ORIGINAL PAPER

Donor InSight: characteristics and representativeness of a Dutch cohort study on blood and plasma donors

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Vox Sanguinis

Background and Objectives More insight into donor health and behaviour may contribute to more efficient and focused strategies regarding donor care and management. Donor InSight (DIS) is a Dutch cohort study of blood and plasma donors. We aimed to outline the objectives and methods of DIS, describe the cohort, and compare it to the active Dutch donor population.

Materials and Methods In 2007-2009 (DIS-I, n = 31 338) and 2012-2013 (DIS-II, 34 826, of whom 22 132 also participated in DIS-I) questionnaire data on demographics, donation, lifestyle, family composition, health and disease were collected. A second follow-up (DIS-III, n = 3046), including donors with differing haemoglobin trajectories, was completed in 2015-2016. DIS-III includes data on genetic determinants, iron and red cell indices. Representativeness of the DIS-I sample for the entire Dutch donor population was assessed by comparing characteristics of both.

Results Donor InSight was initially set up because of a need for more detailed information and evidence as a basis for decision-making in blood banks. DIS-I sample is comparable to the total Dutch donor population in terms of age, body mass index, haemoglobin level, blood pressure, blood type and donation behaviour.

Conclusion Donor InSight is a cohort study representative of the Dutch donor population. It provides evidence to support evidence-based decision making.

Key words: blood donors, demographics, donor health, epidemiology, lifestyle.

Introduction

Blood donor research is an expanding field in which experts in epidemiology, medicine, psychology and sociology collaborate to safeguard a sufficient and safe blood supply [1–4]. Despite recent decreases in the use of blood products, forecasts of increasing blood demands with concomitantly decreasing numbers of donors due to an ageing population stress the need to investigate donor behaviour and health [5]. Greater insight into donor health and donor behaviour could contribute to a more efficient and focused strategy regarding donor care and management and further ensure sufficient blood supply.

It is crucial that a donor pool is stable, healthy, diverse and large enough to ensure availability of all needed blood products. All blood donors are screened prior to

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each donation, in order to estimate whether a donor (1) can cope with the blood (components) loss associated with donation and (2) can donate blood of adequate quality [6, 7]. Two understudied aspects of blood donation are its health effects and donor behaviour. With every donation, fluids and substances like iron, proteins and blood cells are lost and these need to be replaced to maintain homeostasis. A recent study has shown that these replacements can take more time than the widely accepted minimum donation interval of 56 days for whole blood donations [8]. Although blood donation is generally considered to be safe, observations of vasovagal reactions, needle reactions, and fatigue have been reported [9, 10]. Knowledge of health effects and recovery from donation is needed to make sure that donors can safely continue to donate.

The cohort study 'Donor InSight' (DIS) was set up to gain insight into the characteristics and motivation of blood and plasma donors in the Netherlands, and into the health effects of blood donation [11]. Knowledge of both health and behavioural effects of donation contributes to keeping donors healthy and reducing the number of deferred and lapsed donors. The aim of this study is to outline the objectives and methods of DIS, describe the cohort, and compare it to the active Dutch donor population.

Materials and methods

Dutch donor population

In 2009, the Dutch donor population consisted of 404 184 registered voluntary non-remunerated donors aged 18–70 years. Sanquin is the only organisation in the Netherlands authorised to collect and supply blood products. New donors are registered in the blood bank information system (ePROGESA, MAK-SYSTEM International Group, Paris, France), after which donors are invited for an initial eligibility test and blood is drawn for screening and blood typing purposes. Donors must meet several criteria to be eligible to donate [12]. Certain health conditions and high-risk behaviours can lead to temporary or permanent deferral from donation. From their registration in the system, all donors are continuously registered as 'active', except when they are deferred or deregistered. Deregistration either takes place upon the donor's request, or after repeated unsuccessful attempts to contact a donor.

Donor InSight

Donor InSight was initially set up because of a need for more detailed information and evidence as a basis for decision-making in blood banks. The first round of DIS, DIS-I, was initiated to set up a representative cohort of the Dutch donor population regarding donor characteristics, donor motivations and health effects of blood donation. At the second round, DIS-II, the cohort was turned into a dynamic cohort to ensure that new donors would also be represented, by complementing the DIS-I sample with new randomly selected donors. The most recent round, DIS-III, aimed specifically to investigate associations of lifestyle behaviours and genetic factors with blood parameters, thereby making use of the data collected in DIS-I and -II.

