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A novel personalized approach to cardiovascular prevention: the VIVOPTIM programme

Abbreviated title: Cardiovascular prevention: the VIVOPTIM programme

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Summary

Background. – Cardiovascular diseases are a leading cause of mortality, but a substantial proportion are preventable.

Aims. – The Mutuelle Générale de l'Education Nationale (MGEN), a provider of private health insurance in France, has developed the VIVOPTIM programme, a novel digital approach to healthcare based on individualized, multiprofessional, ranked management of cardiovascular risk factors.

Methods. – Between November 2015 and June 2016, eligible individuals (age 30–70 years) from two regions of France were invited to participate. Volunteers completed a questionnaire based on the Framingham Heart Study Risk Score and were assigned to one of three cardiovascular risk levels. VIVOPTIM comprises four components: cardiovascular risk assessment, instruction on cardiovascular diseases and associated risk factors, personalized coaching (telephone sessions with a specially trained healthcare professional to provide information on risk factors and disease management, set individual health targets, monitor progress and motivate participants), and e-Health monitoring.

Results. – Data from 2240 participants were analysed. Significant benefits were observed on mean systolic blood pressure (–3.4 mmHg), weight (–1.5 kg), smoking (–2.2 cigarettes/day) and daily steps (+1726 steps/day (all $P < 0.0001$), though not on weekly duration of exercise (–0.2 hours/week, $P = 0.619$).

Conclusion. – As a result of the positive mid-to-long-term results of the pilot programme on weight, smoking, blood pressure, and uptake of physical activity, the VIVOPTIM programme was extended to the whole of France in 2018 and has the potential to have a genuine impact on patient care and organization of the healthcare system in France.

Résumé

Contexte. – Les maladies cardiovasculaires sont une des principales causes de mortalité, mais une proportion importante de ces décès pourrait être évitée.

Objectifs. – La Mutuelle Générale de l'Education Nationale (MGEN), assurance maladie privée en France, a développé le programme VIVOPTIM, basée sur une prise en charge individualisée, multiprofessionnelle et hiérarchisée des facteurs de risque cardiovasculaire.

Méthodes. – Entre novembre 2015 et juin 2016, les personnes éligibles (âgées de 30 à 70 ans) de deux régions de France ont été invitées. Basé sur le score de risque de Framingham, les volontaires

ont été assignés à l'un des trois niveaux de risque cardiovasculaire. VIVOPTIM comprend quatre volets : une évaluation du risque cardiovasculaire, une information sur les maladies et les facteurs de risque cardiovasculaires, un coaching personnalisé (séances téléphoniques, fixation des objectifs de santé individuels, surveillance des progrès et motivation des participants) et un suivi e-Santé.

Résultats. – Les données de 2240 participants ont été analysées. Des bénéfices significatifs ont été observés sur la pression artérielle ($-3,4$ mmHg), le poids ($-1,5$ kg), le tabagisme ($-2,2$ cigarettes par jour) et le nombre de pas ($+1726$ pas par jour (tout $P < 0,0001$), mais pas sur la durée hebdomadaire de l'exercice ($-0,2$ heure par semaine, $P = 0,619$).

Conclusion. – Grâce aux résultats positifs du programme pilote sur le poids, le tabagisme, la pression artérielle et l'activité physique, le programme VIVOPTIM, étendu à la France entière, a le potentiel d'avoir un fort impact sur les soins et sur l'organisation du système de santé.

KEYWORDS

Prevention;

Blood pressure;

Smoking;

Weight

MOTS CLÉS

Prévention ;

Pression artérielle ;

Tabagisme ;

Poids

Abbreviations: AHA, American Heart Association; CCTIRS, Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé; CNIL, Commission Nationale Informatique et Libertés; MGEN, Mutuelle Générale de l'Education Nationale; SBP, systolic blood pressure; SD, standard deviation.

Introduction

Cardiovascular diseases are the leading cause of mortality, worldwide and in France [1]. However, a considerable number of such deaths are theoretically avoidable [2]. Prevention strategies are known to exert beneficial effects – to varying degrees – on various major risk factors for cardiovascular mortality, i.e. hypertension, diabetes mellitus, smoking and atherogenic dyslipidaemia. In addition to these, other non-independent risk factors are also theoretically modifiable. This is the case for overweight and obesity, a sedentary lifestyle, a non-Mediterranean type diet, social deprivation and chronic stress [3]. Nevertheless, despite this widely acknowledged scientific evidence, the prevalence of these risk factors has not improved within the population, and overweight and obesity have increased [4].

