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Cohort Profile Update

The Healthy Life in an Urban Setting (HELIUS) Study

Galenkamp, Henrike; Koopman, Anitra D.M.; van der Zwan, J.Esi; van den Born, Bert-Jan H.; Lok, Anja; Moll van Charante, Eric P.; Prins, Maria; Verhoeff, Arnoud P.; Zwinderman, Aeilko H.; Stronks, Karien

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Cohort Profile

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Cohort Profile

Cohort Profile Update: The Healthy Life in an Urban Setting (HELIUS) Study

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Keywords: HELIUS study; health inequalities; cohort studies; general population; epidemiology; cardiovascular disease; mental disorders; infectious diseases.

Key Features

- The Healthy Life in an Urban Setting (HELIUS) study is an ongoing prospective multiethnic cohort study in Amsterdam, The Netherlands that started in 2011.
- The principle aim of HELIUS is to investigate the causes of (the unequal burden of) diseases across ethnic groups, with an emphasis on mental disorders, cardiovascular disease, and infectious disease, and their interrelationships.
- Stratified sampling by ethnic group resulted in similar-sized samples of individuals of Dutch, African Surinamese, South-Asian Surinamese, Ghanaian, Turkish, and Moroccan origin.
- Between 2011 and 2015, 24 780 individuals (aged 18–70 years) participated in the baseline examination that consisted of a questionnaire, physical examination, and collection of biological material.
- Between 2019 and 2022, the first follow-up data collection took place among 11 035 participants (aged 22–79 years) with an average follow-up time of 6.4 years. In addition, follow-up data have been collected through linkage with healthcare registries.
- The HELIUS study has several existing collaborations. For new collaborative projects and inquiries, please contact heliuscoordinator@amsterdamumc.nl.

The original cohort

In 2010, the Healthy Life in an Urban Setting (HELIUS) study was designed to provide a knowledge base on inequalities in health and healthcare between the six largest ethnic groups living in Amsterdam, the Netherlands [1, 2]. HELIUS was set up by the Amsterdam University Medical Center and the Public Health Service (GGD) of Amsterdam as a prospective population-based study with stratified sampling across ethnic groups to allow equal sample sizes. Baseline data collection took place between 2011 and 2015, and consisted of

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a questionnaire and physical examination, including the collection of biological material. A total of 24 780 individuals took part, aged 18–70 years (average 43.8 years), with 81% being of non-Dutch origin (South-Asian Surinamese, African Surinamese, Ghanaian, Turkish, or Moroccan).

What is the reason for the new data collection?

The HELIUS study was set up as a prospective cohort study, with repeating measurements during follow-up examinations every 5–10 years to enable longitudinal analyses on the relationship between risk factors and cardiovascular diseases, mental disorders, and infectious diseases. At baseline, participants were asked permission (i) to store biological samples in the HELIUS biobank for future research (93% agreed); (ii) to link their individual data to registries containing data relating to the participants' health (such as hospital admissions, pharmacy data, vaccination programs; 90% agreed); (iii) to request the official causes of death from Statistics Netherlands (87% agreed); and (iv) to approach them for additional studies in the future (substudies; 92% agreed).

The new data collection described in this Cohort Profile Update consists of: a first follow-up data collection (2019–22), linkages with registry data (on risk factors and health outcomes, including mortality), and new laboratory measurements from stored biobank samples.

What will be the new areas of research?

The first follow-up visit enables the study of longitudinal associations with baseline risk factors. The measurement of disease outcomes was therefore the main focus of the follow-up visit compared with the baseline visit in which an extensive set of health determinants was measured. Additional focus areas of the data collection were:

- COVID-19 (serological sub-study with three visits, online questionnaire, linkage with registry data);
- liver stiffness and steatosis;
- vascular aging;
- cancer (through linkage with registry data);
- environmental data (through linkage);
- omics profiling (e.g. genomics, microbiomics, metabolomics).

Who is in the cohort?

Baseline data collection was performed among 24 780 participants, randomly sampled within ethnic groups (Table 1). Between May 2019 and November 2022, all participants who were still alive according to the municipality population register and living in the Netherlands were invited for the first follow-up measurement (HELIUS-2). A total of 371 participants had deceased and 640 participants had moved abroad, leaving 23 769 participants who were eligible for the follow-up measurement. Eligible participants received a written invitation with a response card and a reminder after 4 weeks. In cases of no response, participants from whom a phone number was collected during the baseline data collection were approached by phone. After five unsuccessful attempts, participants were approached one last time by e-mail (if an e-mail address had been collected during the baseline data collection). After a positive response, participants were contacted by phone by the research team to make an appointment for a visit to the research location. A visit to the research location consisted of a questionnaire/interview, physical examination, and collection of biological samples.