Donor InSight-*I*

Objectives of DIS-I were to (1) study donor characteristics and differences between new and regular donors; whole blood and plasma donors; and regional differences, (2) identify motivations and barriers of donation among new and current donors and non-return reasons, and in addition whether these are related to donor characteristics, (3) determine main reasons of temporary and permanent donor deferral and its relation to future donor show behaviour, (4) investigate the effects of different strategies to increase donor show behaviour and (5) study features of the healthy donor effect.

Between April 2007 and April 2009 50 000 'active' donors were invited to participate in DIS-I (Fig. 1). Each month except for July and December a random sample of approximately 2000 'active' donors was selected. An invitation letter with an information brochure, a reply card and a paper-and-pencil questionnaire were sent by mail. After 3 weeks, all non-responders (n = 22 334) received a reminder. Of all 50 000 donors 5210 (10%) replied that they could not or would not participate, mainly because they were not interested, faced time constraints or had concerns based on principles. No response was obtained from 13 452 (27%) donors. Non-responders were more often male (52% vs. 47%) and had donated less often (median number of donations 19 vs. 24). In total, 31 338 (63%) participants returned completed questionnaires.

Donor InSight-*II*

For DIS-II objectives from DIS-I were extended with the aims to (1) investigate strategies to increase and factors that influence donor retention, (2) study health effects of donations and (3) study lifestyle and donor show behaviours.

Between 2012 and 2013 all still eligible 29 532 DIS-I participants were invited for DIS-II. DIS-I donors were considered eligible if they gave consent for participation in future studies, had donated at least once since
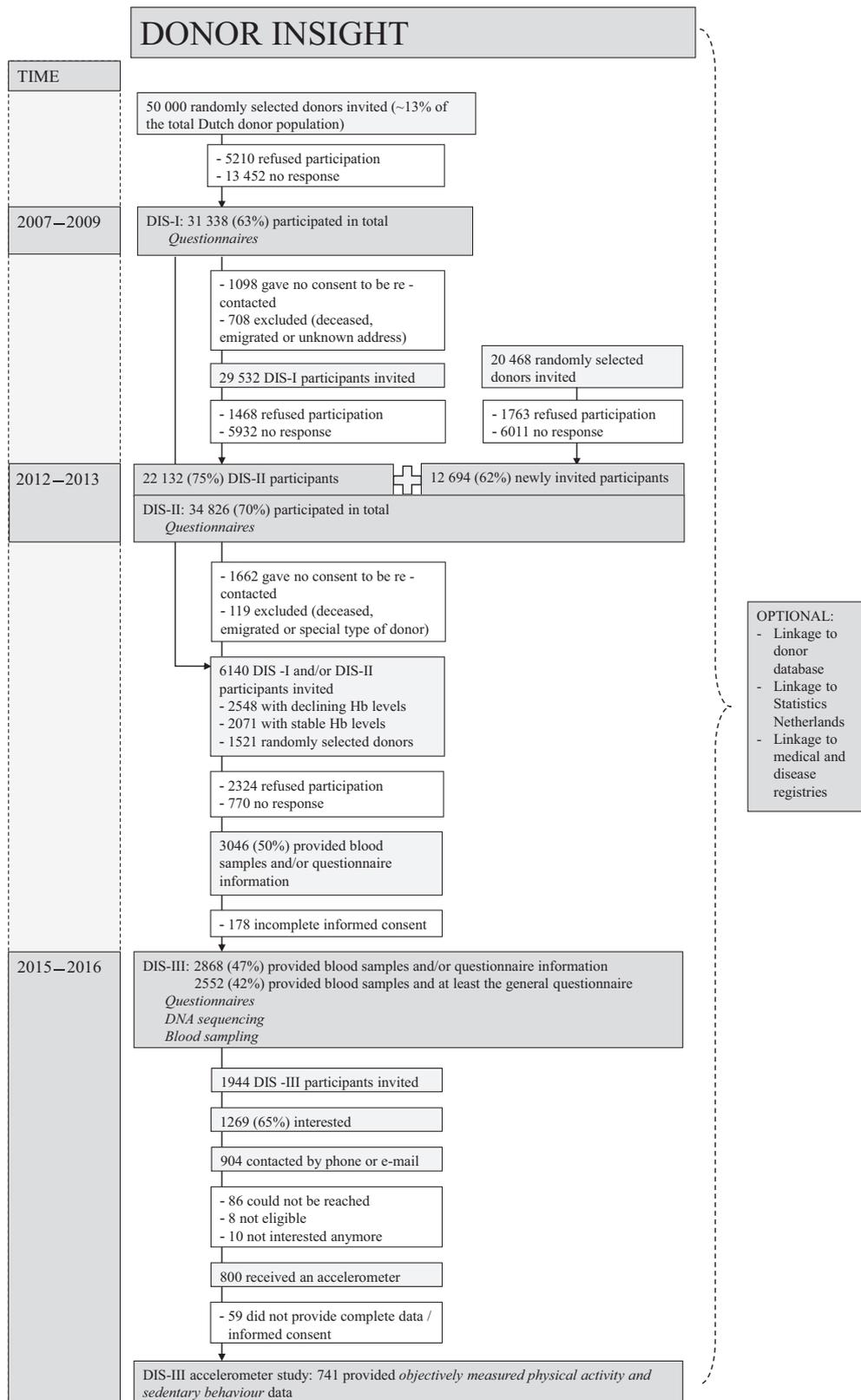
DONOR INSIGHT