The first step in cardiovascular prevention is patient education. Messages of prevention can be provided collectively, via prevention campaigns aimed at the public at large, and are generally initiated by national public services. They can also be individually targeted, in which case they are generally discussed during visits to a healthcare specialist. However, the cost-effectiveness of individualized programmes has been the subject of considerable debate. Targeting high-risk patients increases efficiency, but the benefit to healthcare systems as a whole is less notable than that of non-targeted nationwide interventions, such as campaigns to reduce dietary intake of trans fats or salt [5,6]. Nowadays, in addition to classic healthcare promotion campaigns, patients can also search for information themselves, either on the internet or via the different social networks, and both are endless sources of misleading or false information about cardiovascular prevention. Amongst others are the conspiracy theories, particularly regarding the purported adverse effects of cardiovascular agents used for prevention. The popularity of such stories has a particularly deleterious effect on treatment compliance and even on prescribing habits [7]. This phenomenon came to light by comparing the results of the Esteban study [7] with those of the Nutrition Health national survey between 2006 and 2015 particularly with regard to the prescription of statins. Despite the preventive measures put in place, there has been very little progress over recent decades with regard to the management of cardiovascular risk factors [8].

Patients who are given comprehensive information on measures for cardiovascular risk reduction often see the changes as a complete upheaval of their lifestyle, affecting diet, treatment compliance, physical activity and smoking, to name but a few. Many see these changes as such an

intrusion into their personal life and freedom that they ultimately give up their good resolutions and lose all motivation. From a population perspective, the onset of a considerable number of cardiovascular events can be accounted for by modifiable risk factors [9,10], and therefore innovative motivational strategies have the potential to exert a significant impact on cardiovascular morbimortality.

Given the undeniable inefficacy of both collective and individual cardiovascular prevention strategies to date, the Mutuelle Générale de l'Éducation Nationale (MGEN; General Mutual of National Education) – a provider of private health insurance in France – has developed the VIVOPTIM programme. The primary objective is to provide a novel digital approach to individual wellbeing based on personalized, ranked management of cardiovascular risk factors by a multiprofessional team of healthcare providers. MGEN is a not-for-profit complementary health insurance that covers over four million individuals in France for healthcare costs not covered by the mandatory national health insurance.

This paper presents the details of this pilot project and the clinical results 24 months into the programme. Work is also underway on the medical and economic impact of this programme, and how it is likely to affect the organization of the healthcare system in France in terms of prevention. The results of that branch of our work will be the subject of a dedicated paper.

Patients and methods

Identification and recruitment of participants

Between November 2015 and June 2016, eligible individuals (age 30–70 years) from two regions of France – all of whom were covered by an MGEN complementary health insurance policy – were invited to take part in the study by mail, telephone or during promotional events. At inclusion, volunteers were asked to complete a questionnaire based on the Framingham Heart Study Risk Score for cardiovascular events [11] that included eight questions on individual cardiovascular risk factors. The Framingham Heart Study Risk Score for cardiovascular events was chosen instead of the SCORE scale for several reasons, particularly the upper age limit (which is 74 in the Framingham Heart Study Risk Score versus 65 in SCORE). Global cardiovascular risk was calculated and participants were assigned to one of three risk levels (level 1, 10-year risk of a cardiovascular event <

10%; level 2, 10–20%; level 3, > 20% or previous history of cardiovascular events, diabetes mellitus, hypertension, renal failure or obesity).

General information about cardiovascular risk prevention was provided to level 1 participants. Due to the lack of any likely substantial benefits, this group was not offered a personalized programme. Participants in levels 2 and 3 were asked to complete a more detailed questionnaire (60–80 questions) regarding their cardiovascular risk profile. Based on their answers, patients received suggestions for personalized objectives. There were three types of objectives: healthier diet, increased physical activity and improved personal care. The latter could take different forms, such as a more balanced diet, weight loss, stricter adherence to drug therapy, or reducing cigarette consumption. These objectives were agreed upon during a first motivational telephone interview conducted by a trained nurse, thus concluding the recruitment process.

Data pertaining to participants with a cardiovascular risk level of 2 or 3 who finalized the recruitment process and provided their written consent to participate were included in the statistical analysis. Data pertaining to risk level 1 participants were not included as their exposure to the programme was limited to online information and quizzes on cardiovascular disease and risk factors.