Of all eligible baseline participants, 7336 declined participation in the first follow-up and 5398 could not be reached. In total, 11 035 persons took part in HELIUS-2, of whom 10 639 had a complete baseline examination (questionnaire and physical examination). Response rates (HELIUS-2 participants/eligible participants) varied from 28% in the Turkish-origin group to 67% in the Dutch-origin group. When taking into account that not all participants could be reached, participation rates (HELIUS-2 participants/eligible participants who were reached) varied from 38% in the Turkish-origin group to 71% in the Dutch-origin group.

Demographic characteristics

The distribution of demographic characteristics of the follow-up sample is shown in Table 2. Only the six largest ethnic groups are shown separately because of a low number

Table 1. Response rates of the first follow-up of HELIUS (2019–22; Amsterdam, the Netherlands) by ethnic group

		Ethnic group						
	Total[a,b]	Dutch	South-Asian Surinamese	African Surinamese	Other Surinamese[c]	Ghanaian	Turkish	Moroccan
Baseline participation (HELIUS-1)	**24 780**	**4671**	**3366**	**4458**	**802**	**2733**	**4198**	**4501**
Deceased before follow-up (%)	371 (1.5)	75 (1.6)	76 (2.3)	100 (2.2)	12 (1.5)	42 (1.5)	42 (1.0)	24 (0.5)
Moved abroad (%)	640 (2.6)	94 (2.0)	52 (1.5)	127 (2.8)	14 (1.7)	151 (5.5)	144 (3.4)	53 (1.2)
Declined follow-up (%)	7336 (29.6)	1222 (26.2)	957 (28.4)	1041 (23.4)	210 (26.2)	747 (27.3)	1813 (43.2)	1332 (29.6)
No contact (%)	5398 (21.8)	267 (5.7)	512 (15.2)	1040 (23.3)	197 (24.6)	872 (31.9)	1075 (25.6)	1425 (31.7)
Participation in first follow-up (HELIUS-2)	**11 035**	**3013**	**1769**	**2150**	**369**	**921**	**1124**	**1667**
Participation rate (%)[d]	60%	71%	65%	67%	64%	55%	38%	56%
Response rate (%)[e]	46%	67%	55%	51%	48%	36%	28%	38%
Complete HELIUS-1 and HELIUS-2 data	**10 639**	**2988**	**1732**	**2133**	**255**	**846**	**1075**	**1588**

[a] Including 51 participants of other ethnic backgrounds.
[b] Number was slightly adjusted since the baseline measurement ($n = 24\,789$), as some participants were later found to have attended twice.
[c] Including Javanese and other Surinamese.
[d] Percentage of individuals who took part in HELIUS-2 of those who could be contacted (11 035/(11 035 + 7336)).
[e] Percentage of individuals who took part in HELIUS-2 of those who were eligible among HELIUS baseline participants (11 035/23 769).

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Table 2. Demographic characteristics of HELIUS-2 participants by ethnic group

Characteristic	Total[a]	Ethnic group					
		Dutch	South-Asian Surinamese	African Surinamese	Ghanaian	Turkish	Moroccan
Number of participants	**11 035**	**3013**	**1769**	**2150**	**921**	**1124**	**1667**
Men (%)	4777 (43.3)	1436 (47.7)	769 (43.5)	787 (36.6)	362 (39.3)	536 (47.7)	729 (43.7)
Women (%)	6258 (56.7)	1577 (52.3)	1000 (56.5)	1363 (63.4)	559 (60.7)	588 (52.3)	938 (56.3)
Age in years (SD)	52.6 (12.5)	54.1 (13.1)	53.2 (12.5)	55.9 (11.6)	52.3 (10.3)	47.6 (11.4)	48.4 (12.1)
Age category (range, 22–79 years)							
22–34 (%)[b]	1179 (10.7)	304 (10.1)	192 (10.9)	138 (6.4)	67 (7.2)	182 (16.2)	267 (16.0)
35–44 (%)	1708 (15.5)	470 (15.6)	221 (12.5)	236 (11.0)	120 (13.0)	243 (21.6)	370 (22.2)
45–54 (%)	2675 (24.2)	642 (21.3)	429 (24.3)	435 (20.2)	291 (31.6)	325 (28.9)	464 (27.8)
55–64 (%)	3428 (31.1)	816 (27.1)	566 (32.0)	808 (37.6)	358 (38.9)	322 (28.6)	400 (24.0)
65–79 (%)[b]	2045 (18.6)	781 (25.9)	361 (20.4)	533 (24.8)	85 (9.2)	52 (4.6)	166 (9.9)
First generation: migrants (%)	6559 (81.8)	–	1427 (80.7)	1837 (85.4)	888 (96.4)	826 (73.5)	1244 (74.6)
Second generation: migrants' offspring (%)	1463 (18.2)	–	342 (19.3)	313 (14.6)	33 (3.6)	298 (26.5)	423 (25.4)
Educational level (at baseline)							
1. No schooling or elementary schooling only (%)	1421 (12.9)	76 (2.5)	229 (12.9)	95 (4.4)	243 (26.4)	276 (24.6)	475 (28.5)
2. Lower vocational schooling or lower secondary schooling (%)	2642 (23.9)	370 (12.3)	576 (32.6)	712 (33.1)	339 (36.8)	255 (22.7)	308 (18.5)
3. Intermediate vocational schooling or intermediate/higher secondary schooling (%)	3054 (27.7)	644 (21.4)	518 (29.3)	759 (35.3)	207 (22.5)	325 (28.9)	509 (30.5)
4. Higher vocational schooling or university (%)	3585 (32.5)	1900 (63.1)	438 (24.8)	567 (26.4)	58 (6.3)	229 (20.4)	318 (19.1)
Unknown (%)	333 (3.0)	23 (0.8)	8 (0.5)	17 (0.8)	74 (8.0)	39 (3.5)	57 (3.4)

