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Urban population density and mortality in a compact Dutch city: 23-year follow-up of the Dutch GLOBE study

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ABSTRACT

We investigated the association and underlying pathways between urban population density and mortality in a compact mid-sized university city in the Netherlands. Baseline data from the GLOBE cohort study (N = 10,120 residents of Eindhoven) were linked to mortality after 23 years of follow up and analyzed in multilevel models. Higher population density was modestly related to increased mortality, independently of baseline socioeconomic position and health. Higher population density was related to more active transport, more perceived urban stress and smoking. Increased active transport suppressed the mortality-increasing impact of higher population density. Overall, in dense cities with good infrastructure for walking and cycling, high population density may negatively impact mortality.

1. Introduction

Today, over 70% of Europeans reside in cities and this number is expected to increase in the coming decades (The World Bank, 2017). In order to host more residents, cities can either spread out (e.g. build new housing in the outskirts), or become denser (e.g. build apartment buildings and other high rises within the city's current boundaries). Recent papers advocated the need for 'compact cities', with "short distances that promote increased population density, mixed land use, proximate and enhanced public transport, and an urban form that encourages cycling and walking" (Stevenson et al., 2016; Giles-Corti et al., 2016). Denser populated cities are thought to enhance active transport (e.g. walking, cycling) because of the close proximity of shops, facilities, work and schools which in turn is beneficial to major non-communicable diseases, such as cardiovascular diseases and types of cancers (Sallis et al., 2016). How compactness relates to levels of air pollution and traffic accidents, is still debated. The paradox of intensification states that "ceteris paribus, urban intensification which increases population density will reduce per capita car use, with benefits to the global environment, but will also increase concentrations of motor traffic, worsening the local environment in those locations where it occurs."(Melia et al., 2011) Furthermore, living close together may also be associated with more urban stress, e.g. due to noise pollution, vandalism, crime or lower quality housing. These urban stressors could affect health in a negative way via perceived stress, a bad internal climate, or through unhealthy coping behaviours, such as smoking and alcohol consumption (Lederbogen et al., 2011; Peen et al., 2010; Putrik et al., 2015; Park and Iacocca, 2014). In addition, a closer proximity to shops and facilities may also increase the proximity to tobacco and alcohol outlets which can enhance smoking or drinking behaviour (Finan et al., 2018; Fone et al., 2016).

Most studies advocating compact cities for public health reasons originate in the U.S.A. or Australia where cities, after leaving down town, are generally widely set-up, with the risk of urban sprawl. Urban sprawl negatively affects the accessibility of public transport, local shops and services. In contrast, European cities are often more compact and, in many cases, are very densely populated - also in the outskirts. For example, a middle-sized city of 200,000–250,000 inhabitants in the US has an average population density of just over 1000 inhabitants per square kilometre (e.g. Orlando, Florida: 1017 inhabitants/km2; Madison, Wisconsin: 1173 inhabitants/km2; Fremont, California: 1162 inhabitants/km2). A city of the same size in Europe may have a population density that is more than twice or even five times as high (e.g. Eindhoven, the Netherlands: 2596 inhabitants/km^2; Bordeaux, France: 5000 inhabitants/km^2 (2005); Porto, Portugal: 5736 inhabitants /km^2 (2005)). Access to public facilities is less of an issue in these denser cities. In these urban areas, high levels of population density may reach a 'tipping point', after which the positive health consequences of high

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density do not outweigh the negative ones, related to urban stress. Indeed, evidence from densely populated areas in Europe suggests negative health consequences from increased population density on several health outcomes, including mortality (Chaix et al., 2006; Meijer et al., 2012; Fecht et al., 2016) and mental health (Sundquist et al., 2004). A study from the nineties, undertaken in Japan, hints towards the existence of a curvilinear association of density with mortality where increased urbanization was associated with lower mortality with the exception of inner-city areas with the highest density (Tanaka et al., 1996). This finding is in line with the common notion that mortality in cities is in general lower than in rural areas (Singh and Siahpush, 2014; Chen and Yang, 2014). It also suggests that within densely populated cities, increasing density may not be beneficial for health (Fecht et al., 2016).