Intervention

There were four components to the programme: cardiovascular risk assessment during the inclusion process, education to improve understanding of cardiovascular diseases and associated risk factors, personalized self-management support and follow-up, and e-Health monitoring. These were not intended to replace the patients' usual care provider and did not cover drug prescriptions or clinical management. As long as participants provided their written consent, individual health data (collected during the programme) were also made available to their general practitioners, who could request the data via a dedicated platform on the VIVOPTIM website.

Individuals of all risk levels had access to a website providing information on cardiovascular diseases [12]. This included general data on cardiovascular risk factors (fact sheets, articles, quizzes, videos, personalized recipes, etc.), e-learning sessions, and online communities where participants could share information and provide mutual support.

Personalized self-management support was available for risk level 2 and 3 participants. It comprised up to six telephone coaching sessions conducted by a specially trained nurse or another

healthcare professional (such as a dietician, a medical sports trainer, or a tobaccologist) over the course of a year. The designated referral nurse was in charge of providing information on risk factors and disease management, setting up individual health targets, monitoring progress and providing motivational support to help participants reach their individual objectives. Personal aptitude for change was assessed regularly [13,14] to help the healthcare professionals coach the participants. The content of the coaching could then be adjusted accordingly. A follow-up coaching session took place after an overall participation period of 18 months.

Participants in the risk level 3 group – particularly those with a history of cardiovascular events – were offered e-Health monitoring of weight and blood pressure, using connected scales and a home blood pressure measurement device.

Data collection and reporting

Demographic characteristics, baseline risk factors and disease history were documented in the inclusion questionnaire. Clinical measurements were collected from participants via the online questionnaires and during structured interviews with trained nurses. There were no predefined frequencies or mandatory measures. The frequency of coaching sessions was agreed upon between the referral nurse and the study participant. Clinical criteria included systolic blood pressure (SBP), body weight, cigarette use (defined as current smoking or stopped ≤ 2 years ago) and physical activity (calculated from reports of weekly duration of physical activity and daily steps).

As all health data were self-reported by the participants, in order to reduce bias, we implemented several procedures:

- All measurements for a participant were performed using the same device; the referring nurse ensured the proper use of devices
- Concerning blood pressure measurements, home blood pressure values were systematically preferred to measurements made by the attending physician or another healthcare professional. For group 3 patients, there was a systematic dispatch of a connected blood pressure monitor with systematic teletransmission of blood pressure self-measurement values (Terraillon, Tensioscreen). Group 2 patients either had a home blood pressure self-measurement device – in which case it was these values that were taken into account at the different examination times – or they did not have a home device – in which case it was the blood pressure measurements performed by the

attending physician that were entered into the file. Home blood pressure monitoring was performed according to the recommendations of the French Society of Hypertension [15] (measurements in the seated position, 5 minutes of complete rest before each series of measurements, a series of three measurements in the morning and a series of three measurements in the evening for 3 consecutive days):

- Daily numbers of steps were measured with applications on the volunteers' smartphones, e-watches or activity trackers;
- Weight measurement was performed in the morning in light clothes and bare feet between getting up and breakfast (after the morning toilet).

For each participant, there could be zero, one or multiple values for a given criterion based on individual objectives, individual progression, frequency of use of telemedicine devices and duration of follow-up in the programme. Each participant's involvement in the programme was assessed based on the number of coaching calls, the total duration of those calls and the overall duration of active participation.

An academic scientific committee validated the main study design, including the content of the website and the e-coaching. Both the programme and the study received approval from the appropriate ethics and administrative committees: the Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé (CCTIRS; French Advisory Committee on Information Processing in the Field of Health) (Dossier n°15.216bis dated 13 May 2015), and the Commission Nationale Informatique et Libertés (CNIL; French Data Protection Authority) (Délibération n°2015 273 dated 13 July 2015).

Statistical analysis

The population eligible for clinical evaluation was made up of all risk level 2 and 3 participants who completed the recruitment process and provided their informed consent. In addition to the total population, five groups were also defined for the statistical analysis, corresponding to the clinical criteria assessed (SBP, body weight, cigarette use, weekly duration of physical activity, and daily steps). For each given criterion, the corresponding group comprised all participants who underwent at least two criteria assessments at intervals in excess of 1 month. It is important to note that each participant could belong to several groups as they could declare values for several clinical criteria.

