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Ethnic disparities in out-of-hospital cardiac arrest: A population-based cohort study among adult Danish immigrants

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Summary

Background Ethnicity might impact out-of-hospital cardiac arrest (OHCA) risk, but it has scarcely been studied in Europe. We aimed to assess whether ethnicity influenced the risk of OHCA of cardiac cause in Danish immigrants and its interplay with risk factors for OHCA and socioeconomic status.

Methods This nationwide study included all immigrants between 18 and 80 years present in Denmark at some point between 2001 and 2020. Regions of origin were defined as Africa, Arabic countries, Asia, Eastern Europe, Latin America, and Western countries. OHCAs with presumed cardiac cause were identified from the Danish Cardiac Arrest Registry.

Findings Overall, among 1,011,565 immigrants, a total of 1,801 (0.2%) OHCAs (median age 64 (Q1-Q3 53–72) years, 72% males) occurred. The age- and sex- standardized (reference: Western countries) incidence of OHCA (/1,00,000 person-years) was 34.6 (27.8–43.4) in African, 34.1 (30.4–38.4) in Arabic, 33.5 (29.3–38.2) in Asian, 35.6 (31.9–39.6) in Eastern European, and 16.2 (9.0–27.2) in Latin American immigrants. When selecting Western origin as a reference, and after adjusting on OHCA risk factors, Arabic (HR 1.18, 95%CI 1.04–1.35; P=0.01), Eastern European (HR 1.28, 95%CI 1.13–1.46; P<0.001), and African origin (HR 1.34, 95%CI 1.10–1.63; P<0.01) were associated with higher risk of OHCA, whereas Latin American origin (HR 0.58, 95%CI 0.35–0.0.96; P=0.03) was associated with lower risk of OHCA. Comparable results were observed when adjusting on education level and economic status.

Interpretation This study emphasizes that ethnicity is associated with OHCA risk, even when considering traditional cardiac arrest risk factors.

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[1] Equal contribution to the article.

Keywords: Out-of-Hospital Cardiac Arrest; Ethnicity; Immigrants; Registry; Epidemiology

Research in context

Evidence before this study

We searched MEDLINE, Embase, and the Cochrane database using the search terms "cardiac arrest" AND "ethnicity" AND "incidence" or "sudden death" AND "ethnicity" AND "incidence", to identify studies assessing incidence of cardiac arrest according to ethnicity published in English until August 31st, 2021. Studies showed that Black Americans have higher risk of out-of-hospital cardiac arrest (OHCA) as compared to White Americans. There is little evidence about the risk of OHCA in other populations.

Added value of this study

This study, comprising more than one million immigrants, captured new ethnicities, such as Arabic or Eastern European, revealing that these individuals have higher risk of OHCA as compared to Western immigrants. Moreover, we implemented traditional risk factors of OHCA and socioeconomic status into the models and the increased risk of cardiac arrest persisted adjustment on these variables.

Implications of all the available evidence

The identification of ethnic disparities is crucial to understand pathophysiological implications, tailor prediction and prevention of OHCA, and direct further research. These findings may provide foundation to reduce cardiac arrest inequalities, especially when related to ethnicity.

Introduction

Out-of-hospital cardiac arrest (OHCA) remains a major public health concern, with an estimated annual incidence of 500,000 cases in Europe, accounting for 50% of cardiovascular deaths.[1]

Traditional risk factors for cardiac arrest comprise of cardiovascular risk factors, heart diseases such as myocardial infarction or heart failure, and socioeconomic parameters.[2] Nevertheless, race and ethnicity may also play a key role. Previous studies have pointed out racial differences regarding sudden cardiac death occurrence in the US. Although income and social status partly explain differences,[3,4] sudden cardiac death remains two-fold higher in Black individuals compared to White individuals after adjustment on these characteristics.[5,6]

Up to now, the respective impacts of ethnicity, cardiovascular burden, and socio-economic factors on cardiac arrest outcome have not been studied, especially in a European context. In Denmark, immigrants account for >10% of the population and come from diverse regions all over the world (Africa, Arabic countries, Eastern Europe, Western Countries, Latin America, and Asia).[7] Moreover, they are given a unique identification number like all other Danish citizens, allowing for follow-up in nationwide registries. The Danish set-up, combining exhaustive registries and a high rate of immigration, offers appropriate tools to evaluate this issue.

We aimed to assess whether ethnicity influenced the risk of OHCA of cardiac cause in Danish immigrants and how traditional risk factors for OHCA and socioeconomic status interplayed with the results.

Methods

Study population

In this nationwide study, all immigrants between 18 to 80 years present at some point in Denmark between June 1st, 2001, and December 31st, 2020, were included. The age limit was defined to ensure a homogeneous study population with reliable diagnosis of OHCA. The immigrant status was defined as a person born abroad whose parents are both foreign citizens, or as a person born in Denmark whose parents have foreign citizenship. An exhaustive picture of the immigration status is possible in Denmark as every citizen staying more than three months in the country is obligated to obtain a residence permit, an administrative procedure during which data about country of origin, date of immigration, and date of emigration are collected. These data are publicly available on Statistics Denmark (https://www.dst.dk). Immigrants were categorised according to their region of origin: Africa, Arabic countries, Asia, Eastern Europe, Latin America (comprising Mexico, Central and South America), and Western countries (see classification in *Supplementary Material 1)*. The immigrant's region of origin was used as a proxy for ethnicity. Figure 1 shows the selection process and a description of the Danish immigration pattern is detailed in Supplementary Material 2. Data about ethnicity were reported according to the Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals.[8] The Danish Data Protection Agency approved the use of data for this study project (ref.no: 2007-58-0015/GEH-2014-017 I-Suite no: 02735). In Denmark, retrospective register-based studies do not require approval from the research ethics committee system. The data is structured in such