[a] Including 391 participants with other ethnic backgrounds.
[b] Age categories adjusted because of low numbers in age categories 15–24 and 75–84 years, respectively.

of participants in the other Surinamese ($n = 369$) and other origin ($n = 22$) groups. In all ethnic groups, more women took part in the first follow-up visit than men. Participation rates were higher for individuals aged between 45 and 54 years and between 55 and 64 years. Most participants were migrants themselves (first-generation, range 74%–96%) as compared with the offspring of migrants (second-generation, range 4%–27%). On average, Dutch-origin participants had the highest educational level and Ghanaian-origin participants had the lowest. At baseline, these variations in educational level reflected the Amsterdam situation [1].

Representativeness of the first follow-up

Those who participated in the follow-up data collection were, at baseline, generally older than those who did not. In addition, they were more often first-generation migrants and more often had intermediate or higher educational levels (Figure 1 and Supplementary Table S1). In most ethnic groups, participants of the first follow-up less often had diabetes or self-reported cardiovascular disease at baseline compared with those who did not participate in the first follow-up (Supplementary Table S2). In addition, they smoked less and more frequently met the physical-activity guideline criteria. Finally, participants included at follow-up less often reported depressive symptoms. Results were fairly similar after excluding participants who had deceased or moved abroad between HELIUS-1 and HELIUS-2 (Supplementary Table S3).

What has been measured?

First follow-up in total sample

While HELIUS baseline included a broad range of determinants of health, this follow-up data collection focused on a smaller set of outcome measures, predominantly related to mental health and cardiovascular disease. In addition, more in-depth measurements were performed in smaller samples (see next paragraph). Table 3 describes the measurements that were taken at both measurement waves. Where possible, methods were aligned between the two rounds. An important difference is that, at baseline, participants filled in the questionnaire (paper or digital version) at home, with help from an interviewer if needed. At follow-up, all questions were asked by the research nurse at the research location.

Follow-up measurements in subgroups

Specific measurements were taken in smaller subgroups between 2020 and 2023. Firstly, between 2020 and 2022, a longitudinal serological study was performed to study ethnic inequalities in the epidemiology of COVID-19 [3]. During three study visits among a subsample of ~2500 participants (six largest ethnic groups, random samples), SARS-CoV-2-specific antibodies were determined and an interview was conducted containing questions on COVID-19-related symptoms, the uptake of control measures, wellbeing, risk of exposure (work environment, contacts, traveling), and severity of disease (Supplementary Table S4). In addition, an online questionnaire was sent to all HELIUS baseline participants for whom we had an e-mail address and was filled in by 4450 participants. Questions focused on perceived changes in finances, health behaviors, mental health factors, and use of non-COVID-19 healthcare due to the COVID-19 pandemic [4]. Secondly, in an additional visit after the HELIUS follow-up visit, a FibroScan was performed in ~400 participants (all ethnic groups) to measure liver stiffness and liver steatosis [5]. Participants were selected based on a high risk of metabolic dysfunction-associated steatotic liver disease or were included in the control group. Finally, vascular aging was studied in a subsample of ~3000 participants of Dutch, South-Asian