Descriptive statistics were performed to determine the demographic characteristics, cardiovascular history, and cardiovascular and metabolic risk factors of the six populations, i.e. the overall population and the five groups. Descriptive statistics were also computed for the clinical criteria and for measurements of individual involvement in the programme. Results are presented as frequencies and percentages for categorical variables, and as means and standard deviations (SDs) for continuous variables. For each clinical criterion, the progression between inclusion and the end of the individual follow-up period was estimated for individuals in the corresponding group. As previously mentioned, none of the inter-measurement intervals were mandatory. Furthermore, participants could drop out before the end of the scheduled 18-month follow-up period. Consequently, where required, the last reported criteria measure for each individual was carried forward to the end of the total duration of 18 months. To assess the progression of each clinical criterion, Student's paired *t* test was performed with a type I error of 5% and under the null hypothesis of an absence of progression. If the *t* test was significant, a linear regression model was fitted to the data. A step-down procedure with a threshold of 0.2 was used to select the final covariates from among those tested, i.e. sex, age, criteria measurements at inclusion and a history of cardiovascular events. All analyses were performed using SAS software (version 9.4; SAS Institute, Carry, NC) and R (version 3.5.1) for graphical display.

Results

Fig. 1 shows the final numbers of participants in the study population and in each of the five groups, with details of reasons for exclusion. There were 2240 participants in the overall population, of whom 827 declared at least two SBP values at intervals > 1 month. Likewise, there were 1411, 79, 148 and 83 participants who declared at least two values at intervals > 1 month for weight, cigarette use, duration of exercise and daily number of steps, respectively.

In the overall population, the mean age of participants was 62.0 ± 7.2 years and 59.3% were male (Table 1). Many patients had risk factors for cardiovascular disease: 11.3% were in secondary cardiovascular prevention, 9.1% had diabetes, 37.8% hypertension and 22.9% obesity, but few (7.4%) were active smokers. Overall, 72.1% of the study population were risk level 3 (high calculated global cardiovascular risk). Individual characteristics in each of the five groups were generally similar to those of the whole population (Table 1). Logically, involvement in the programme was higher for the five groups (Table 1).

Fig. 2 shows the statistically significant effects of the interventions on SBP (-3.4 mmHg, $P < 0.0001$), weight (-1.5 kg, $P < 0.0001$), smoking (-2.2 cigarettes/day, $P < 0.0001$), and daily steps ($+1726$ steps/day, $P < 0.0001$), though not on weekly duration of exercise (-0.2 hours/week, $P = 0.619$).

For the progression of each clinical criterion, a linear regression model was fitted to the data by a step-down procedure to assess the covariates (age, sex, parameter's level at inclusion, cardiovascular risk factors and presence of a cardiovascular disease). None of the multivariable models were statistically significant, as only a marginal part of variance could be explained by the models ($< 10\%$, data not shown), and no parameter entered any of the four multivariable models. We therefore failed to identify any specific determinants of the clinical benefits.

Discussion

The salient findings of the VIVOPTIM intervention pilot programme are that this innovative, individualized, multiprofessional, ranked management of cardiovascular risk factors had statistically significant beneficial effects on SBP, weight, smoking and daily number of steps, though not on weekly duration of exercise, after a mean follow-up period of 14 months.

We postulate that the two main explanations for our positive results are the design of the VIVOPTIM programme and the characteristics of the study population. With regards to the latter, we observed several discrepancies compared to other population-based French cohorts [7,8,16]. For example, the smaller proportion of active smokers (7.4% in VIVOPTIM vs 18.0 in the CONSTANCES cohort [15] and 21.7% in the Esteban study [7,8]) suggests a relatively health-conscious population [17]. Positive results in a highly selected population of health-conscious motivated volunteers need to be confirmed at the population level, but we believe that the design of the programme also helps to motivate the participants and thus the positive results. Indeed, we considered that the management of lifestyle changes required the support of specialists capable of providing both technical support (e.g. tobaccologist, dietician, sports instructor) and psychological support (referral nurse specially trained in motivational interviews, active listening and coaching skills).