TIME	

50 000 randomly selected donors invited (~13% of the total Dutch donor population)

- 5210 refused participation
- 13 452 no response

2007–2009

DIS-I: 31 338 (63%) participated in total
Questionnaires

- 1098 gave no consent to be re-contacted
- 708 excluded (deceased, emigrated or unknown address)

29 532 DIS-I participants invited

| 20 468 randomly selected donors invited |

- 1468 refused participation
- 5932 no response

- 1763 refused participation
- 6011 no response

2012–2013

22 132 (75%) DIS-II participants | 12 694 (62%) newly invited participants

DIS-II: 34 826 (70%) participated in total
Questionnaires

- 1662 gave no consent to be re-contacted
- 119 excluded (deceased, emigrated or special type of donor)

6140 DIS -I and/or DIS-II participants invited
- 2548 with declining Hb levels
- 2071 with stable Hb levels
- 1521 randomly selected donors

- 2324 refused participation
- 770 no response

3046 (50%) provided blood samples and/or questionnaire information

- 178 incomplete informed consent

2015–2016

DIS-III: 2868 (47%) provided blood samples and/or questionnaire information
2552 (42%) provided blood samples and at least the general questionnaire
Questionnaires
DNA sequencing
Blood sampling

1944 DIS -III participants invited

1269 (65%) interested

904 contacted by phone or e-mail

- 86 could not be reached
- 8 not eligible
- 10 not interested anymore

800 received an accelerometer

- 59 did not provide complete data / informed consent

DIS-III accelerometer study: 741 provided *objectively measured physical activity and sedentary behaviour* data

OPTIONAL:
- Linkage to donor database
- Linkage to Statistics Netherlands
- Linkage to medical and disease registries

Fig. 1 Donor InSight flowchart.

registration as donor, were not deceased and had not moved to an untraceable address. Of the DIS-I donors invited, 22 132 (75%) participated in DIS-II. A new random sample of 20 468 active donors was also invited for DIS-II, of whom 12 694 (62%) participated. Reminders were sent to all initial non-responders (n = 21 178). Of all 50 000 donors invited for DIS-II, 3231 donors replied that they could not or would not participate. In total, 34 826 (70%) participants completed the DIS-II questionnaire (Fig. 1).

Donor InSight-*III*

The objectives of DIS-III were to (1) investigate genetic and lifestyle behaviour determinants in relation to declining vs. stable Hb levels and donation-related iron deficiency, (2) assess whether identified genetic factors can improve the performance of previously developed prediction models, (3) study genetic determinants of iron metabolism in relation to their iron status and red blood cell indices and (4) investigate associations of Hb trajectories and iron deficiency with several health symptoms in whole blood donors.

Between April 2015 and December 2016 6140 DIS-I and/or DIS-II participants were invited to participate in DIS-III. DIS participants of whom the Hb level of their first donor screening was known were considered eligible. Three groups of DIS participants were invited. A group of donors with stable (n = 2071) and a group with declining (n = 2548) Hb levels were distinguished by fitting growth mixture models on Hb measurements [13]. These models were fitted on whole blood donors who registered between January 1, 2005 and December 31, 2012 and had at least one visit after the first donation. A third group was randomly selected (n = 1521) from DIS-I and/or DIS-II participants. An invitation letter with information brochure including a link to online questionnaires, and a pictorial blood loss assessment chart (PBAC) for women only [14] were sent by mail. After 2 weeks, all non-responders (n = 4530) received a reminder. Starting from 2 weeks after the reminder, remaining non-responders (n = 3652) were contacted by phone with a maximum of three attempts. Non-responders of whom e-mail addresses were known also received a reminder by e-mail (n = 1331). Of all 6140 donors invited for DIS-III, 2324 donors replied that they could or would not participate, mainly because of health reasons and time constraints. A total of 770 donors could not be reached. In total 3046 (50%) participants provided blood samples and/or questionnaire information for DIS-III of whom 2868 (47%) participants provided informed consent. In total 2552 participants provided blood samples and completed at least the general questionnaire (Fig. 1).