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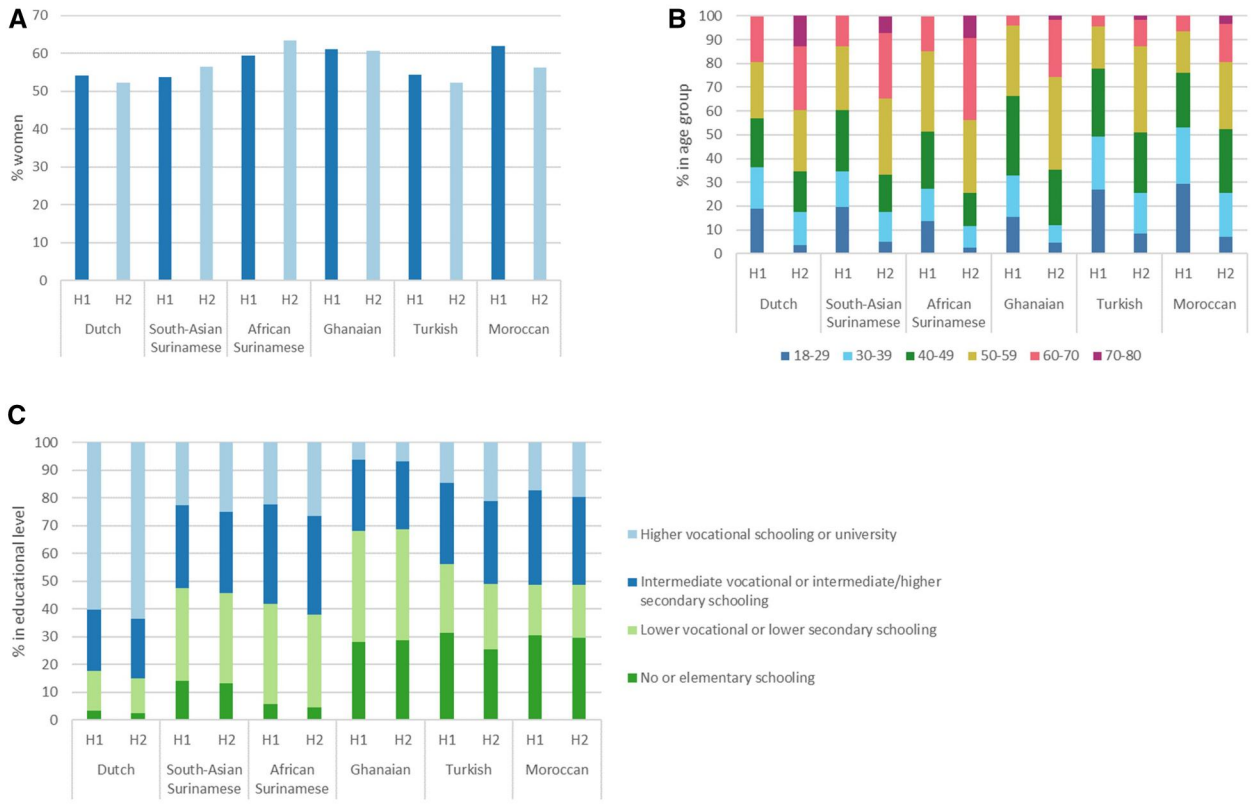

Figure 1. Demographic characteristics of HELIUS participants at HELIUS baseline (H1) and follow-up (H2) by ethnic group. (A) Percentage women; (B) percentage participants in each age group; (C) percentage of participants in each educational level.

Surinamese, and Moroccan origin (aged 35–65 years) through carotid ultrasound examination [6], followed by carotid and brain magnetic resonance imaging (MRI) ($n \sim 570$) and cardiac MRI ($n \sim 150$) (Table 3).

Linkage with health registries and other databases

Until 2024, linkages were established on an individual level for different health outcomes, including diabetes and cardiovascular diseases (CVD), infectious diseases, (all-cause) mortality, and cancer (Supplementary Table S5). In addition, data on environmental exposures (including safety, food environment, air pollution) were obtained at the neighborhood or postal code level. Finally, data on healthcare use (hospitalization, medication use) were obtained via linkages.

Laboratory measurements in stored baseline samples

During baseline examination, ancillary fasting blood and morning urine samples were collected and stored in the HELIUS biobank. In addition, in subsamples, we collected feces samples and vaginal swabs, amongst others. Additional measurements and analyses that have been performed on these stored samples are listed in Supplementary Table S6.

What has it found? Key findings and publications

A list of all publications that are based on data from the HELIUS study is available at https://www.heliusstudy.nl/nl/researchers/publications. In this section, we highlight the key findings until January 2024.