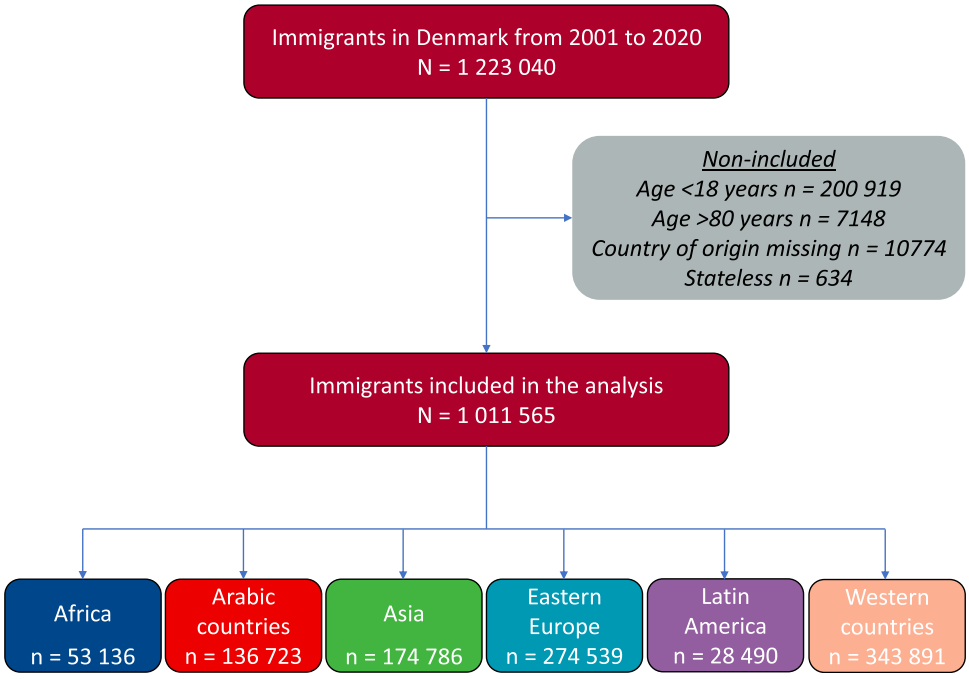

Figure 1. Flow-chart. Between 2001 and 2020, 1,223,040 individuals immigrated to Denmark. 82.4% were included in the analysis.

a way that individual patient identification is not possible but individual linkage between registers is allowed.

Data source

Using the unique civil registration number that all Danish residents are assigned, we linked information from five national administrative registries. 1/*The Danish National Population Register* provides information on age, sex, vital status, immigrant status, country of origin, dates of immigration and emigration. 2/*The Danish National Patient Register* records all hospital admissions, ambulatory hospital visits and related diagnosis using the International Classification of Diseases (ICD-10) and allowed us to collect the medical history of each individual.[9,10] 3/*The Danish Education Register* provides information on education status, which was defined by the highest completed education classified according to the International Standard Classification of Education system, (UNESCO, 2011)[11] and was divided into three groups: a/ Lower secondary education including elementary school, primary school, and high school (ISCED 0-2), b/ Upper secondary education including college and short secondary education (ISCED 3), and c/ Tertiary education including bachelor's degree (Bachelor of Arts; BA), master's degree (Master of Arts; MA), and doctoral degree or equivalent (ISCED 4-8). 4/*The Danish Household Income Register* provides information on the household income calculated as average income over a 2-year period from the date of follow-up start to account for yearly variations and minimising potential influence of illness, corrected for inflation to year 2015 and weighted according to number of people in the household. The final study population was divided into quartiles according to income. Quantiles were calculated according to the income of the total population. 5/*The Danish Cardiac Arrest Registry* (DANCAR) is an exhaustive ongoing nationwide registry collecting all OHCAs with a resuscitation attempt occurring in Denmark since June 1st, 2001, the data of which is collected as stated in the Utstein resuscitation registry template.[12,13]

Outcome

The main outcome was OHCA from presumed cardiac cause, which was defined excluding suicide attempts, road traffic accidents, trauma, drug overdose and other medical disorders. The capture of cardiac arrest cases is exhaustive, because the EMS system is activated for all emergencies concerning cardiac arrest, and the definition excludes cases with obvious late signs of death (e.g., rigor mortis) for which resuscitative efforts are not initiated. Importantly, EMS personnel are required to complete a case report form for the Danish Cardiac Arrest Registry for each OHCA.

Statistics

Preparation of this report was carried out in accordance with the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.[14]

Continuous data are presented as mean (SD) or median (IQR), depending on the distribution, and categorical data are presented as n (%). In order to respect data confidentiality, in accordance with Statistics Denmark Research Services' policy, only aggregated results with tables containing at least three observations per cell were presented.

The incidence of OHCA and corresponding 95% confidence intervals (CIs) were calculated according to the region of origin between June 1st, 2001 and December 31st, 2020. Estimates are presented as unadjusted and adjusted according to age and sex ratio of immigrants from the Western countries group.

No medical history was available before immigration when immigrants entered Denmark between 2001 and 2020. To be able to adjust for the medical history, and socioeconomic status, we considered a delayed entry of one year, meaning that medical history was collected during the 12 months after June 1st, 2001, if the individual had already immigrated to Denmark before this date, or during the 12 months after his/her immigration date (see details in Supplementary Material 3).

To investigate differences in OHCA risk between ethnicities we used Cox proportional-hazards models using age as the underlying time scale. Because of delayed entry, follow-up started on June 1st 2002 if the individual had already immigrated to Denmark before June 1st, 2001, or 12 months after immigration date if the individual immigrated after June 1st, 2001. People were censored at the age of OHCA, death, emigration, or end of follow-up (December 31st, 2020), whichever came first. Proportional hazards were tested using Schoenfeld residuals.

Data were presented as Hazard Ratios (HR) and 95% CI. Model 1 was adjusted for sex, age, history of ischaemic heart disease, history of heart failure, and type 2 diabetes. Stratification on sex, age, history of ischaemic heart disease, history of heart failure, and type 2 diabetes were performed. Interactions between region of origin, sex, type 2 diabetes and heart failure were also tested by including a cross-product term of sex and heart failure by region of origin group, and a cross-product term of sex and type 2 diabetes by region of origin group in separate models. Model 2 was furthermore adjusted on education level and income.

The data management and statistical analysis were performed using SAS version 9.4 ("SAS Institute Inc., Cary, NC, USA") and R version 4.1.1. A two-sided *P*-value <0.05 was considered statistically significant.