Of all DIS-participants, a vast majority (27 450 (88%) of DIS-I and 28 790 (83%) of DIS-II participants) gave informed consent for linkage to the blood bank information system, external databases and public registries such as cancer registries. DIS was approved by the Medical Ethical Committee Arnhem-Nijmegen in the Netherlands and for DIS-III by the Medical Ethical Committee of the Academic Medical Center, Amsterdam, the Netherlands. All participants gave their written, informed consent.

Measurements

An overview of all data collected during DIS-I, -II and -III is provided in Table 1. The questionnaire for DIS-I was self-administered, mainly multiple choice, covered six topics in Dutch. During DIS-II, the same, slightly updated questionnaire was used. These questionnaires were, with exception of the questions about donation, adapted from the Nijmegen Biomedical Study questionnaire [15]. In addition, several psychological constructs were inquired with regard to donation behaviour. This included constructs of the Theory of Planned Behaviour and were based on previously published measures and concepts such as trust and altruism [16–18].

Donor InSight-III participants were requested to complete questionnaires on symptoms associated with iron deficiency; general health (SF12); [19] the international physical activity questionnaire (IPAQ); [20] a shortened version of a food frequency questionnaire (FFQ) [21], designed to estimate iron intake; and questions on alcohol use, smoking and medication, adapted from the DIS-I and -II questionnaires. Furthermore, female participants were again asked to fill out questions about their menstruation patterns, pregnancies and contraceptive use. In DIS-III the PBAC was used to quantify menstrual blood loss [14].

Blood sampling, genotyping and accelerometers (DIS-III)

Blood for DIS-III was sampled at all blood bank collection sites throughout the Netherlands. Four blood samples (12 ml in total) were taken from the sampling pouch during a routine blood donation if donors were eligible. If a donor was deferred from donation or not willing to make a full donation (n = 836, 29% of all blood samples), blood was sampled through venepuncture. Blood samples were sent to Amsterdam and processed within 24 h after donation. Blood samples for zinc protoporphyrin (ZPP; Model 206D, Aviv Biomedical, Lakewood, NJ) were stored in EDTA whole blood at 4–6°C and measured within 10 days after sampling. Full blood counts (XT-2000, Sysmex, Kobe, Japan) were performed immediately after

Table 1 Donor InSight measurements

Phase	Measurements	Topic	Item
Continuously updated	Linkage to the Dutch donor database:	Donor and donation(s) information	Number and timing of donation, donor screening, including blood pressure, haemoglobin level and deferral
DIS-I 2007–2009	Questionnaire:	Demographic characteristics	Age, sex, household composition, ethnicity, education and employment
		Donation	Experiences with the blood bank and blood donation, including short-term effects and potential motivators for and barriers to blood donation
		Lifestyle	Diet, smoking, alcohol use, physical activity and travel behaviour
		Health and disease	Current health status, medication use and medical history
		Family	Family composition, family members giving or receiving blood, events of cancer, myocardial infarction and stroke in the family
		Females	Menstruation pattern, contraceptive use, menopause, reproductive organ surgery and pregnancies
DIS-II 2012–2013	Questionnaire:	Demographic characteristics	Age, sex, household composition, ethnicity, education and employment
		Donation	Experiences with the blood bank and blood donation, including short-term effects and potential motivators for and barriers to blood donation
		Lifestyle	Diet, smoking, alcohol use, physical activity and travel behaviour
		Health and disease	Current health status, medication use and medical history
		Family	Family composition, family members giving or receiving blood, events of cancer, myocardial infarction and stroke in the family
		Females	Menstruation pattern, contraceptive use, menopause, reproductive organ surgery and pregnancies
DIS-III 2015–2016	Questionnaire:	Demographic characteristics	Age, sex, ethnicity
		Lifestyle	Diet and iron intake (FFQ), physical activity (IPAQ), smoking, alcohol use
		Health Status	General health (SF-12), medication use
		Iron-deficiency-related symptoms	Restless legs syndrome, cognitive functioning, pica, fatigue
		Females	Menstruation pattern, contraceptive use, menopause, reproductive organ surgery and pregnancies, pictorial blood loss assessment chart (PBAC)
	Measurements:	DNA isolation and sequencing	Single nucleotide polymorphisms
		Full blood count and haemolysis	Including Hb, Ht, MCV, MCH, MCHC, RBC, WBC, PLT
		Iron metabolism	Ferritin, zinc protoporphyrin
		Blood lipid profile	High density lipoprotein cholesterol, total cholesterol and triglyceride levels
		Physical activity	Accelerometer data
Optional	Linkage to:	Databases and disease registries	