The aim of this paper is to investigate the influence of population density on all-cause and cause specific mortality in a densely populated European city: the city of Eindhoven, a middle-sized city hosting a technical university situated in the South-East of the Netherlands, which grew from 190,000 inhabitants in 1990 to 227,100 inhabitants in 2017 - which makes it the fifth largest city in the Netherlands currently. Furthermore, potential mediating factors will be studied. Both positive mediators, expected to be associated with increased density and healthy behaviour (i.e. physical activity) and negative mediators (i.e. urban stressors, or inadequate coping responses, such as smoking) will be explored. The conceptual model describing these potential mediators is visualized in Fig. 1. We adjusted all analyses for indicators of individual and neighbourhood level socioeconomic position (SEP). Those with a lower SEP may be more likely to live in highly populated areas, but also to be less physically active, live in lower quality housing and experience higher mortality levels (Stringhini et al., 2017). Related, neighbourhood deprivation and population density may be correlated, and associations between neighbourhood deprivation and mortality are well-reported (Pickett and Pearl, 2001). Similarly, as a worse health status may sort people into specific neighbourhoods (potentially with higher population density), and may lead to higher mortality, we also adjusted for baseline health status.

2. Methods

2.1. Study population

Data for this study were collected among a stratified sample of the adult population of the city of Eindhoven in the Netherlands, that participated in the prospective cohort study GLOBE (a Dutch acronym for 'Health and Living Conditions of the Population of Eindhoven and surroundings'). At baseline, in 1991, a postal survey was send out to a random sample, stratified by age, degree of urbanization, and socioeconomic position, of non-institutionalized Dutch persons aged 14–75 years living in Eindhoven and surrounding municipalities (response rate 70.1%, N = 18,973). There were no significant differences in response rates by age, sex, social class (zip code), marital status and level of urbanization. The majority of the participants (n = 10,450, 52.7%) were inhabitants of the city of Eindhoven (the fifth largest city of the Netherlands with approximately 190,000 inhabitants in 1991) and lived in 86 different neighbourhoods (average size of a neighbourhood is ca. 2200 residents, with an approximate inter quartile range of 1000–3200). More detailed information on the objectives, study design, and data collection of the Dutch GLOBE study can be found elsewhere (Mackenbach et al., 1994; Van Lenthe et al., 2014). The use of personal data in the GLOBE study is in compliance with the Dutch Personal Data Protection Act and the Municipal Database Act and has been registered with the Dutch Data Protection Authority (number 1248943).

2.2. Measures

2.2.1. Mortality

Mortality data up to and including December 31st, 2014 were obtained from Statistics Netherlands. We were able to link 10,125 participants to the register data (96.9%). Participants were censored at their date of death or end of follow-up. During the almost 24 years of follow-up, 3024 individuals (29,9%) died from all causes. In addition to all-cause mortality, we also investigated the three major groups of cause specific mortality: cancer mortality, cardiovascular mortality, and respiratory mortality. Cause of death was recorded based on the International Statistical Classification of Diseases and Related Health Problems (ICD) of the World Health Organisation (WHO) (World Health Organization, 2004). Until 1996, the ICD-9 codes were used. From 1996 onwards, ICD-10 is used. Cancer mortality included ICD-10 codes C00-D48 (ICD-9: 140–239). Cardiovascular mortality included ICD-10 codes I00-I99 (ICD-9: 390–459). Respiratory mortality included ICD-10 codes J00-J99 (ICD-9: 460–519).

2.2.2. Population density

Population density was derived in 1992 from routinely collected descriptive statistical information about neighbourhoods from the statistical division of Eindhoven municipality. The average number of