Role of the funding source

The funder had no role in the study design, data collection, data analysis, interpretation, or writing of the report.

Results

Baseline characteristics

Between 2001 and 2020, 1,011,565 immigrants were registered in Denmark: 53,136 were from Africa, 136,723 from Arabic countries, 174,786 from Asia, 274,539 from Eastern Europe, 28,490 from Latin America and 343,891 from Western countries. Baseline characteristics are presented in Table 1. Median age was 27 (IQR 22–37) years and 51% were males. Prevalence of cardiovascular risk factors and previous disease was low.

OHCA incidence

Overall, 1,801 (0.2%) OHCA occurred during a median follow-up time of 4.8 (IQR 1.3–17.0) years: 125 in Africans, 402 in Arabic immigrants, 259 in Asians, 379 in Eastern Europeans, 16 in Latin Americans, and 620 in Western immigrants. Median age at OHCA was 64 (IQR 53–72) years, and 72% were males. Characteristics of individuals who experienced OHCA according to region of origin are presented in Table 2.

Crude incidence of OHCA (/per 100,000 person-years) was 19.9 (95% CI 16.6–23.7) in African, 22.6 (95% CI 20.4–24.9) in Arabic, 17.9 (95% CI 15.8–20.2) in Asian, 19.9 (95% CI 17.9–22.0) in Eastern European, 9.0 (95% CI 5.0–14.6) in Latin American, and 28.0 (95%CI 25.8–30.3) in Western immigrants.

The incidence of OHCA over time according to region of origin is represented in Figure 2. OHCA incidence increased over time for Western and Arabic countries immigrants, whereas it remained low in immigrants from Latin America. OHCA incidence was consistently higher among males across regions of origin (Figure 3). The difference of OHCA incidence according to sex was the highest among Arabic countries' immigrants, whereas it was the lowest among Latin American immigrants.

Figure 4 shows the incidence of OHCA within the different ethnicities according to decades of age. OHCA incidence increased gradually with age in the six regions.

When standardized to the age and sex of the Western countries' immigrants, the incidence of OHCA (/per 100,000 person-years) was 34.6 (95% CI 27.8–43.4) in African, 34.1 (95% CI 30.4–38.4) in Arabic, 33.5 (95% CI 29.3–38.2) in Asian, 35.6 (95% CI 31.9–39.6) in Eastern European, and 16.2 (95% CI 9.0–27.2) in Latin American immigrants.

Multivariable analysis

Using delayed entry resulted in considering a population of 798,304 individuals, in which 1,758 OHCA occurred (0.2%).

In a multivariable Cox-regression model (Figure 5, Model 1) adjusted for age, sex, type 2 diabetes, history of heart failure and history of ischaemic heart disease,

	Africa (*n* = 53,136)	Arabic countries (*n* = 136,723)	Asia (*n* = 174,786)	Eastern Europe (*n* = 274,539)	Latin America (*n* = 28,490)	Western countries (*n* = 343,891)	Total (*n* = 1,011,565)
Age	29 [22, 36]	31 [23, 39]	28 [23, 35]	27 [22, 36]	28 [24, 34]	26 [22, 38]	27 [22, 37]
Male sex	28,528 (53.7)	76,626 (56.0)	74,966 (42.9)	153,515 (55.9)	13,010 (45.7)	167,582 (48.7)	514,227 (50.8)
Medical history							
Hypertension	602 (1.1)	2,340 (1.7)	1,551 (0.9)	3,012 (1.1)	201 (0.7)	6,075 (1.8)	13,781 (1.4)
Type 2 diabetes	223 (0.4)	933 (0.7)	594 (0.3)	387 (0.1)	20 (0.1)	483 (0.1)	2,640 (0.3)
Ischaemic heart disease	91 (0.2)	908 (0.7)	401 (0.2)	657 (0.2)	29 (0.1)	896 (0.3)	2,982 (0.3)
Heart failure	37 (0.1)	180 (0.1)	85 (0.0)	145 (0.1)	5 (0.0)	299 (0.1)	751 (0.1)
Atrial fibrillation	30 (0.1)	146 (0.1)	73 (0.0)	217 (0.1)	14 (0.0)	481 (0.1)	961 (0.1)
Stroke	12 (0.0)	77 (0.1)	60 (0.0)	103 (0.0)	10 (0.0)	216 (0.1)	478 (0.0)
Cancer	102 (0.2)	314 (0.2)	227 (0.1)	464 (0.2)	67 (0.2)	1,060 (0.3)	2,234 (0.2)
Chronic kidney disease	75 (0.1)	111 (0.1)	90 (0.1)	89 (0.0)	5 (0.0)	112 (0.0)	482 (0.0)
Income group							
Quartile 1: 1 to 184,567 DKK	11,856 (31.4)	27,198 (25.3)	28,173 (26.4)	63,457 (33.9)	4,602 (29.5)	51,030 (28.3)	186,316 (29.3)
Quartile 2: 184,568 to 321,593 DKK	10,920 (28.9)	31,093 (28.9)	23,619 (22.2)	53,177 (28.4)	2,994 (19.2)	31,628 (17.5)	153,431 (24.2)
Quartile 3: 321,593 to 486,947 DKK	9,130 (24.2)	34,148 (31.8)	28,888 (27.1)	39,795 (21.3)	3,252 (20.8)	33,239 (18.4)	148,452 (23.4)
Quartile 4> 486,947 DKK	5,847 (15.5)	14,978 (13.9)	25,929 (24.3)	30,824 (16.5)	4,772 (30.6)	64,531 (35.8)	146,881 (23.1)
Missing	15,383 (28.9)	29,306 (21.4)	68,177 (39.0)	87,286 (47.5)	12,870 (45.2)	163,463 (10.0)	376,485 (37.2)
Education level							
Lower secondary	18,680 (35.2)	58,059 (42.5)	32,516 (18.6)	26,003 (9.5)	2,882 (10.1)	20,675 (6.0)	158,815 (15.7)
Upper secondary	10,248 (19.3)	28,118 (20.6)	24,959 (14.3)	67,282 (24.5)	3,948 (13.9)	51,233 (14.9)	185,788 (18.4)
Tertiary	9,629 (18.1)	23,310 (17.0)	50,467 (28.9)	79,307 (28.9)	10,237 (35.9)	105,570 (30.7)	278,520 (27.5)
Missing	14,579 (27.4)	27,236 (19.9)	66,844 (38.2)	101,947 (37.1)	11,423 (40.1)	166,413 (48.4)	388,442 (38.4)
OHCA	125 (0.2)	402 (0.3)	259 (0.1)	379 (0.1)	16 (0.1)	620 (0.2)	1,801 (0.2)
Follow up, *years*	13 [5, 20]	17 [6, 20]	5 [2, 17]	4 [1, 12]	2 [1, 11]	3 [1, 12]	5 [1, 17]
Total observed time, *years*	628,051	1,780,188	1,445,768	1,909,196	177,761	2,214,410	8,155,374