processing, after which this EDTA whole blood sample was used to determine free haemoglobin (EON plate reader, Biotek, NH, USA) and to determine haemolysis levels 28 days after blood sampling. Ferritin was measured using plasma from lithium heparin tubes (Architect Ci8200, Abbott Laboratories, IL, USA) and were stored at -80°C. Total cholesterol, high density lipoprotein cholesterol and triglycerides were also measured from lithium heparin tubes (Cobas C systems, Roche/Hitachi, Mannheim, Germany). Both ferritin and blood lipid levels were measured within 12 months after blood sampling. DNA was extracted from EDTA whole blood samples stored at -30°C. A part of the entire genome was analysed, including high-throughput genotyping using the UK Biobank Axiom Array (Thermo Fisher, Waltham, MA, USA) that contains 820 967 single nucleotide polymorphisms (SNP) and insertion/deletion (INDEL) markers [1, 22].

A subset of DIS-III participants were invited through the DIS-III questionnaire to additionally participate in an accelerometer study to objectively assess physical activity and sedentary behaviour (wGT3X-BT and GT3X Actigraph, Pensacola, FL, USA). Accelerometers provide information on activity as counts per minute (cpm). Activity was categorized as sedentary ≤99; light-intensity 100–2019; moderate-intensity 2020–5998; and vigorous-intensity ≥5999 cpm. according to the well-established Troiano (2008) cut-off points [23].

Data used to assess characteristics and representativeness of DIS

For the current analyses, data on demographics, lifestyle, health and disease, and donor and donation information were used. Level of education was defined as the highest level of education completed, being primary education, prevocational secondary education and lower general secondary education (categorized as low education), senior secondary vocational training, senior general secondary education and pre-university education (categorized as medium education), or higher professional education and university (categorized as high education). Household composition was measured as living alone, living alone with children (categorized as living alone (with children)), living with spouse or partner, living with spouse or partner and children (categorized as living with partner (and children)), living with parents/family/friends, living as a student in a dorm/with roommates and other (categorized as other). Employment was measured using the question "To which group do you belong?" with the options (multiple answers possible): employed, retired, off work due to illness, unemployed/searching for a job, disabled, housewife/-man, student with a job, student without a job and other (categorized as other). Part-time and full-time employment were categorized by using the question "If you have paid work, how many hours do you work during an average week?". Using information from these two questions, employment was categorized as full-time (≥36 h/week), part-time, student/unemployed and retired. Employment, household composition and education were measured once, these questions were asked only in DIS-II in case the donor did not participate in DIS-I.

Physical activity regarded medium to high intensity workouts for DIS-I and -II; participants were asked to for instance include mountain biking, but exclude cycling to work or playing chess. The IPAQ-short form was used in DIS-III [24] to estimate time spent in moderate to vigorous physical activity (MVPA) and sedentary behaviour. In a subset of the DIS-III sample sedentary behaviour and physical activity were also objectively measured using accelerometers. MVPA and sedentary behaviour are reported as mean minutes per day.

Smoking was measured as current smoker, former smoker and, never smoked. Alcohol consumption was measured as less than once a week, 1–2 days/week, 3–5 days/week and (almost) every day. The presence of medical conditions was assessed in DIS-I and DIS-II by asking whether these conditions had ever been diagnosed by a physician. In DIS-III name of (prescribed) medication or vitamin, preparations and reason for prescription was requested. Answers were categorized according to the World Health Organization recommended Anatomical Therapeutic Chemical classification system [25]. To enable comparison in terms of donor (demographic) and donation information of the DIS-I sample to the total donor population, data on all active and non-active donors on the 31st of December 2009, corresponding with the timing of DIS-I, were extracted including all whole blood and plasma donations made in 2007-2009. Age at 31-12-2009 (years), height (m), weight (kg), body mass index (BMI, kg/m^2), mean Hb (mmol/l, mean of measurements in 2007–2009), mean systolic and diastolic blood pressures (SBP and DBP, mm Hg, mean of all measurements in 2007–2009), mean donation interval (mean of all intervals between donations in 2007–2009) and total number of donations in 2007–2009 were obtained or calculated from this database.