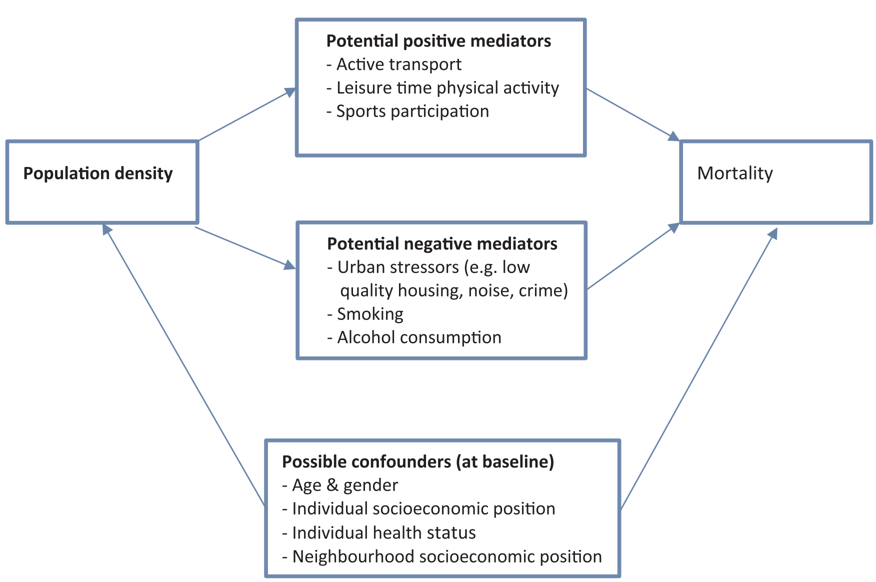

Fig. 1. Conceptual model describing the expected relationship between population density and mortality.

people residing per 1 square hectometre (hm^2) was recorded for each neighbourhood in the city of Eindhoven. Population density was linked to the residential area of GLOBE participants by a unique neighbourhood code (assigned to each neighbourhood by Statistics Netherlands). For ease of interpretation, the indicator of density was centred around the mean and divided by ten, and therefore one-unit increase represents ten more people per hm^2.

2.2.3. Potential mediators

2.2.3.1. Perceived urban stressors. Perceived urban stressors were stressors related to the direct residential neighbourhood of the participant and their housing situation. The urban stressors were measured via self-reported questionnaires in 1991. All participants were asked to indicate whether or not they dealt with any of the listed situations in the past 12 months: 1) Noise nuisance from your neighbours; 2) Traffic noise, noise from passing airplanes, street noise, noise from businesses in your neighbourhood; 3) Bad odour/air pollution because of traffic, industry or businesses; 4) Problems with vandalism, pollution, crime etc. in your street or neighbourhood; 5) Coldness and draught in your house; 6) Misted windows or windows covered in condensation in your living room; 7) Damp problems in your house and the formation of mildew on the walls, furniture, fabrics.

2.2.3.2. Health behaviour. Physical activity indicators were also measured via self-reported questionnaires in 1991. Active transport was assessed as ‘How long on average do you walk or cycle to and from your work and to and from the store a day?’. Respondents could enter the average minutes a day. Due to the strongly skewed distribution, active transport was dichotomized into ‘yes, participates in active transport’ for those respondents who reported at least 5 min each day, versus ‘no, does not participate in active transport’ for those respondents who reported no or less than 5 min of active transport a day.

Leisure time physical activity was assessed via the question ‘How many hours of your leisure time do you spend gardening, cycling, walking or walking the dog in a week in total?’. Respondents could respond with (1) (Almost) never, (2) Less than 1 h, (3) 1–2 h, or (4) 2 h or more. The variable was dichotomized into ‘yes, is physically active during leisure time’ for those respondents who answered any physical activity (responses 2, 3 and 4), versus ‘no, does not participate in any leisure time physical activity’ for those respondents who reported to participate (almost) never in leisure time physical activities.

Sports participation was assessed via the question ‘Do you exercise?’ with the instruction to not include any mind sports. Respondents could respond with (1) (Almost) never, (2) Yes, less than 1 h, (3) Yes, 1–2 h, or (4) Yes, 2 h or more. The variable was dichotomized into ‘yes, participates in sports’ for those respondents who answered yes to the above question (responses 2, 3 and 4), versus ‘no, does not participate in sports’ for those respondents who reported to (almost) never exercise.

Smoking status was self-reported in 1991 and based on the question “Do you smoke?”. It was dichotomized to non-smokers (including former smokers and never smokers) and smokers (current smokers).

Alcohol consumption was self-reported at baseline (1991) as the number of days per week the person consumed alcohol and the average number of alcoholic beverages (glasses) consumed per drinking day. This information was used to identify current drinkers ($>$ 7 glasses of alcoholic beverages each week) and non- or light drinkers (7 or less alcoholic beverages per week), based on the most recent guidelines of the Dutch Health Council (“Don’t drink any alcohol or in any case, drink no more than 1 alcoholic beverage a day”) (Gezondheidsraad, 2015).

2.2.4. Neighbourhood- and individual level confounders

To adjust for neighbourhood socioeconomic position, we included the percentage of households with low education in a neighbourhood as a confounder. This measure was also derived in 1992 from routinely collected descriptive statistical information from neighbourhoods from the statistical division of Eindhoven municipality and could be linked via neighbourhood code as well.