The medical literature has reported on countless intervention programmes that focus on cardiovascular risk factors [18]. Over 20 years ago, an American Heart Association (AHA) task force on the primary prevention of coronary heart disease concluded that: 'if the burden of coronary heart

disease in American society is to be substantially reduced, primary prevention must be improved' and 'Risk factor modification in the general public and persons at high risk offers the best opportunity for effectively reducing the prevalence of coronary heart disease in the United States'. [19]. Later, a Cochrane review [18] highlighted the impact that lifestyle interventions have on total mortality, as well as fatal and non-fatal cardiovascular events when tailored to particular categories of patients, such as high-risk patients with hypertension or diabetes. Nevertheless, in terms of the impact of these interventions on modifiable risk factors, the marked heterogeneity between trials made pooled results of 'dubious validity' [18]. More recently, another meta-analysis [20] concluded that multifactorial lifestyle interventions lowered blood pressure, total cholesterol, body mass index and waist circumference, at both 6 and 12 months, and increased physical activity at 12 months. For the authors, multifactorial lifestyle interventions clearly represent a valid tool for reducing cardiovascular risk factors and should be implemented in at-risk groups and in primary prevention [20]. In Sweden, a community and primary care-based intervention demonstrated beneficial effects on blood pressure, glycaemia and smoking [21]. In overweight and obese patients, a systematic review and network meta-analysis on the impact of long-term lifestyle programmes on weight loss and cardiovascular risk factors found that a combination of diet and exercise was more effective than either diet or exercise alone [22]. The existing literature on multifactorial lifestyle interventions is extremely heterogeneous: very few studies have lasted longer than 6–12 months and, to our knowledge, none have assessed the impact of individualized management of cardiovascular risk factors for > 1 year, such as was conducted in the VIVOPTIM pilot programme.

Our study has several limitations. First, given that the study population of volunteers was highly selected, our positive results cannot be directly extrapolated to the population at large: the male/female and geographical distributions were similar, but the mean age was about 6 years older than that of the 250,000 MGEN-eligible members [23]. Second, because most data were patient-reported, discrepancies in comparison with the real world cannot be excluded, although teletransmission of data and corroboration with coaches did limit the risk. Third, because interventions were both qualitatively and quantitatively heterogeneous, individually tailored to each participant, with the potential support of one or more healthcare professionals, it was not easy to quantify or accurately assess their impact. Fourth, follow-up duration was also extremely diverse, ranging between 1 and 24 months, according to the participants' genuine motivation to change their lifestyle. Fifth, since it was

difficult to invite volunteers and subsequently tell them that they had been randomized to the control group without any intervention, there was no control group in the present study.

From a financial standpoint, the VIVOPTIM programme is in keeping with both a conceptual and an operational commitment. Conceptual, because the primary objective was to show that this comprehensive end-to-end approach to patient care has beneficial effects on individual cardiovascular risk profiles and ultimately reduces the incidence of cardiovascular accidents; and operational, since the aim was to implement this approach as extensively as possible.

In light of the optimistic results of the VIVOPTIM pilot programme to date, the board of directors of the MGEN decided to extend the programme to the whole of France as from July 2018. With this in mind, and in light of the analysis of the results of the pilot phase, the following noteworthy decisions have been made: (1) future inclusion in the programme will be both simpler and quicker; (2) cardiovascular risk assessment will be optimized; (3) the number of coaching sessions will be increased (up to seven); (4) a module of stress management will be added as a complement to lifestyle changes; and (5) management of interactive content will be improved, with a particular focus on leveraging individual motivation.

In conclusion, despite the limitations, the VIVOPTIM pilot programme has shown extremely promising results on weight, smoking, blood pressure, and uptake of physical exercise. This programme has the potential to have a meaningful impact on patient care and organization of the healthcare system in France.

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Disclosure of interest

All authors received honoraria from the MGEN for their participation as members of the VIVOPTIM committees.

Author contributions

All authors contributed to the conception or design of the work. Jacques Blacher, Virginie Femery and Anne Dubois contributed to the acquisition, analysis and interpretation of data for the work. All other authors contributed to analysis and interpretation of data of the work. Jacques Blacher and Virginie Femery drafted the manuscript. All authors critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Figure legends

Figure 1. Flow chart of the VIVOPTIM programme.

^a Participants with < 2 reported values (or 2 values reported within < 1 month).

Figure 2. A. SBP, B. weight, C. cigarette use, D. weekly duration of physical exercise and E. daily steps at inclusion and the end of follow-up. Bars show means, error bars show SDs. The results of the univariate *t* test on progression between inclusion and the end of individual follow-up are shown. CI, confidence interval; SBP: systolic blood pressure; SD, standard deviation.

Table 1 Characteristics of the overall population and the five groups.