Statistics

Descriptive results of the DIS-I, -II and -III population in terms of demographic characteristics, donation, lifestyle behaviours and health and disease are reported as numbers and proportions for binary data, or mean values ± standard deviations or medians with interquartile ranges in case of normally distributed or skewed continuous data

respectively. Mean values ± standard deviations for age, height, weight, BMI, Hb, SBP and DBP, median donation intervals (with interquartile ranges) and proportions of donors with 0, 1–3, 4–6, 7–9 or 10 or more donations, of participants with blood type A, B, AB or O, and of whole blood donors are presented.

Results

Representativeness DIS-I

In Table 2, characteristics of both the DIS population and the total active donor population on December 31st 2009 are summarised. This table shows that the DIS population is very similar to the total active donor population. Only the number of donations differed, DIS donors were more likely to have made a larger number of donations in 2007–2009 as compared with all donors.

Characteristics of DIS-I, -II and -III

Characteristics of the DIS-I, -II and -III populations are shown in Tables 3, 4 and 5 respectively. Approximately

one-third of the donors participating in DIS-I and -II completed higher professional education or university (34–37% and 36–39% in DIS-I and -II respectively), which is more than in the general Dutch population (32% of the Dutch 25–64 year old) [26].

Donor InSight donors were mainly living with a partner (and children), DIS-I: 74–86% and DIS-II: 77–84%, and often full-time employed (DIS-I: 19–68% and DIS-II: 35–37%). The percentage of smokers ranged from 8 to 17% (DIS-I – DIS-III), which is lower compared with the general Dutch population (23% among adults in 2016) [27] and consumption of alcohol 1–2 days per week ranged from 24 to 33. The prevalence of hypertension, high cholesterol and diabetes was relatively low in comparison with the general Dutch population: ranging from 1% (women with diabetes) to 16% (men with hypertension) in DIS-I and from 1% (diabetes) to 15% (hypertension) in DIS-II [11].

Discussion

Donor InSight is a unique cohort study on randomly selected donors from the Dutch donor population and comprises data regarding epidemiological and psychosocial

Table 2 Characteristics of the Donor InSight I sample and the total active donor population, based on data from the donor database as of on 31-12-2009

	DIS–I sample		Active donor population	
	Men (*n* = 14 782)	Women (*n* = 16 556)	Men (*n* = 182 751)	Women (*n* = 211 794)
Age (years)	51 ± 12	44 ± 13	48 ± 13	42 ± 15
Height (cm)	182 ± 7	169 ± 6	182 ± 7	170 ± 6
Weight (kg)	84 ± 14	70 ± 13	83 ± 14	70 ± 13
BMI (kg/m²)	26 ± 3	25 ± 4	26 ± 3	25 ± 4
Haemoglobin (mmol/l)	9·4 ± 0·6	8·5 ± 0·6	9·3 ± 1·2	8·2 ± 1·5
SBP (mm Hg)	134 ± 13	126 ± 14	134 ± 13	125 ± 14
DBP (mm Hg)	81 ± 8	78 ± 8	81 ± 8	77 ± 8
Donation interval (days)	105 (80–161)	152 (124–209)	107 (79–168)	147 (113–208)
Donations in 2007–2009 (%)				
0	507 (3)	978 (6)	8599 (5)	22 254 (11)
1–3	2060 (14)	4213 (26)	43 167 (24)	76 325 (36)
4–6	3140 (21)	5501 (33)	39 260 (22)	59 975 (28)
7–9	2933 (20)	4126 (25)	31 512 (17)	38 110 (18)
10	6133 (42)	1726 (10)	60 213 (33)	15 130 (7)
Blood type, %				
A–/A+	8/33	8/32	7/32	7/30
B–/B+	2/8	2/8	2/8	2/7
AB–/AB+	1/3	1/3	1/3	1/3
O–/O+	10/36	11/35	9/36	10/34
Whole blood donors (%)	11 565 (78)	13 826 (84)	143 652 (79)	165 456 (78)

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Continuous data are shown as mean ± standard deviation, donation interval as median (interquartile range), numbers of donors *n* (%) are shown for categories.