***Table 1*: Baseline characteristics of all immigrants (with or without OHCA) at start of follow-up.**

Data are presented as n (%) or median [interquartile range] ± SD.

Abbreviations: DKK, Danish krone; OHCA, out-of-hospital cardiac arrest. Comorbidities were assessed during the 12 months after June 1st, 2001, if the individual had already immigrated to Denmark before this date, or during the 12 months after his/her immigration date.

	Africa (*n* = 125)	Arabic countries (*n* = 402)	Asia (*n* = 259)	Eastern Europe (*n* = 379)	Latin America (*n* = 16)	Western countries (*n* = 620)	Total (*n* = 1 801)
Age at OHCA	56 [44, 66]	60 [50.0, 68.8]	62 [53, 70]	60 [51, 71]	69 [57.5, 74.0]	68 [60.8, 74.0]	64 [53, 72]
Male sex	94 (75.2)	332 (82.6)	181 (69.9)	260 (68.6)	9 (56.2)	417 (67.3)	1,293 (71.8)
Medical history							
Hypertension	13 (10.4)	≤52 (≤12.9)	47 (18.1)	58 (15.3)	≤3 (≤18.8)	128 (20.6)	300 (16.7)
Type 2 diabetes	4 (3.2)	27 (6.7)	17 (6.6)	11 (2.9)	0 (0.0)	12 (1.9)	71 (3.9)
Ischaemic heart disease	≤7 (≤5.6)	31 (7.7)	9 (3.5)	13 (3.4)	≤3 (≤18.8)	27 (4.4)	88 (4.9)
Heart failure	≤3 (≤2.4)	15 (3.7)	8 (3.1)	≤8 (≤2.1)	0 (0.0)	11 (1.8)	47 (2.6)
Atrial fibrillation	≤3 (≤2.4)	5 (1.2)	≤3 (≤1.2)	≤3 (≤0.8)	0 (0.0)	10 (1.6)	22 (1.2)
Stroke	0 (0.0)	0 (0.0)	≤3 (≤1.2)	5 (1.3)	0 (0.0)	≤3 (≤0.5)	9 (0.5)
Cancer	≤3 (≤2.4)	≤3 (≤0.7)	≤3 (≤1.2)	≤3 (≤0.8)	0 (0.0)	6 (1.0)	14 (0.8)
Chronic kidney disease	≤3 (≤2.4)	6 (1.5)	≤3 (≤1.2)	0 (0.0)	0 (0.0)	≤3 (≤0.5)	11 (0.6)
Income group							
Quartile 1	31 (26.3)	93 (24.2)	52 (21.2)	83 (23.2)	6 (37.5)	76 (13.4)	341 (20.2)
Quartile 2	37 (31.4)	117 (30.5)	74 (30.2)	124 (34.7)	4 (25.0)	162 (28.5)	518 (30.7)
Quartile 3	31 (26.3)	117 (30.5)	69 (28.2)	≤87 (≤24.4)	≤3 (≤18.8)	140 (24.6)	447 (26.5)
Quartile 4	19 (16.1)	57 (14.8)	50 (20.4)	≤63 (≤17.6)	≤3 (≤18.8)	191 (33.6)	383 (22.7)
Missing	7	18	14	22	0	51	112
Education level							
Lower secondary	41 (32.8)	153 (38.1)	102 (39.4)	98 (25.9)	4 (25.0)	137 (22.1)	535 (29.7)
Upper secondary	41 (32.8)	≤115 (≤28.6)	78 (30.1)	146 (38.5)	≤3 (≤18.8)	244 (39.4)	627 (34.8)
Tertiary	19 (15.2)	69 (17.2)	43 (16.6)	66 (17.4)	7 (43.8)	158 (25.5)	362 (20.1)
Missing	24 (19.2)	≤65 (≤16.2)	36 (13.9)	69 (18.2)	≤3 (≤18.8)	81 (13.1)	277 (15.4)

***Table 2*: Baseline characteristics of patients with OHCA at start of follow-up.**
Data are presented as n (%) or median [interquartile range] ± SD.
Abbreviations: OHCA, out-of-hospital cardiac arrest. Comorbidities were assessed during the 12 months after June 1st, 2001, if the individual had already immigrated to Denmark before this date, or during the 12 months after his/her immigration date.

immigrants from Africa (HR 1.34, 95% CI 1.10–1.63; *P*<0.01), Arabic countries (HR 1.18, 95% CI 1.04–1.35; *P*=0.01), and Eastern Europe (HR 1.28, 95% CI 1.13–1.46; *P*<0.001) had a higher risk of OHCA as compared to Western countries' immigrants, whereas immigrants from Latin America had a lower risk (HR 0.58, 95% CI 0.35–0.96; *P*=0.03). The OHCA risk of Asian immigrants (HR.1.14, 95% CI 0.95–1.33; *P*=0.08) was not different as compared to Western countries' immigrants. No interaction between region of origin and sex, region of origin and heart failure, or region of origin and type 2 diabetes were found when tested in a separate model (*P* for interaction = 0.251, 0.345, and 0.904, respectively). When not stratifying on traditional risk factors, HR in each country region were the same, and HR (95%CI) for OHCA incidence according to male sex, heart failure, type 2 diabetes and ischaemic heart disease were 2.51 (2.27–2.79), 5.80 (4.14–8.14), 2.56 (1.97–3.13), and 1.76 (1.35–2.29), respectively.