Individual socioeconomic position was measured using the highest attained educational level of the participant at baseline. Based on the International Standard Classification of Education (ISCED) we defined four categories: 1—high (higher professional education and university; ISCED 5–7); 2—middle (intermediate professional and higher general education; ISCED 3–4); 3—low (lower professional and intermediate general education; ISCED 2); and 4—lowest (primary education; ISCED 0–1) (UNESCO, 1997). Educational level is has proved to be a good indicator of socio-economic position in the Netherlands (Van Berkel-Van Schaik and Tax, 1990).

Health status at baseline was derived from the 1991 postal survey and was measured as none (0) or 1 or more chronic conditions (1) such as hypertension, diabetes mellitus and arthritis. All analyses were adjusted for age (in years) and gender.

2.3. Statistical analyses

Participants with missing values for the individual- or neighbourhood-level confounders were excluded from all analyses (n = 5). Thus, the main analyses were carried out with n = 10,120 participants, residing in 86 neighbourhoods (mean number of participants per neighbourhood: n = 118, minimum n = 4, maximum n = 373).

To examine neighbourhood differences in mortality, Cox multilevel models with Weibull distribution were used (mixed-effects Weibull regression) with a neighbourhood level intercept and individuals nested within neighbourhoods. Survival time was defined as time since baseline. In the cause-specific models, observations were right-censored in case of death from another cause. The crude models (Model 0) were adjusted for age, gender, having chronic conditions at baseline and accounted for neighbourhood-level variance. Model 1 additionally included population density. Model 2 was additionally adjusted for individual educational level and Model 3 additionally adjusted for neighbourhood educational level.

Sensitivity analysis with respect to the influence of socioeconomic position were carried out in a subsample of the data. In these analyses, the additional role of average neighbourhood income and crowding were explored (see Online Material).

Mediation was tested via a stepwise approach (Baron and Kenny, 1986). First, the association between population density and mortality was estimated. Second, the association between density and the potential mediators was estimated. Third, the association between the potential mediators and mortality was estimated, while adjusting for population density. Only those factors that were related to both population density and mortality were considered to be valid mediators. Finally, the estimated association between population density and mortality, while adjusting for the mediators was compared to the estimated association between population density and mortality without adjustment for the mediator. Attenuation of the estimated association was considered evidence for mediation. The detailed mediation methods are described in the Online Material.

3. Results

Participants were on average 47 years old and just under half of them had one or more chronic conditions at baseline (Table 1). The surveyed neighbourhoods had an average population density of 46.58 residents per hectare (4658 per km^2), and an average of 118 people per neighbourhood participated in the GLOBE baseline measurement. After 23 years, 29.9% of the participants had passed away, mainly due to cancer (10.2%) or cardiovascular diseases (9.2%), with a mean survival time of 21 years. No leisure time physical activity and no active transport were reported by respectively 16.5% and 18.6% of the sample. Over half of the respondents (56.2%) reported no sports

Table 1
Descriptive statistics of GLOBE participants (n = 10,120) at baseline (1991) and neighbourhoods of Eindhoven (n = 86).

	Mean (SD) or %	Range
Individual variables		
Age in years	47.45 (16.26)	14 – 74
Female	52.29%	
Having 1 or more chronic conditions	46.48%	
Educational level		
Low	23.99%	
Medium low	38.11%	
Medium high	22.17%	
High	15.72%	
Mortality	29.88%	
Cancer mortality	10.21%	
Cardiovascular mortality	9.15%	
Respiratory mortality	3.14%	
Other	5.88%	
Survival time in years	21.05	3.76 – 23.75
Health behaviour		
No leisure time physical activity *(missing = 1.61%)*	16.50%	
No active transport *(missing = 7.51%)*	18.57%	
No sport participation *(missing = 1.45%)*	56.21%	
Smoking *(missing = 1.34%)*	37.45%	
Alcohol consumption > 7 glasses/week *(missing = 5.42%)*	34.09%	
Perceived urban stressors		
Noise nuisance from neighbours *(missing = 2.28%)*	10.07%	
Noise nuisance from traffic, airplanes, street, business *(missing = 2.33%)*	16.07%	
Bad odour/pollution due to traffic, industry, business *(missing = 2.71%)*	15.53%	
Problems with vandalism, pollution, crime, etcetera *(missing = 2.46%)*	15.00%	
Coldness and draught in house *(missing = 2.30%)*	17.27%	
Misted or condensed windows *(missing = 2.37%)*	16.46%	
Damp problems in house and formation of mildew *(missing = 2.24%)*	10.44%	
Neighbourhood variables		
Population density (average number of persons per hectare)	46.58 (26.58)	0.3 – 124
% low educated in neighbourhood	20.51 (11.57)	0 – 44.09
GLOBE respondents in neighbourhood	118	4 – 373

participation. Current smoking and alcohol consumption of > 7 glasses/week were reported by respectively 37.5% and 34.1%. The different housing and neighbourhood stressors were reported by 10.1–17.3% of the respondents.