Variables	Total (n = 2240)	SBP (n = 827)	Weight (n = 1411)	Cigarette use (n = 79)	Duration of exercise/week (n = 148)	Number of steps/day (n = 83)
Cardiovascular risk factors						
Age (years)	62.0 ± 7.2	63.2 ± 6.7	62.2 ± 7.2	60.5 ± 7.2	61.2 ± 7.6	61.8 ± 7.5
Female	912 (40.7)	351 (42.4)	592 (42.0)	25 (31.6)	60 (40.5)	31 (37.3)
Risk level 2	624 (27.9)	98 (11.9)	291 (20.6)	16 (20.3)	23 (15.5)	15 (18.1)
Risk level 3	1616 (72.1)	729 (88.1)	1120 (79.4)	63 (79.7)	125 (84.5)	68 (81.9)
Chronic renal failure	27 (1.2)	15 (1.8)	18 (1.3)	3 (3.8)	3 (2.0)	2 (2.4)
Previous CV event	253 (11.3)	115 (13.9)	186 (13.2)	13 (16.5)	22 (14.9)	11 (13.3)
Hypertension	846 (37.8)	431 (52.1)	581 (41.2)	25 (31.6)	66 (44.6)	29 (34.9)
Diabetes	203 (9.1)	87 (10.5)	140 (9.9)	8 (10.1)	14 (9.5)	7 (8.4)
Prediabetes	334 (14.9)	128 (15.5)	222 (15.7)	13 (16.5)	26 (17.6)	11 (13.3)
Dyslipidaemia	734 (32.8)	306 (37.0)	505 (35.8)	25 (31.6)	50 (33.8)	25 (30.1)
Smoking ^a	166 (7.4)	42 (5.1)	81 (5.7)	79 (100)	9 (6.1)	2 (2.4)
Clinical characteristics at inclusion						
Weight (kg)	77.8 ± 14.7	78.3 ± 15.2	79.8 ± 15.1	77.4 ± 14.8	80.7 ± 15.2	82.3 ± 14.4
BMI (kg/m ²)	26.9 ± 4.7	27.2 ± 4.5	27.6 ± 4.6	26.3 ± 4.6	28.0 ± 4.4	28.3 ± 4.5
Obese	512 (22.9)	203 (24.5)	394 (27.9)	16 (20.3)	50 (33.8)	26 (31.3)
Overweight	839 (37.5)	339 (41.0)	572 (40.5)	33 (41.8)	65 (43.9)	41 (49.4)
SBP (mmHg)	129.0 ± 9.7	130.1 ± 12.4	129.4 ± 12.0	127.2 ± 11.5	129.9 ± 11.9	130.3 ± 10.0
Physical activity at inclusion						
Duration of exercise (hours/week)	2.8 ± 3.8	3.1 ± 4.0	3.0 ± 4.0	3.8 ± 4.8	3.1 ± 4.7	3.0 ± 3.7
Number of steps (steps/day)	6314 ± 1581	5609 ± 2422	5471 ± 2455	6774 ± 1884	5335 ± 2201	5592 ± 2269
Involvement in the programme						
Number of coaching	4.2 ± 2.7	6.2 ± 2.0	5.5 ± 2.3	5.7 ± 2.3	6.1 ± 1.9	6.0 ± 2.0

calls						
Total duration of	126.8 ±	203.1 ±	173.2 ±	181.5 ± 106.4	199.4 ± 97.1	195.0 ± 96.2
coaching (minutes)	104.8	102.3	100.8			
Duration of active	9.5 ± 8.6	15.1 ± 9.6	13.0 ± 5.6	13.7 ± 5.4	14.5 ± 5.3	14.7 ± 6.4
participation						
(months)						

Data are expressed as mean ± standard deviation or number (%). BMI: body mass index; CV:

cardiovascular; SBP: systolic blood pressure; SD: standard deviation.

^a Current smoker or stopped ≤ 2 years ago.

Figure 1 [Note to journal: besides style alterations, please remove brackets round superscript a's]