Finally, when adjusting for education level and income (Figure 5, Model 2), HR in each country region were similar as when adjusting on traditional risk factors for OHCA. When compared to Western immigrants, immigrants from Africa, Arabic countries and Eastern Europe had higher risk of OHCA, in contrast to Latin American immigrants who had a lower risk.

Discussion

Our findings indicate that the risk of OHCA is significantly different among immigrants according to their region of origin. Compared to Western countries' immigrants, African, Arabic countries', and Eastern countries' immigrants had higher risk of OHCA, whereas Latin American immigrants had a lower risk. These results were persistent after adjustment on traditional risk factors for OHCA, but also on socio-economic factors.

Population of the study

The population studied here was young (mean 26.6 to 29.8 years vs. approximately 45 to 63 years at start of follow-up in other studies),[3,6,15] which explains the low prevalence of ischaemic heart disease,[6] and the low incidence of OHCA.[16] Nevertheless, the settings of the current study, assessing more than one million individuals, allowed for a balanced analysis, preventing overestimation of the effect of ischemic heart disease on OHCA.

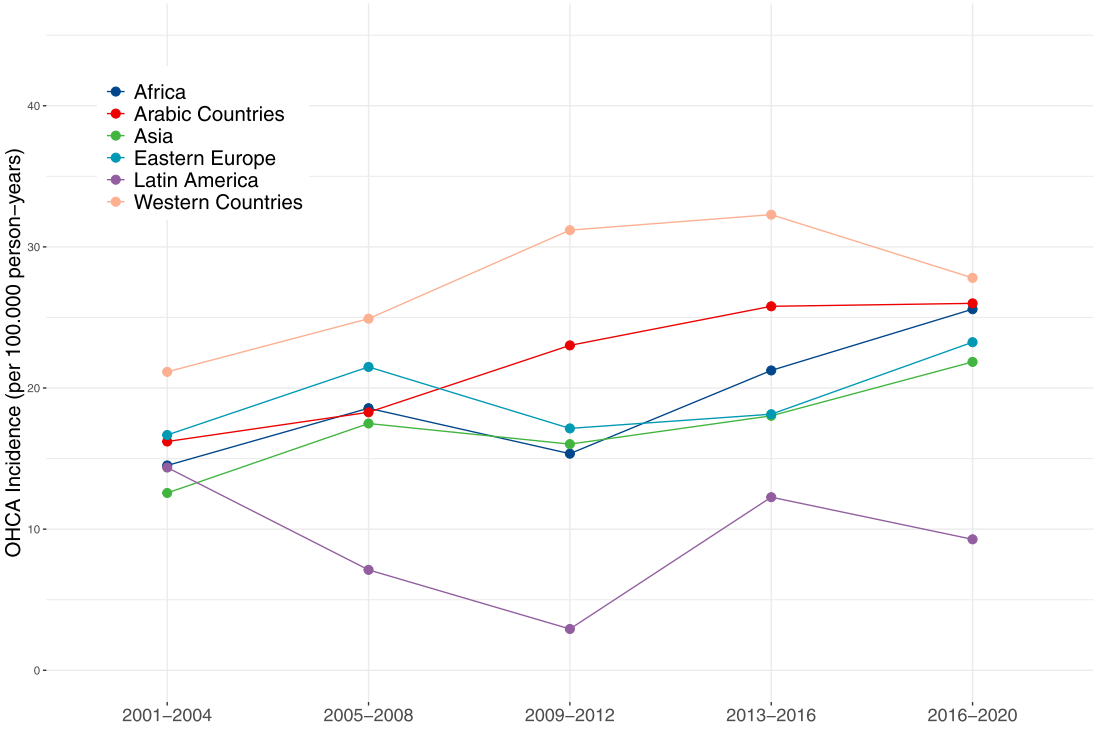

Figure 2. Crude OHCA incidence according to time and to region of origin. Dots represent crude OHCA incidence per 100,000 person-years. From 2001 to 2020, OHCA incidence increased in individuals from each region of origin, except in individuals from Latin America.

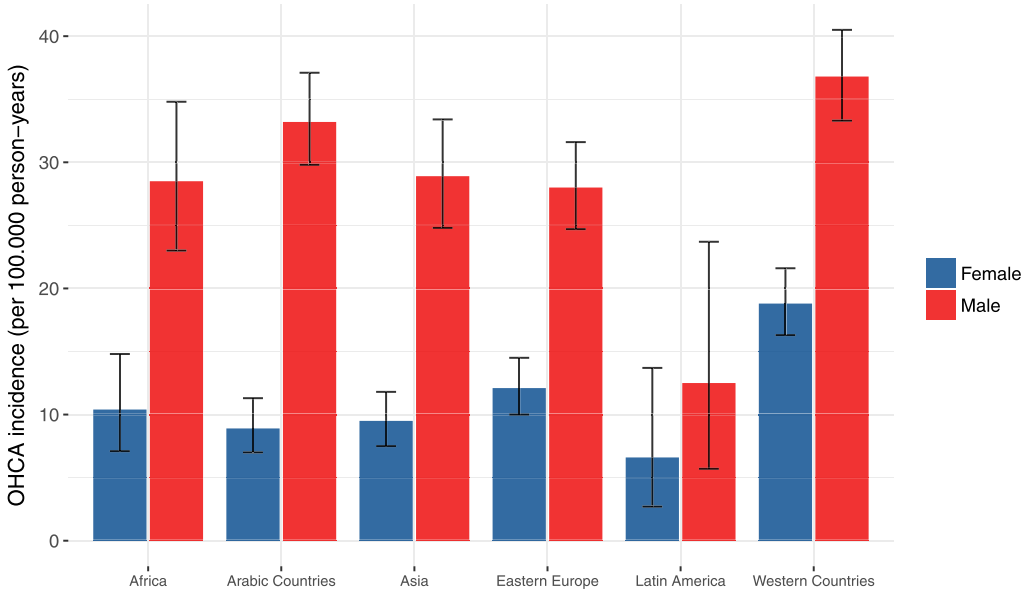

Figure 3. Crude OHCA incidence according to sex and to region of origin. OHCA incidences and 95% confidence intervals are presented. Crude OHCA incidence was consistently higher in males than in females. However, this difference was smaller in individuals from Latin America.