Cardiovascular diseases

HELIUS has shown that there are substantial inequalities in cardiovascular health between ethnic groups, particularly in the prevalence of diabetes, diabetes-related complications, hypertension, and chronic kidney disease [7–10]. Diabetes in particular is two to four times more common among individuals with a migration background compared with the Dutch host population and also has an onset at a much younger age [7]. Potential explanatory mechanisms for inequalities in diabetes include ethnic differences in the prevalence of hypertension and obesity. However, also in normal-weight individuals, cardiometabolic risk remains increased [11]. HELIUS has shown that the relation between diabetes and measures of body composition, including body mass index (BMI) and waist circumference, differs across ethnic groups [12]. This finding from HELIUS and other studies has contributed to ethnicity-specific recommendations for the case-finding of type 2 diabetes in the Netherlands [13].

Individuals of Ghanaian, African Surinamese, and South-Asian Surinamese descent exhibit a higher risk of hypertension compared with other ethnic groups—a risk that cannot be fully explained by variations in well-known risk factors such as BMI, physical activity, and educational level [14]. For this reason, the recent European guideline on cardiovascular disease prevention recommends multiplying factors to take into account the additional CVD risk imposed by ethnicity. Additionally, recent risk estimations based on a large Dutch GP Research Network

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Table 3. Overview of measurements that were taken in both HELIUS-1 and HELIUS-2, or only in HELIUS-2

	Baseline HELIUS-1 (2011–15) ($n \sim 25\,000$)	Follow-up HELIUS-2 (2019–22) ($n \sim 11\,000$)
Variables in questionnaire/interview		
Marital status	X	X
Occupational status	X	X
Smoking	X	X
Alcohol intake	X	X
Self-reported history of high blood pressure	X	X
Self-reported history of diabetes	X	X
Self-reported myocardial infarction	X	X
Self-reported Dotter/bypass surgery	X	X
Self-reported cerebrovascular events	X	X
Mastery (Pearlin–Schooler Mastery Scale)	X	X
Depressive symptoms (PHQ-9)	X	X
Stressful life events	X	X
Physical examination		
Current medication use (name, frequency, indication)	X	X
Anthropometry (weight, height, and circumferences of waist, hip)	X	X
Blood pressure (sitting position, 5 min of rest, WatchBP Home, Microlife)	X	X
Laboratory measurements fasting blood		
Glucose, hemoglobin A1c (HbA1c), hemoglobin, triglycerides, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) (calculated), creatinine	X	X
Aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), gamma-glutamyl transferase (GAMMA-GT), thrombocytes		X
Laboratory measurements morning urine		
Microalbumin, creatinine	X	X
Feces (subsamples)		
Fecal microbiome (16S)	X $n = 6029$	X $n \sim 8000$
Stored feces samples	X $n = 6046$	X $n \sim 8000$
Swabs (subsamples)		
Nasal and throat swabs	X $n = 6631$	X $n \sim 2000$
Oral swabs		X $n \sim 2000$
NAFLD In the healthy Life in an urban sEtting (NILE) study		
Physical exam: transient elastography (FibroScan), anthropometry, blood pressure, heart rate, collection of blood (hepatitis B and C)		X $n \sim 400$
Questionnaire: 36-Item Short Form Health Survey (SF-36), physical activity, diet, alcohol, smoking, drugs, hypertension, diabetes, medication		X $n \sim 400$
Vascular aging sub-study		
Visit 1: Carotid ultrasound examination		X
Questionnaire: diet, sleep, physical activity		$n \sim 3000$
Visit 2: Carotid and brain MRI		X $n \sim 570$
Visit 3: Cardiac MRI		X
Physical examination: blood pressure, electrocardiogram, Nexfin measurement		$n \sim 150$

[a] An extensive list of measures of the baseline examination can be found in the initial HELIUS cohort profile (1).

database suggest an increased risk of death from CVD among various ethnic minority groups, potentially warranting lower risk thresholds for cardiovascular screening [15].

Mental disorders

A higher prevalence of depressive symptoms was found in all migrant groups in HELIUS compared with those with Dutch origin, especially in Turkish and South-Asian Surinamese individuals [16, 17]. In addition, for substance (ab)use, post-traumatic stress disorder (PTSD), and suicidal ideation, we found an increased risk in those with a migration background [18–21]. An exception is the regular use of alcohol, which is more common in those with Dutch origin [22]. Disparities were also observed in risk factors for depressed mood, including childhood maltreatment [23], perceived ethnic discrimination [21], specific dietary patterns [24], socioeconomic factors [17], and environmental factors [25].