Table 3 Demographic and lifestyle characteristics of the Donor InSight I sample

	DIS–I sample			
	Men (*n* = 14 782)		Women (*n* = 16 556)	
	Whole blood donors (*n* = 11 565)	Other[a] (*n* = 3217)	Whole blood donors (*n* = 13 826)	Other[a] (*n* = 2730)
Demographic characteristics				
Education				
Medium	3905 (34)	1072 (34)	5102 (37)	939 (35)
High	4232 (37)	1149 (36)	4675 (34)	921 (34)
Household				
Living alone (with children)	1246 (11)	349 (11)	2574 (19)	592 (22)
Living with partner (and children)	9820 (85)	2770 (86)	10 309 (75)	2008 (74)
Other	499 (4)	89 (3)	943 (7)	118 (4)
Employment[b]				
Full-time	7935 (68)	2134 (66)	2768 (19)	552 (20)
Part-time	1528 (13)	415 (13)	8067 (58)	1557 (56)
Retired	1582 (14)	513 (16)	589 (4)	160 (6)
Other	583 (5)	161 (5)	2554 (18)	509 (18)
Lifestyle and health status				
Current smoker	1935 (17)	450 (14)	2244 (16)	403 (15)
Alcohol consumption				
<once/week	2281 (20)	661 (21)	4993 (36)	888 (33)
1–2 days a week	3543 (31)	936 (29)	3374 (24)	663 (24)
3–5 days a week	2757 (24)	707 (22)	1931 (14)	418 (15)
(Almost) every day	2265 (20)	692 (22)	1475 (11)	311 (12)
Physical activity (hours sports/week)	2·5 (1·5 − 4·0)	3·0 (2·0 − 4·5)	2·0 (1·3 − 3·0)	2·0 (1·5 − 3·5)
Hypertension[c]	1880 (16)	504 (16)	1751 (13)	413 (15)
High cholesterol[c]	1176 (10)	309 (10)	664 (5)	157 (6)
Diabetes mellitus[c]	193 (2)	63 (2)	141 (1)	38 (1)

Binary data are shown as numbers (%), continuous data are shown as mean ± standard deviation, or as median (interquartile range) in case of skewed data.

[a]The category 'other donors' mainly contains plasmapheresis donors.

[b]Due to the possibility of multiple answers per donor, the sum of the number of donors per categories may exceed the total number of donors.

[c]As diagnosed by a physician.

aspects of blood donation. As shown in this study, DIS-I donors are representative of the Dutch donor population.

Differences in age, number of donations and the larger number of donations in 2007–2009 between the DIS-sample and the Dutch donor population is probably due to the fact that donors who participated in DIS were randomly selected from the active donor population at different time points in the period 2007–2009. In equal circumstances, a random selection of the active donor population in April 2007 will obviously be older in December 2009 than the active donor population at that point. Furthermore, donors who stopped donating will be present in the DIS population, but not in the active total donor population in December 2009. Vice versa, the total donor population includes recently registered donors who could not have been part of DIS. Indeed, the total donor population includes 2·6% newly registered donors, while only 0·1% of the DIS donors were newly registered.

Multiple other large studies among blood donors have also collected questionnaire and biological data, though with different study aims and study populations. The INTERVAL study, for example, is a randomized controlled trial assigning donors to different donation intervals [1]. The Danish Blood Donor study invited all donors visiting the blood bank who had donated at least once [4]. Last, the Donor Iron Status Evaluation (RISE) study investigated four groups of donors (male and female, frequent and first-time/reactivated) [28]. So a unique aspect of DIS is that the inclusion into DIS was not directly linked to actual donations, thereby enhancing the participation of potentially less motivated donors and donors with blood types that are less frequently requested [2–4].

Table 4 Demographic and lifestyle characteristics of the Donor InSight II sample

| | DIS–II sample | | |
	DIS–I participants (*n* = 22,132)	Newly recruited[a] (*n* = 12,694)	Total (*n* = 34,826)
Demographic characteristics			
Education[b]			
Medium	7679 (35)	4721 (37)	12 400 (36)
High	7959 (36)	4967 (39)	12 926 (37)
Household			
Living alone (with children)	3161 (14)	1873 (15)	5034 (14)
Living with partner (and children)	18 529 (84)	9766 (77)	28 295 (81)
Other	405 (2)	1037 (8)	1442 (4)
Employment			
Full-time	8322 (35)	5029 (37)	13 351 (36)
Part-time	7741 (33)	4496 (33)	12 237 (33)
Retired	3844 (16)	1307 (10)	5151 (14)
Other	3806 (16)	2698 (20)	6504 (17)
Lifestyle and health status			
Current smoker	2658 (12)	1704 (13)	4362 (13)
Alcohol consumption			
<once/week	5685 (29)	3504 (31)	9189 (30)
1–2 days a week	5934 (30)	3709 (33)	9643 (31)
3–5 days a week	4473 (23)	2405 (21)	6878 (22)
(Almost) every day	3481 (18)	1630 (14)	5111 (17)
Physical activity (hours sports/week)	2 (1–4)	2 (2–4)	2 (1–4)
Hypertension[c]	3092 (15)	1227 (10)	4319 (13)
High cholesterol[c]	1628 (8)	540 (4)	2168 (7)
Diabetes mellitus[c]	449 (2)	153 (1)	602 (2)

Binary data are shown as numbers (%), continuous data are shown as mean ± standard deviation, or as median (interquartile range) in case of skewed data.