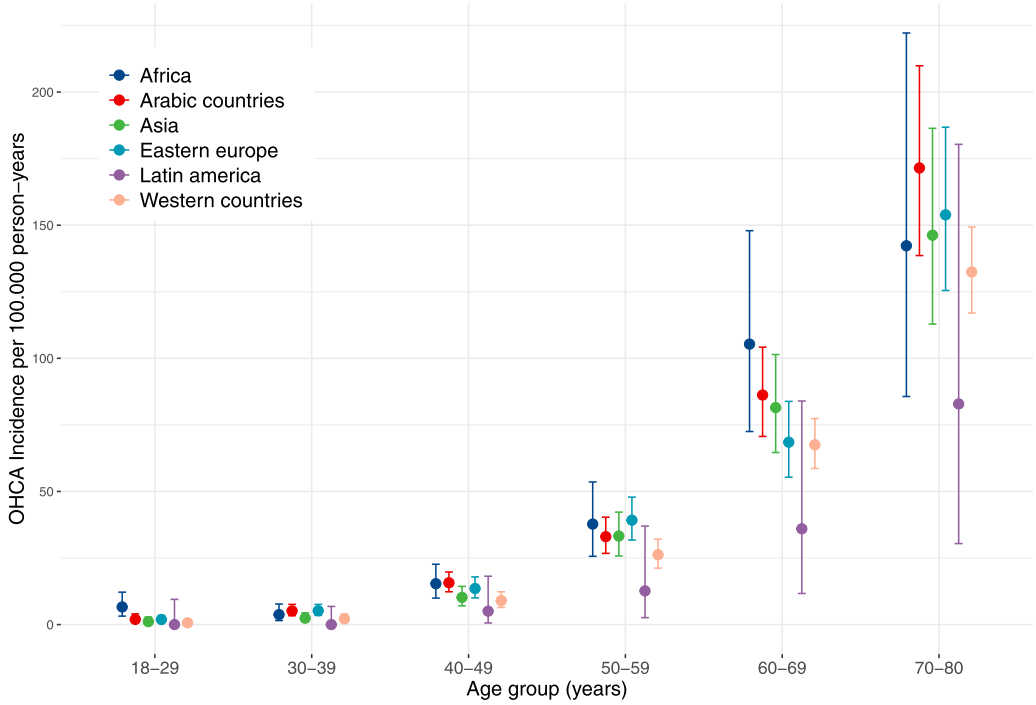

Figure 4. Crude OHCA incidence according to age and to region of origin. OHCA incidences and 95% confidence intervals are presented. Crude OHCA incidence increased consistently with age whatever the region of origin.

The second peculiarity was education as 20% had a tertiary education. In comparison, 15% of the Danish and 11% of the French populations had a tertiary education in 2010, whereas in the world's poorest countries, less than 1% had completed tertiary education.[17] The high education attainment could be another explanation for the low prevalence of cardiovascular disease.[18]

OHCA risk according to ethnicity

Up to now, most of the data available on ethnicity and OHCA were collected in the U.S. Black Americans had twice higher risk of sudden cardiac death compared to White Americans,[19,20] whereas Hispanics and Asians had lower risk.[21,22] Except for Asian immigrants, we showed similar results with lower incidence of OHCA after adjustment in Latin Americans, but we also found higher OHCA risk in African, Arabic countries, and Eastern European immigrants. The main difference from previous works is that, beyond Black/White/Hispanic and Asian distinction, we could capture new ethnicities such as Arabic or Eastern European in the same register allowing for direct comparison. Moreover, the Danish setting, using a prospective nationwide register, allows an exhaustive picture of all OHCAs for almost two decades. Over this time period the OHCA incidence increased in almost all the region groups. This trend might be due to of a better awareness of OHCA in the general population, but also because of the implementation of an electronic OHCA registration form from 2016, which may have contributed to increase the capture of OHCA.

Weight of traditional OHCA risk factors as compared to ethnicity

This study is the second one to show that ethnicity impacts OHCA risk independently of traditional risk factors for cardiac arrest.[6] Deo et al. used advanced parameters such as cholesterol levels, alcohol use or physical activity as covariates, whereas we present results in a larger population. Nevertheless, we found that traditional risk factors were associated with much higher risk of OHCA as compared to region of origin. For instance, heart failure was associated with four times greater risk of OHCA as compared to African region.

Reasons for ethnic disparities regarding risk of OHCA

The impact of ethnicity on cardiac arrest may be due to differences in genetic background, diet, preventive use of health-care services, socio-economic status, or lifestyle factors.[23–26] Nevertheless, even if genetics is a fast-growing field with lots of promise, up to now, we have little scientific evidence explaining disparities regarding cardiac arrest risk.[27,28] In the present work, ethnic differences regarding OHCA risk