Regarding the interplay between mental health and cardiometabolic diseases, we found that depressive symptoms and trauma/PTSD were associated with obesity [26], metabolic syndrome [20], and hypertension [27]. Finally, recent HELIUS studies on the gut–brain axis showed that the substantial ethnic differences in depression are related to ethnic differences in microbiome diversity, independently of socioeconomic status (SES), lifestyle, and medication use [28].

Infectious diseases

Research on infectious diseases in HELIUS has focused on the epidemiology of human papillomavirus [29], viral hepatitis B, C, and E [30, 31], *chlamydia* [32], *Helicobacter pylori* [33], and, more recently, COVID-19 [3]. Ghanaian, Turkish,

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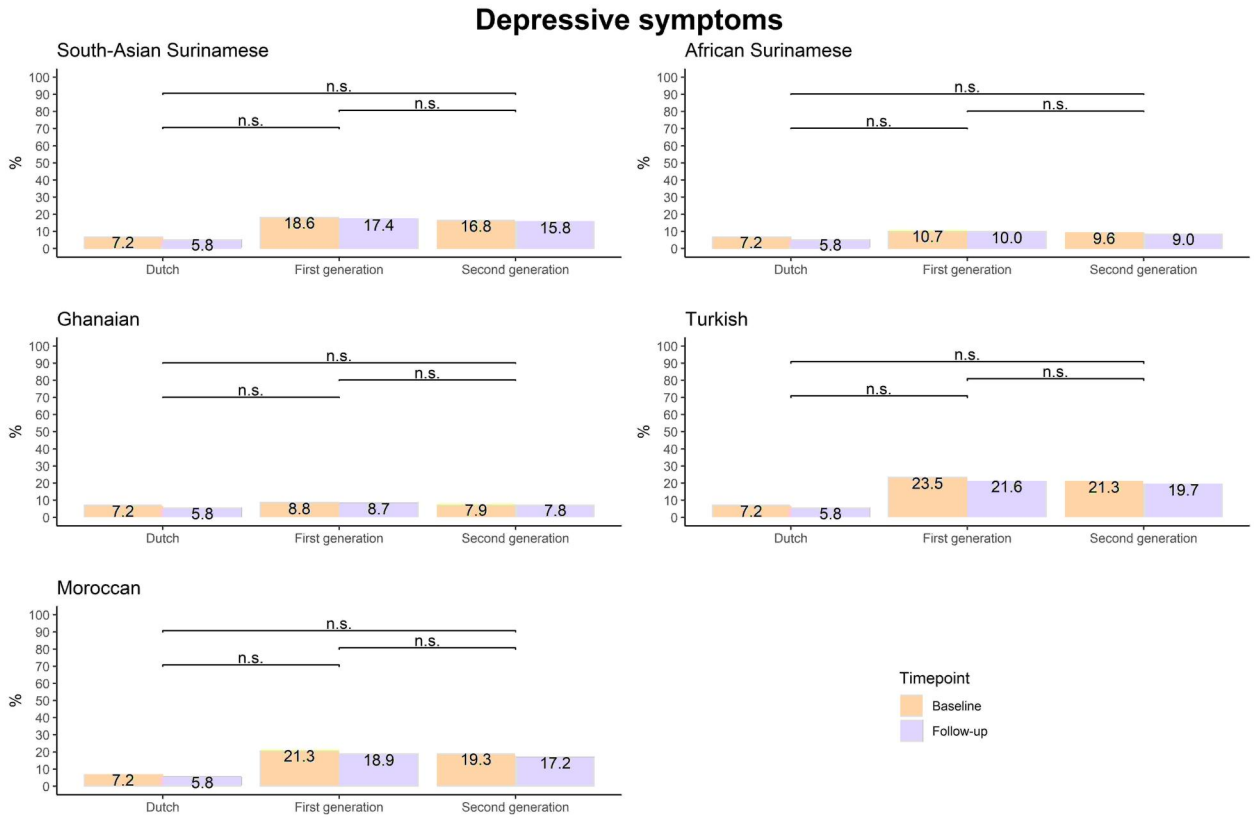

Figure 2. Depressive symptom prevalence at baseline and follow-up by migration generation compared with the Dutch-origin group and differences between groups over time based on Generalized Estimating Equations analysis. N.s. = nonsignificant.

and African Surinamese first-generation migrants were found to be at increased risk of chronic hepatitis B infection and many were unaware of their infection whereas hepatitis C prevalence was low among all ethnic groups [24]. These results were used by the Dutch Health Council in their advice to the Minister of Health, Welfare and Sport in the Netherlands to limit screening for these infections to key populations and this advice was adopted [34].