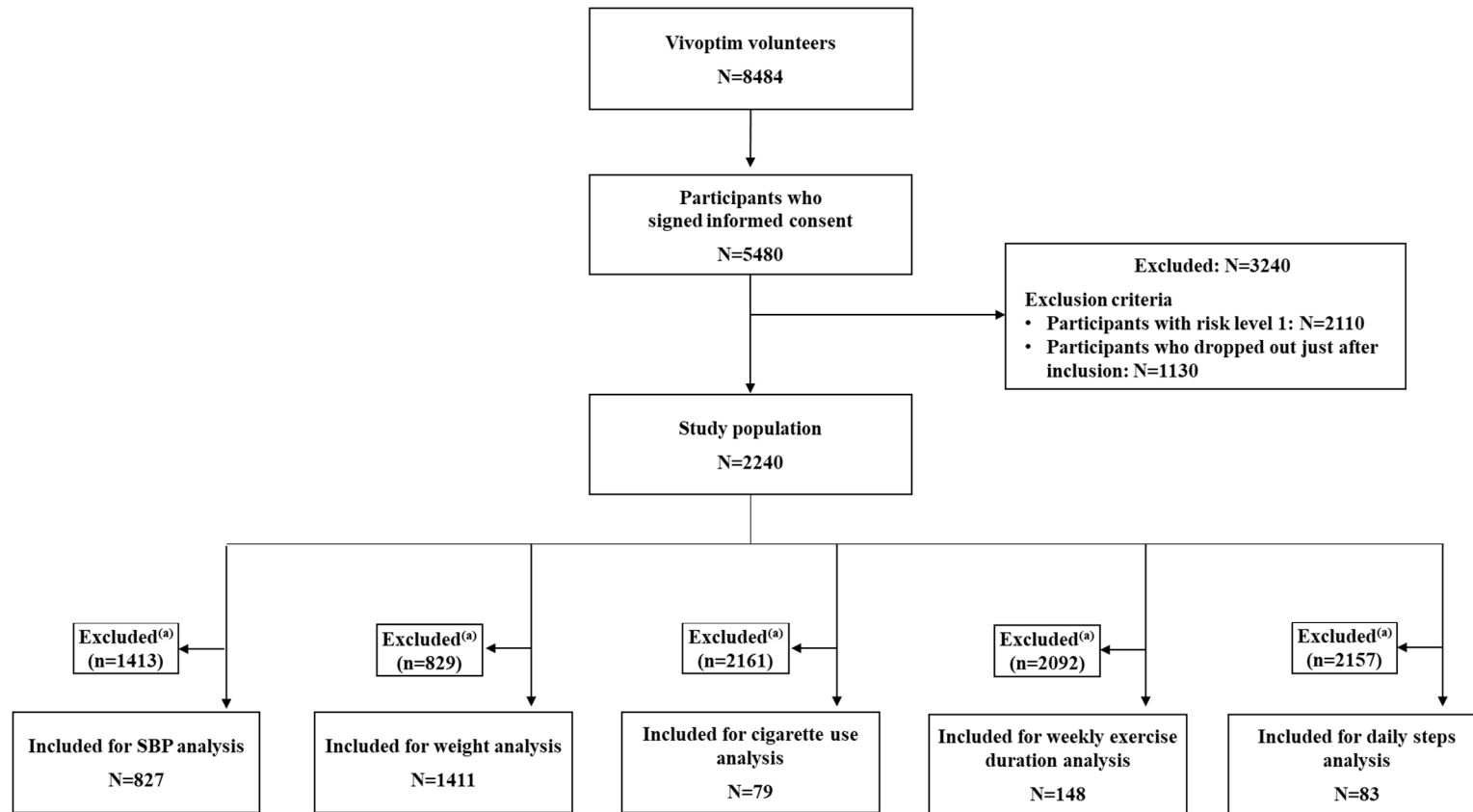
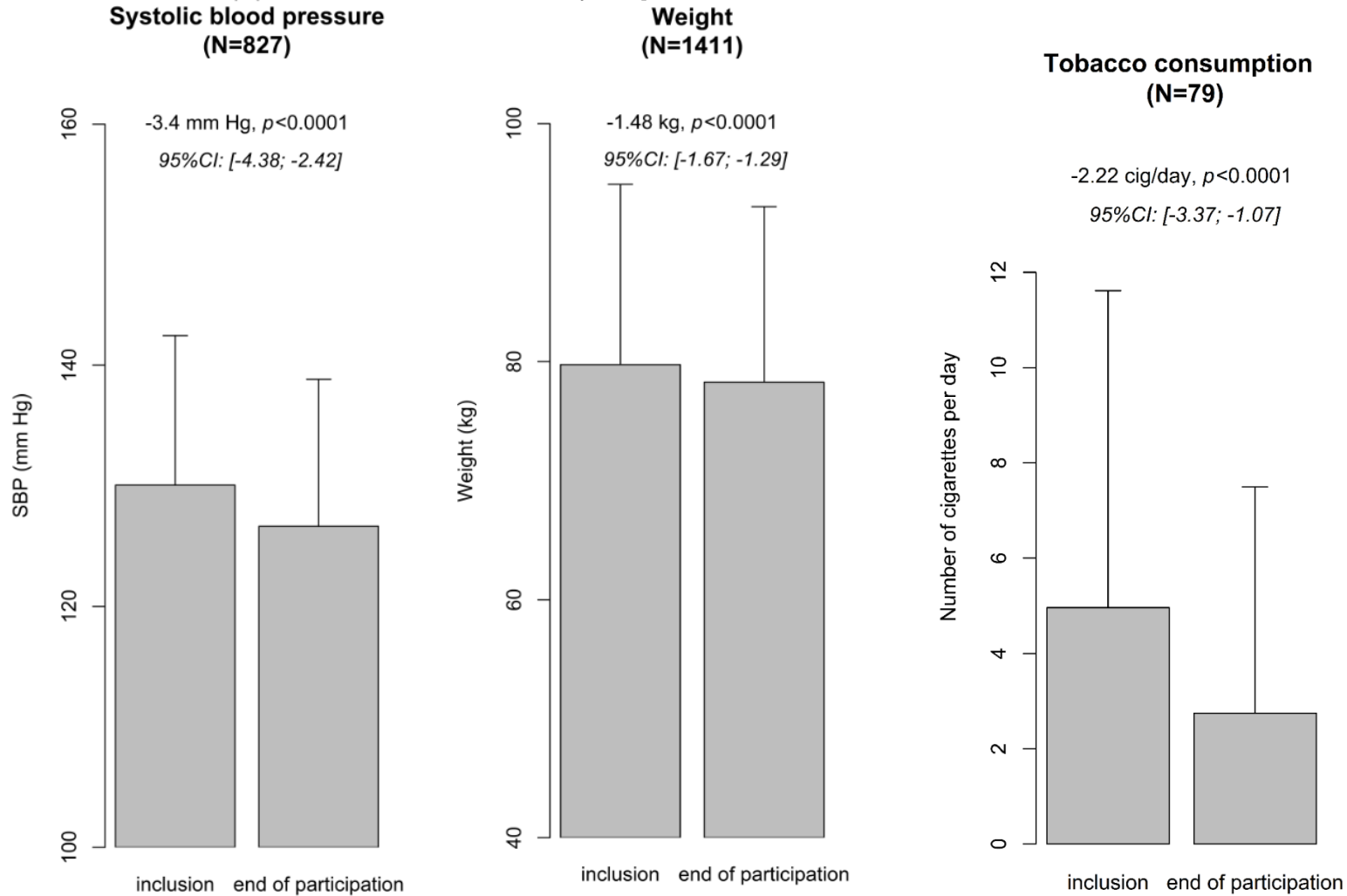
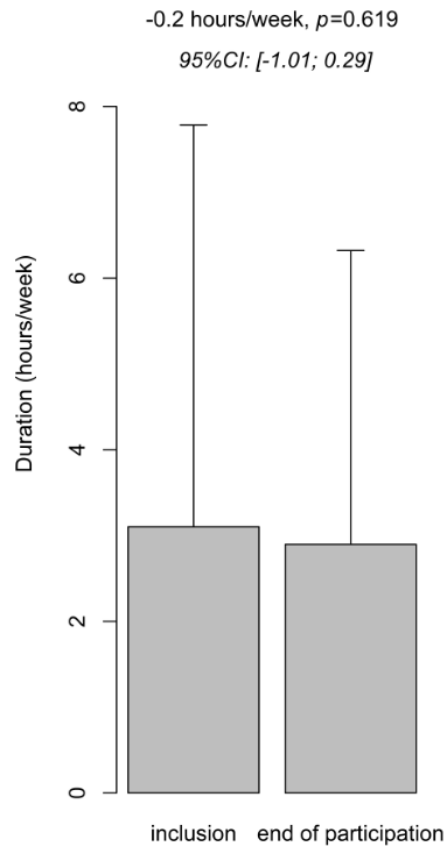


Figure 2 [Note to journal: besides style alterations, please replace titles with A, B, etc. but add “n = 827” etc. under bars. If titles are kept, please alter “Tobacco consumption” to “Cigarette use”, “Daily walking distance” to “Daily steps”. Please alter y axis of D to “Exercise duration (hours/week)”. Suggest alter numbers to 1 decimal place]



**Weekly duration of exercise
(N=148)**



**Daily walking distance
(N=83)**