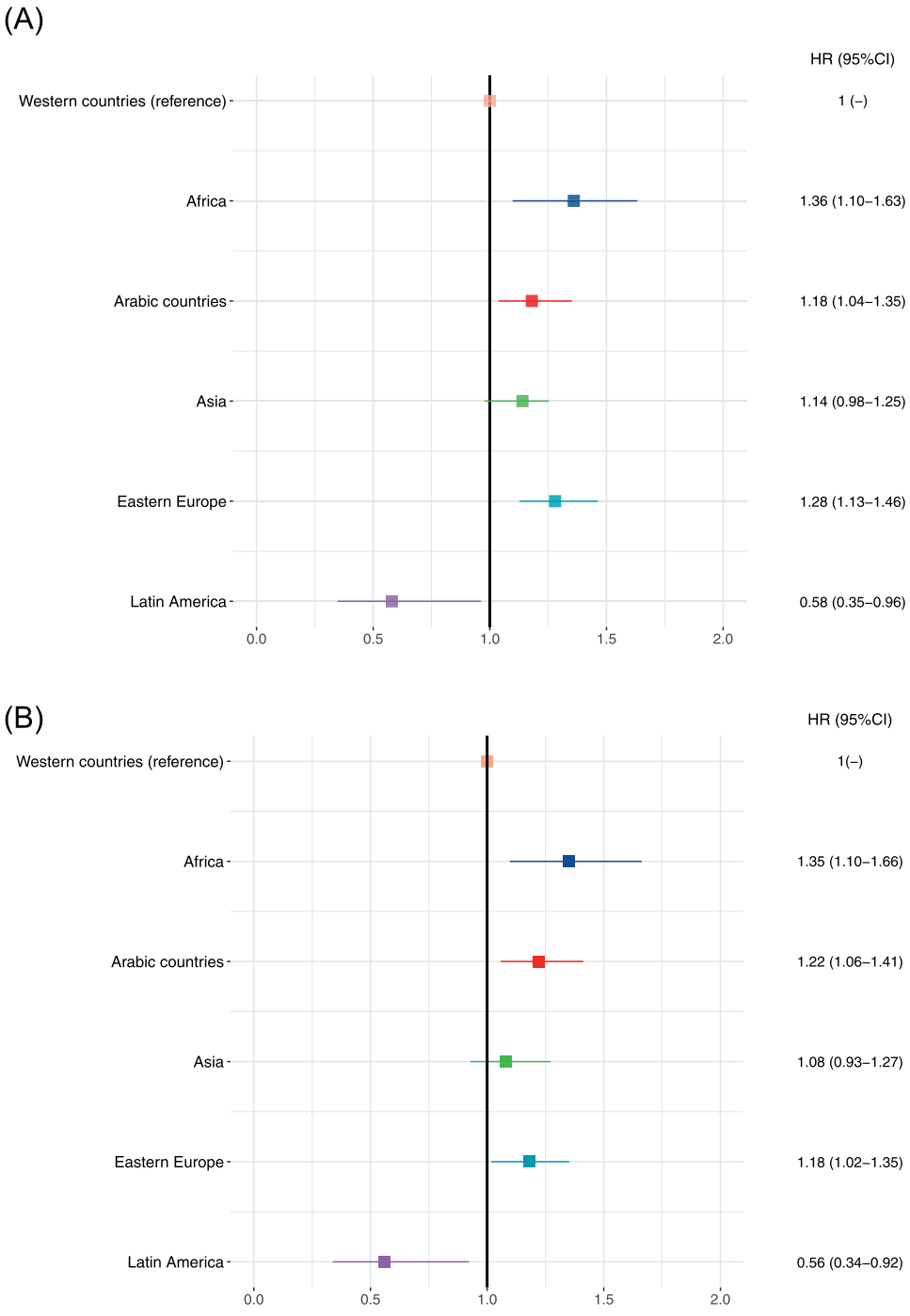

Figure 5. Risk of OHCA according to region of origin using multivariable Cox-regression models. Hazard ratios and 95% confidence interval are presented. Model 1 (panel A) is adjusted on sex, age, history of ischaemic heart disease, history of heart failure, and type 2 diabetes. Model 2 (panel B) is adjusted on education level and income. In both models, the risk of OHCA was higher in individuals originating from Africa, Arabic countries and Eastern Europe, whereas it was lower in individuals from Latin America.

persisted after adjustment on education and income. A first step to investigate why the OHCA risk is different across ethnic groups would be to perform autopsy and molecular autopsy to more accurately identify the underlying cause of death in each individual.[29–31]

A call for reducing ethnic disparities regarding OHCA

The terms "race" and "ethnicity" are somewhat subjective as they are social constructs without scientific or biological meaning and are changing over time. We have chosen to use the term ethnicity, which is more inclusive of a sense of shared identity, as the groups have their own cultural context, traditions, history and language. While literature about disparities is flourishing, data about ethnicity and race in other countries than the U.S is scarce. One reason may be the lack of registers in respective countries, but also because data collection regarding ethnicity/race is not allowed in some countries. Appraisal of OHCA risk in ethnic groups other than Western individuals is crucial to understand pathophysiological implications, tailor prediction of OHCA, and direct further research. Ethnicity might be a source of disparities, and reducing inequalities related to cardiac arrest is critical.

Limitations

Our work has several limitations. Only immigrants who arrived in Denmark were included, generating a "healthy worker" selection, and an OHCA incidence underestimation.[32,33] Moreover, we suspect that health status was different across groups, but the multivariable analysis took the comorbidity burden into account and allowed OHCA risk comparison among the different regions of origin. Secondly, country of origin was used to determine ethnicity, which could be misclassified in rare cases where an individual had immigrated to Denmark from a country other than his original region of origin. Nevertheless, unless the misclassification was systematic, it would tend toward attenuating estimates of group differences, thus not invalidating the findings. Furthermore, information clarifying the reason for immigration was not available in the registers used for this study. As far as we know, no previous work has defined world regions in the cardiac arrest literature, so we aimed to define homogeneous groups according to regions of origin. Third, important subcategories (e.g. the Latin American population who can be Latin American Indigenous peoples or African descent) with different cultures, languages, and diets exist within different groups which could not be identified here. Finally, in some subgroups, such as Latin America, the number of observed OHCA events was not large and may not provide sufficient power to detect differences.

Conclusion

This study assessed OHCA incidence among more than 1 million adult immigrants in Denmark. After adjusting for all traditional risk factors for cardiac arrest, Arabic, Eastern European, and African origin were associated with higher risk of cardiac arrest from cardiac cause, whereas Latin American origin was associated with lower risk of cardiac arrest.

Contributors

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Jacob Tfelt- Hansen: conceptualisation, supervision, conceptualisation, writing – original draft
All authors revised the manuscript for important intellectual content.

Data sharing statement

Data are available after formal request to and acceptance by Statistics Denmark and the Danish Data Protection Agency.

Declaration of interests

We declare no competing interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lanepe.2022.100477.