Studies that were set up during the COVID-19 pandemic showed that SARS-CoV-2 incidence was higher in the ethnic minority groups compared with the Dutch-origin group. Inequalities became wider during the second wave versus the first wave of infections, which may imply that very stringent measures during the first wave of infections likely prevented ethnic disparities in the initial spread of the virus, but subsequent less rigorous measures might have resulted in a more rapid spread in the ethnic minority groups [3]. In line with these findings, we found that the risk of COVID-19 hospitalization was higher in all ethnic minority groups, but the risk of adverse outcomes after COVID-19 hospitalization was similar [35]. Additionally, individuals with a migration background and those in lower education or occupation categories were more susceptible to adverse changes across various life domains, including health behavior, mental wellbeing, and access to non-COVID-19 healthcare [4].

Inequalities over time and across generations

Beneath the surface of ethnic health disparities lies the hypothesis that they may diminish with time as migrants establish longer-term residence in the Netherlands. However, studies from HELIUS have shown that ethnic inequalities often persist into the second generation [17] and that they are similar across subgroups of residence duration and acculturation [36].

The data that were collected during the first follow-up measurement enable a comparison between 2011–15 and 2019–2022 (average follow-up 6.4 years). In this time frame, Generalized Estimating Equations analysis showed that inequalities between groups with and without a migration background continued to persist. Furthermore, at both time points, migrants from the first and second generations had a similar risk of unfavorable health outcomes. For example, we found no change in the increased risk of depressive symptoms that first- and second-generation migrants have compared with their Dutch counterparts (Figure 2). The same applied to hypertension prevalence, although the prevalence in all groups increased over time (Figure 3). It remains to be seen whether other health outcomes show similar patterns, but current findings do not support the hypothesis of decreasing ethnic inequalities across generations or over time.

What are the main strengths and weaknesses?

Strengths of the study include the inclusion of a large number of migrants and their offspring from several major ethnic groups living in the same city. While our findings suggest that ethnic minority groups have an increased risk for adverse health outcomes, no specific group consistently exhibits a greater risk across the broad spectrum of diseases. This emphasizes the need to differentiate between individual ethnic groups.

A second strength is the collection of a wide range of multi-domain measurements. This enables the investigation of (i) ethnic inequalities in several health outcomes and cross-

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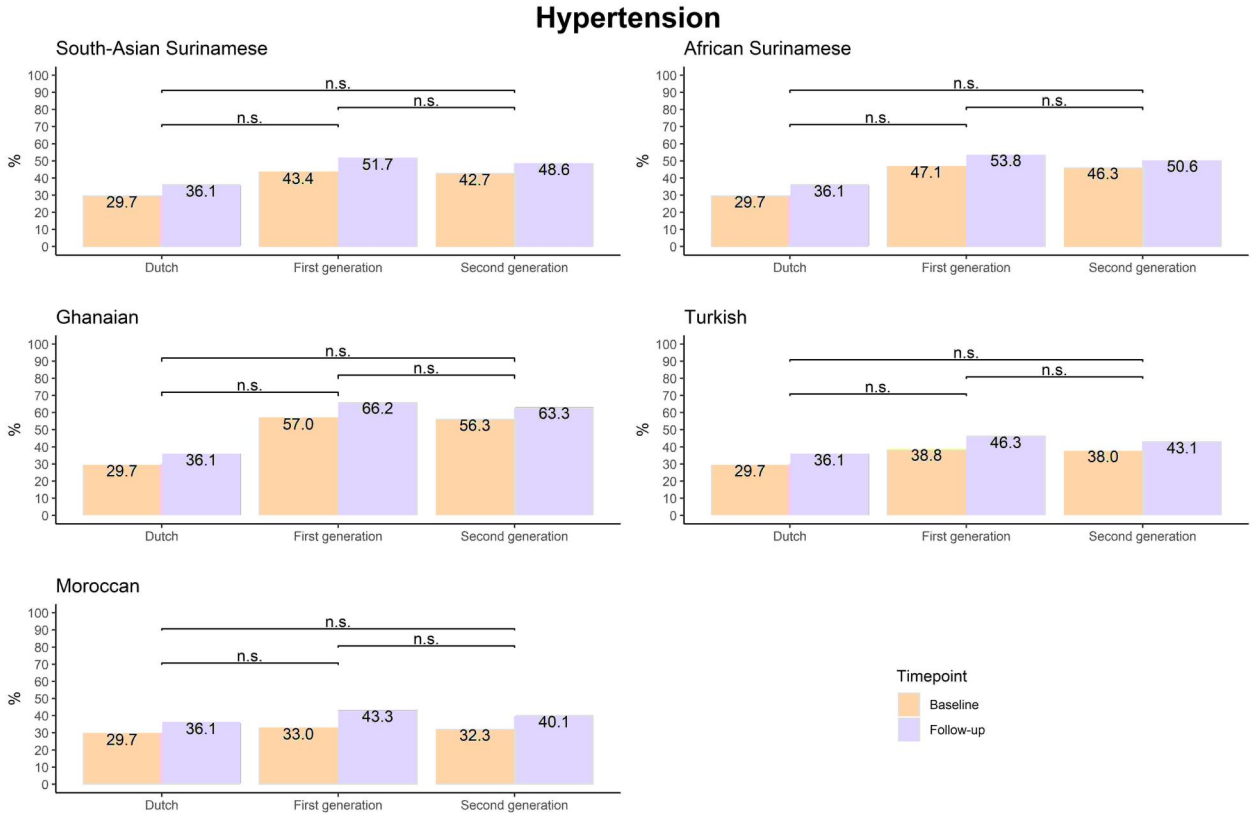