[a]These donors did not participate in DIS-I and were newly recruited for DIS-II.

[b]Due to the possibility of multiple answers per donor, the sum of the number of donors per categories may exceed the total number of donors.

[c]As diagnosed by a physician.

Strengths of DIS include the large study population and high representativeness of the Dutch donor population. This makes the study particularly useful for donation-related research questions for which the donor database is lacking information. Due to its prospective design and multiple measurements DIS also provides a unique opportunity to study questions in fields like public health, social sciences, epidemiology, (bio)statistics, genetics and haematology. The DIS cohort is a relatively healthy cohort that can serve as control sample [29]. Another strength is the objectively measured physical activity and sedentary behaviour in a subset of the DIS-III sample. Benefits of the study set-up are that (1) many repeated measurements with different intervals are available from the donor database and (2) additional data can be obtained relatively easily because (still donating) participants return to donation centres and are generally very willing to participate in research which is reflected in the DIS response rates ranging from 42 to 70%. Other

strengths include the possibility of linking study results to the donor database and to morbidity and mortality data. A potential weakness is the selective study population because of (1) the voluntary nature of donation, (2) donor screening procedures and (3) non-response to study invitations [11]. As with all studies, but particularly in the present circumstances, one should keep in mind that extrapolation of conclusions to the general population should be done with great caution.

Donor InSight data provide many more research opportunities because of the longitudinal questionnaire information, but also the biomedical and genetic data. Information on genetic markers can be used for research purposes, such as to study associations between Alzheimer's disease and blood donation, between iron indices and autoimmune/inflammatory disorders or between blood donation and cancer common variants.

Donor InSight is a cohort study of a representative sample of the Dutch donor population. The cohort can

Table 5 Characteristics of the Donor InSight III sample

	DIS–III sample[a]			
	Stable Hb levels (*n* = 744)	Declining Hb levels (*n* = 987)	Random sample (*n* = 821)	Total (*n* = 2552)
Sex				
Male	250 (34)	502 (51)	393 (48)	1145 (45)
Lifestyle and health status				
Current smoker	58 (8)	81 (9)	63 (8)	202 (9)
Alcohol consumption				
<once/week	291 (39)	336 (34)	250 (31)	877 (34)
1–2 days a week	190 (26)	255 (26)	204 (25)	649 (25)
3–5 days a week	125 (17)	180 (18)	168 (21)	473 (19)
(Almost) every day	84 (11)	116 (12)	142 (17)	342 (13)
Physical activity				
MVPA IPAQ (min/day)	51 (26–116)	51 (21–108)	56 (20–124)	51 (21–113)
Sitting IPAQ (min/day)	480 (300–720)	480 (300–660)	420 (240–600)	480 (300–660)
MVPA accelerometer (min/day)[b]	31 (22–49)	28 (18–43)	29 (17–43)	29 (19–45)
Sedentary behaviour accelerometer (min/day)[b]	533 ± 93	558 ± 82	552 ± 85	549 ± 87

IPAQ, International Physical Activity Questionnaire; MVPA, moderate to vigorous physical activity.

Binary data are shown as numbers (%), continuous data are shown as mean ± standard deviation or as median (interquartile range) in case of skewed data.

[a]Donors who provided blood samples and completed (at least) the general questionnaire.

[b]Subset of DIS-III participants with accelerometer data: stable Hb *n* = 212, declining Hb *n* = 278, random sample *n* = 251, total *n* = 741.

been used to study donor characteristics, motivations and barriers of donation, donor deferral in relation to future donor show behaviour and the healthy donor effect. Currently the DIS cohort is used to study lifestyle behaviours and genetic determinants of Hb trajectories. The DIS data may provide answers to many research questions that cannot at all be analysed by our research team.

Acknowledgements

Funding

Author Contributions

KvdH conceived the idea of the paper. KvdH, TCT and RdG wrote, reviewed and edited the manuscript. KH, EMM, FJP, FA, WLAMdK provided critical feedback on the manuscript. All authors read and approved the final manuscript.

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