References

1 Gräsner J-T, Lefering R, Koster RW, et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: a prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. *Resuscitation*. 2016;105:188–195.
2 Reinier K, Rusinaru C, Chugh SS. Race, ethnicity, and the risk of sudden death. *Trends Cardiovasc Med*. 2019;29:120–126.
3 Zhao D, Post WS, Blasco-Colmenares E, et al. Racial differences in sudden cardiac death. *Circulation*. 2019;139:1688–1697.
4 Reinier K, Nichols GA, Huertas-Vazquez A, et al. Distinctive clinical profile of blacks versus whites presenting with sudden cardiac arrest. *Circulation*. 2015;132:380–387.
5 Chan PS, Nichol G, Krumholz HM, et al. Racial differences in survival after in-hospital cardiac arrest. *JAMA*. 2009;302:1195–1201.

6 Deo R, Safford MM, Khodneva YA, et al. Differences in risk of sudden cardiac death between blacks and whites. *J Am Coll Cardiol*. 2018;72:2431–2439.
7 Official statistics about immigration in Denmark. https://www.dst.dk/en/Statistik/emner/borgere/flytninger/ind-og-udvandring.
8 Flanagin A, Frey T, Christiansen SL, Manual of Style Committee AMA. Updated guidance on the reporting of race and ethnicity in medical and science journals. *JAMA*. 2021;326:621–627.
9 Madsen M, Davidsen M, Rasmussen S, Abildstrom SZ, Osler M. The validity of the diagnosis of acute myocardial infarction in routine statistics: a comparison of mortality and hospital discharge data with the Danish MONICA registry. *J Clin Epidemiol*. 2003;56:124–130.
10 Kümler T, Gislason GH, Kirk V, et al. Accuracy of a heart failure diagnosis in administrative registers. *Eur J Heart Fail*. 2008;10:658–660.
11 Unesco Education Classification. http://uis.unesco.org/en/topic/international-standard-classification-education-isced.
12 Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA*. 2013;310:1377–1384.
13 Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest: a statement for healthcare professionals from a task force of the International Liaison committee on resuscitation (American heart association, European resuscitation council, Australian and New Zealand council on resuscitation, heart and stroke foundation of Canada, interamerican heart foundation, resuscitation council of Southern Africa, resuscitation Council of Asia); and the American heart association emergency cardiovascular care committee and the council on cardiopulmonary, critical care, perioperative and resuscitation. *Circulation*. 2015;132:1286–1300.
14 Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18:805–835.
15 Reinier K, Sargsyan A, Chugh HS, et al. Evaluation of sudden cardiac arrest by race/ethnicity among residents of Ventura County, California, 2015–2020. *JAMA Netw Open*. 2021;4:e2118537.
16 Lynge TH, Risgaard B, Banner J, et al. Nationwide burden of sudden cardiac death: a study of 54,028 deaths in Denmark. *Heart Rhythm*. 2021;18:1657–1665.
17 tertiary education. https://ourworldindata.org/tertiary-education#enrollment-in-tertiary-education.
18 Woodward M, Peters SAE, Batty GD, et al. Socioeconomic status in relation to cardiovascular disease and cause-specific mortality: a comparison of Asian and Australasian populations in a pooled analysis. *BMJ Open*. 2015;5:e006408.
19 Becker LB, Han BH, Meyer PM, et al. Racial differences in the incidence of cardiac arrest and subsequent survival. The CPR Chicago Project. *N Engl J Med*. 1993;329:600–606.
20 Cowie MR, Fahrenbruch CE, Cobb LA, Hallstrom AP. Out-of-hospital cardiac arrest: racial differences in outcome in Seattle. *Am J Public Health*. 1993;83:955–959.
21 Gillum RF. Sudden cardiac death in Hispanic Americans and African Americans. *Am J Public Health*. 1997;87:1461–1466.
22 Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. *Circulation*. 2001;104:2158–2163.
23 Park JH, Cha K-C, Ro YS, et al. Healthy lifestyle factors, cardiovascular comorbidities, and the risk of sudden cardiac arrest: a case-control study in Korea. *Resuscitation*. 2022. S0300-9572(22)00098-3.
24 Chiuve SE, Fung TT, Rexrode KM, et al. Adherence to a low-risk, healthy lifestyle and risk of sudden cardiac death among women. *JAMA*. 2011;306:62–69.
25 Jonsson M, Ljungman P, Härkönen J, et al. Relationship between socioeconomic status and incidence of out-of-hospital cardiac arrest is dependent on age. *J Epidemiol Community Health*. 2020;74:726–731.
26 Cockerham WC, Bauldry S, Hamby BW, Shikany JM, Bae S. A comparison of black and white racial differences in health lifestyles and cardiovascular disease. *Am J Prev Med*. 2017;52:S56–S62.
27 Burke A, Creighton W, Mont E, et al. Role of SCN5A Y1102 polymorphism in sudden cardiac death in blacks. *Circulation*. 2005;112:798–802.
28 Sun AY, Koontz JI, Shah SH, et al. The S1103Y cardiac sodium channel variant is associated with implantable cardioverter-defibrillator events in blacks with heart failure and reduced ejection fraction. *Circ Cardiovasc Genet*. 2011;4:163–168.
29 Winkel BG, Holst AG, Theilade J, et al. Nationwide study of sudden cardiac death in persons aged 1–35 years. *Eur Heart J*. 2011;32:983–990.
30 Stiles MK, Wilde AAM, Abrams DJ, et al. 2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families. *Heart Rhythm*. 2021;18:e1–50.
31 Tseng ZH, Ramakrishna S, Salazar JW, Vittinghoff E, Olgin JE, Moffatt E. Sex and racial differences in autopsy-defined causes of presumed sudden cardiac death. *Circ Arrhythm Electrophysiol*. 2021;14:e009393.
32 Rawshani A, Svensson A-M, Zethelius B, Eliasson B, Rosengren A, Gudbjörnsdottir S. Association between socioeconomic status and mortality, cardiovascular disease, and cancer in patients with Type 2 diabetes. *JAMA Intern Med*. 2016;176:1146–1154.
33 McDonald JT, Kennedy S. Insights into the 'healthy immigrant effect': health status and health service use of immigrants to Canada. *Soc Sci Med*. 2004;59:1613–1627.