Figure 3. Hypertension prevalence at baseline and follow-up by migration generation compared with the Dutch-origin group and differences between groups over time based on Generalized Estimating Equations analysis. N.s. = nonsignificant.

links between these outcomes; and (ii) a wide range of explanatory factors that represent the causal pathway through which ethnicity is linked to the incidence and prognosis of health conditions [2]. The HELIUS study confirmed conclusions from previous research that ethnic inequalities in health are at least partly socioeconomic in nature. However, the novelty of the HELIUS analyses lies in the insights generated on categories of explanatory factors other than SES, e.g. perceived discrimination [16], diversity of vaginal and gut microbiota composition [37, 38] and group-level determinants such as the food environment and social norms regarding body weight [39].

The thorough study of inequalities in health in a multiethnic population is achieved not only through recurring measurement rounds with intervals of several years, but also by leveraging the existing cohort structure to establish substudies in a relatively short timeframe. We effectively used this opportunity, e.g. during the COVID-19 pandemic. The representativeness of the sample at baseline is another strength, which provides a basis for extrapolating results to the total population [8]. This is particularly valuable for baseline studies and studies that use follow-up data from registries, as only a limited number of participants did not give consent for linkages. At the same time, the relatively limited sample size at the first follow-up poses a threat to this representativeness, as groups who did and did not participate in the follow-up measurement round differed with regard to demographic and health characteristics. Another limitation is the unknown validity of some of our questionnaires and physical measurements in non-European-descent populations, which may still mask an unknown proportion of health disparities across ethnic groups. Although some measures have been checked for cross-cultural validity [40], this is not possible with all measures, as gold standards are often not present. Finally, an inherent limitation of studying a large number of participants by using an extensive set of measurements is that this provides information regarding the health status at that particular moment and that the time between two measurement rounds is relatively long.

Can I get hold of the data? Where can I find out more?

The HELIUS data are owned by the Amsterdam University Medical Center, location Academic Medical Center, in Amsterdam, the Netherlands. Any researcher can request the data by submitting a proposal to the HELIUS Executive Board as outlined at http://www.heliusstudy.nl, by e-mail to Dr Henrike Galenkamp (heliuscoordinator@amsterdamumc.nl). The HELIUS Executive Board will check proposals for compatibility with the general objectives, ethical approvals, and informed consent forms of the HELIUS study. There are no other restrictions to obtaining the data and all data requests will be processed in the same manner. For linked data, additional conditions for reuse may apply. To allow the sharing of microbiome data collected in HELIUS with (inter)national researchers, 16S rRNA sequence analysis (accession codes EGAD00001004106, EGAD00001009732) and virome sequencing (accession code EGAD00001008765) have been stored at the European genome-phenome archive (EGA).

Ethics approval

The HELIUS study is performed in line with the principles of the Declaration of Helsinki. The HELIUS study has been

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approved by the Ethical Review Board of the Academic Medical Center Amsterdam (Protocol ID NL32251.018.10; approval numbers 10/100# 10.17.1729; 2010_100#B201997). Written informed consent was obtained from all individual participants included in the study.

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Author contributions

All authors contributed to the study conception and design. H.G. and K.S. conceived the present manuscript. H.G., A.K., J.Z., B.B., M.P., and K.S. drafted the paper. H.G. and J.Z. performed the analyses. H.G. finalized writing the paper. A. L., E.M.C., A.V., and A.Z. were involved in reviewing previous versions of the paper in detail. All authors read and approved the final manuscript.

Supplementary data

Supplementary data are available at *IJE* online.

Conflict of interest: All authors declare they have no conflicts of interest.

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Use of artificial intelligence (AI) tools

Not applicable.

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Cohort Profile