Increased population density was associated with an increased risk of all-cause mortality, even after adjusting for both individual and neighbourhood-level socioeconomic position (Table 2). Point estimates of the association between population density and cause-specific mortality were slightly larger than the association between density and all-cause mortality, but the accompanying confidence intervals were wider and included the null (Table 3).

Increased population density was positively associated with smoking and with experiences of problems with 'noise nuisance from neighbours', 'vandalism, pollution, crime, etcetera in the neighbourhood', and 'damp in the house and the formation of mildew'. When adopting a more lenient cut-off value (90% CI), increased population density was also associated with 'experiencing coldness and draught in the house' and 'misted or condensed windows'. Of these potential mediators, only smoking and experiencing coldness or draught in the house were associated with an increased risk of all-cause mortality. Smoking was also associated with cancer, cardiovascular and respiratory mortality. Additionally, increased population density decreased the odds of reporting no active transport, and no active transport was related to an increased risk of all-cause mortality. No active transport was also associated with cardiovascular mortality and respiratory mortality. None of the perceived urban stressors were related to the cause-specific mortality outcomes. An overview of these results is presented in the Online Material.

The estimated association between population density and all-cause mortality did not attenuate after additional adjustment for 'coldness and draught in the house' (Table 4). The inclusion of smoking in the model did mildly attenuate the association between population density and mortality (Table 5). Including active transport in the regression models, slightly increased the association between population density and mortality (Table 6). Similar results were found for the cause-specific mortality outcomes and are presented in the Online Material.

4. Discussion

In the compact, mid-sized city of Eindhoven, the Netherlands, higher population density was modestly related to a higher all-cause mortality, also after taking socioeconomic position and baseline health status into account. Higher population density was related to more active transport, but also to more perceived urban stress (e.g. noise from neighbours, vandalism, pollution, and lower quality housing conditions) and smoking. Whereas active transport was associated with lower mortality, urban stressors showed weak associations with mortality. Thus, the health-enhancing impact of increased active transport did somewhat compensate for the increased mortality risk of high population density, but overall, higher density was related to higher mortality.

Table 2
Cox multilevel models (mixed-effects Weibull regression) for all-cause mortality in GLOBE participants (n = 10,120) living in neighbourhoods of Eindhoven (n = 86).

	Model 0		Model 1			Model 2			Model 3		
Neighbourhood level variance	*0.017*	*0.007–0.042*	*0.010*	*0.003–0.032*		*0.005*	*0.001–0.032*		*0.004*	*0.000–0.038*	
			HR	95%CI	p	HR	95%CI	p	HR	95%CI	p
Population density			1.048	1.026–1.070	0.000	1.037	1.016–1.058	0.000	1.028	1.007–1.050	0.009
Educational level											
High						1.000			1.000		
Medium high						1.096	0.952–1.263	0.202	1.082	0.939–1.247	0.273
Medium low						1.147	1.012–1.299	0.031	1.121	0.988–1.271	0.076
Low						1.437	1.265–1.633	0.000	1.390	1.220–1.584	0.000
% low educated in neighbourhood									1.051	1.006–1.098	0.025

All models were adjusted for age, gender and chronic conditions at baseline
10 persons/hectare.

Table 3
Cox multilevel models (mixed-effects Weibull regression) for cause-specific mortality in GLOBE participants (n = 10,120) living in neighbourhoods of Eindhoven (n = 86).

