it is possible that participants prioritized dietary rather than physical activity goals.

Our findings did not show significant differences between groups in terms of biochemical measurements. On the contrary, previous researches[33–36] had shown that exercise can be beneficial in improving subjects lipid

profile. In this study the intensity of our intervention program was probably not sufficiently high to allow for a comparison with the programs adopted within other projects.[37–39]

Stratifying by cancer screening program, we found that, while among participants in the breast cancer screening the effect of the interventions was limited to a reduction in the red and processed meats consumption, among the participants in the colon cancer screening, positive changes compared to the CG were also observed for the consumption of extra-virgin oil, whole grain, legumes, and alcohol. Observing a result for red meat in both programs could be due to the fact that people are aware that high consumption of red and processed meat is implicated in the development of cardiovascular disease (CVD), and colon cancer.[40,41] On the other hand, the higher sensitivity to the interventions among the participants in the colon cancer screening program, suggests that people are probably quite aware of the relationship between diet on colon cancer occurrence.

Similar results have been found by studies conducted on sub-populations at-risk for colon cancer and, more in general, by studies that investigated interventions aimed to encouraging lifestyle changes in order to reduce the risk of colon cancer.[42–46] Smith-Warner et al.[42] reported an increase from 7.3 servings of fruits and vegetables at baseline to 11.9 servings at 12 months of follow-up, after a 1-year structured dietary intervention. Similarly, Robb et al.[43] found an increase in fruit and vegetable intake 6 months after a standard leaflet on healthy lifestyle plus a brief, tailored feedback. Participants in the bowel health to better health (BHBH) lifestyle intervention[44] significantly increased their fiber intake, likely due to an increase in the consumption of cereals. In the Project PREVENT,[45] a multisite randomized clinical trial, a significant increase in multivitamin intake and a significant decrease in red meat consumption was estimated in the treated group compared to the controls. In the randomized controlled trial BeWEL,[46] the authors evaluated the impact of diet and physical activity intervention among attendees in colorectal cancer screening program. After 12 months, changes in body weight, physical activity, eating and drinking habits were observed in the intervention arm. A third of participants achieved the clinically relevant goal of 5% weight loss, and almost a quarter achieved the program target of 7% weight loss. In addition, a decrease in fat intake and an increase in fruit and vegetable consumption and physical activity were also found.

The failure to increase physical activity among the colon cancer screening participants is in line with the results from other lifestyle interventions conducted in a similar context.[43–45]

The effects observed in the breast cancer screening group were limited. This is not in line with the literature that provides evidence of a certain efficacy of lifestyle interventions in similar contexts. The largest program of lifestyle interventions "Well-Integrated Screening and Evaluation for Women Across the Nation" (WISEWOMAN) program, in conjunction with the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), indicated that the program had been successful in reducing hypertension, BMI, and dietary fat as well as in increasing physical activity.[17] In the ALPHA study,[47] where postmenopausal women were randomized to undertake 45 min of moderate to vigorous exercise five times a week, after a 1-year follow-up period the intervention groups showed significantly greater losses in adiposity markers (body weight, body fat, subcutaneous abdominal fat) than the controls. The "Get healthy after Breast cancer" study,[48] did not find any significant changes in fruit or vegetable servings per day or takeaways and fast food frequency per week; instead a statistically significant effect from baseline to 6 months for weight loss and total physical activity minutes per week was found.

The limited effect of the active interventions observed within the breast cancer screening program in the Sti.Vi study may have several explanations. First of all, in our study, compliance to the courses was quite low within the breast cancer screening program (31.8% of the participants did more than one absence to the courses), so participants recruited through this program and randomized to the active interventions likely reacted more similarly to the controls and, consequently, the average effect of the interventions resulted to be diluted. The low adherence to the active interventions also stresses the need for the development of innovative strategies to enhance participants retention. Furthermore, the recruitment of younger participants through breast cancer screening compared to colorectal screening may influence the perceived risk participants have relating to unhealthy lifestyles. Finally, it should be considered that the awareness of the association between unhealthy lifestyles and breast cancer could be quite low among general public.

The Sti.Vi study used the screening channel to reach individuals, with the idea that screening may be a favorable moment to perform lifestyle interventions.[14–22] The study was not aimed at evaluating the efficacy of proposing the interventions in this specific setting, but with a participation rate lower than the expected (12% of enrolled participant did not accomplish the baseline visit and 24.8% of the participants did more than one absence to the course), it seems to contradict the hypothesis that the screening is an ideal context. Furthermore, we know that lifestyle interventions nested within screening programs reach only those people who choose to adhere to the program, who likely are a selected subgroup of the population. For this reason, the results of the present study could be poorly generalizable to the whole population.

When interpreting the results of our study, it should be also considered that the outcomes have been measured

through self-report questionnaires. These are an easy and relatively cheap tool, but it is well-known that people are often biased with what they report on their own experiences. For example, individuals are more likely to report information that is considered to be "clinically" acceptable or preferred. Self-reporting could have brought to an overestimation of the adherence to healthy behaviors. In future studies, actual food consumption or changes should be verified through objective measures as metabolic parameters. Finally, as a limitation of this study, we would like to stress that the questionnaire was not validated.

In conclusion, the findings of the Sti.Vi study support the hypothesis that communicating health education messages though courses where the participants learn to choose and properly cook the "right" foods and to perform simple physical exercises can increase awareness and induce behavioral changes. In particular, we found that active interventions can induce diet changes compared to the CG consisting in an information booklet about diet and physical exercise. However, the low participation rate among breast and colorectal cancer screening attendees and the poor compliance to the courses suggest that it is important and necessary to develop innovative strategies to enhance participants' retention, with the ultimate goal of increasing awareness and inducing positive lifestyle changes.

Authors' contribution

Design of the study: NS, FG, CA, AP, CS, and LG. Data collection: FG, CA, NS, and LG. Data analysis: ER, MB, and EC. Drafting of the paper: ER, MB, and LG. All authors reviewed and approved the final draft of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical standards disclosure

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Ethics Committee of AOU Città della Salute e della Scienza. Written informed consent was obtained from all subjects/patients. The trial was registered in ClinicalTrials.gov (NCT03118882).

Significance for public health

Unhealthy diets, physical inactivity, alcohol and tobacco consumption are among the leading risk factors for non-communicable diseases. A number of cancer cases could be prevented by eating a healthy diet, maintaining a healthy weight and being more active. The Sti.Vi randomized trial, conducted among cancer screening participants, aimed to increase awareness about these risk factors and tried to induce changes in diet and physical activity habits. Our results suggest that the application of active interventions can help achieve this aim of changing habits, particularly relating to modification in diet. However, low compliance rates with these programs suggests that this process requires the application of innovative strategies to enhance participants' retention.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental material

Supplemental material for this article is available online.

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