	Model 0		**Model 1**			**Model 2**			**Model 3**		
Cancer mortality											
Neighbourhood level variance	*0.000*	*0.000–0.000*	-			-			-		
			HR	**95%CI**	**p**	**HR**	**95%CI**	**p**	**HR**	**95%CI**	**p**
Population density			1.043	1.011–1.076	0.008	1.036	1.003–1.069	0.030	1.033	0.999–1.068	0.059
Educational level											
High						1.000			1.000		
Medium high						0.974	0.773–1.228	0.823	0.969	0.768–1.223	0.792
Medium low						1.118	0.916–1.366	0.273	1.108	0.904–1.358	0.322
Low						1.272	1.032–1.567	0.024	1.254	1.011–1.557	0.040
% low educated in neighbourhood									1.018	0.950–1.090	0.619
Cardiovascular mortality											
Neighbourhood level variance	*0.036*	*0.010–0.131*	*0.028*	*0.006–0.120*		*0.024*	*0.005–0.123*		*0.021*	*0.004–0.127*	
			HR	**95%CI**	**p**	**HR**	**95%CI**	**p**	**HR**	**95%CI**	**p**
Population density			1.053	1.014–1.093	0.006	1.041	1.003–1.080	0.036	1.029	0.989–1.070	0.152
Educational level											
High						1.000			1.000		
Medium high						1.267	0.989–1.640	0.072	1.245	0.962–1.613	0.096
Medium low						1.176	0.931–1.486	0.175	1.141	0.900–1.445	0.275
Low						1.563	1.234–1.978	0.000	1.495	1.174–1.904	0.001
% low educated in neighbourhood									1.072	0.986–1.165	0.104
Respiratory mortality											
Neighbourhood level variance	*0.157*	*0.061–0.405*	*0.150*	*0.059–0.381*		*0.137*	*0.052–0.360*		*0.131*	*0.049–0.354*	
			HR	**95%CI**	**P**	**HR**	**95%CI**	**p**	**HR**	**95%CI**	**p**
Population density			1.072	1.000–1.149	0.049	1.056	0.985–1.132	0.126	1.041	0.967–1.121	0.282
Educational level											
High						1.000			1.000		
Medium high						0.637	0.398–1.018	0.059	0.624	0.390–0.999	0.050
Medium low						1.030	0.709–1.496	0.879	0.996	0.683–1.453	0.984
Low						1.451	0.996–2.115	0.052	1.386	0.943–2.036	0.097
% low educated in neighbourhood									1.092	0.930–1.282	0.283

All models were adjusted for age, gender and chronic conditions at baseline
10 persons/hectare.

4.1. Interpretation of results and comparison to previous studies

Two previous multilevel studies also reported a positive association between population density and all-cause mortality (Meijer et al., 2012; Nakaya et al., 2014). Both however, studied the association in a context of rural areas or lower population densities than in Eindhoven. For example, in a study in Danish parishes the cut-off point for the quartile with the highest density was 165 persons per km^2 (Meijer et al., 2012). Thus, while those residing in the most as compared to the least dense parishes appeared to have higher mortality rates, absolute density levels in the dense Danish parishes were presumably substantially lower than in Eindhoven. A Japanese study, reporting a similar association, was conducted in middle-sized Japanese cities and excluded metropolitan areas (Nakaya et al., 2014). Despite a tendency towards higher mortality rates for cancer, and ischaemic heart diseases (IHD) among residents of the most densely populated neighbourhoods, we were unable to show significant associations. Chaix and colleagues (Chaix et al., 2006) however, reported a dose-response association between population density and chronic obstructive pulmonary disorder and lung cancer mortality and an association with ischaemic heart disease mortality among participants aged 55 years and older. One potential explanation is that the latter study used lung cancer mortality, whereas we aggregated all types of cancer. Often mentioned explanations for an association between population density and mortality includes air pollution, which has a specifically large impact on lung cancer. To the best of our knowledge, our finding that active transport to some extent suppressed the association between population density and mortality, has not been reported before. However, this finding is in line with the often-posed argument that more compact cities enhance walking or cycling due to shorted distances to shops, facilities, schools and work (Sallis et al., 2016). Furthermore, although housing-related urban stressors such as experiencing coldness and draught in the house were associated both with population density and mortality, there was no indication that these stressors mediated the association between

Table 4
Mediation analyses for all-cause mortality exploring the role of 'Cold and draught in the house' (n = 9887).

	Model without mediator			**Model with mediator**			**Change in point estimate**
	HR	**95%CI**	**p**	**HR**	**95%CI**	**p**	
Population density (10 persons/hectare)	1.028	1.006–1.050	0.011	1.028	1.006–1.050	0.011	–
Educational level							
High	1.000			1.000			
Medium high	1.086	0.941–1.252	0.261	1.084	0.940–1.250	0.269	
Medium low	1.126	0.991–1.279	0.068	1.122	0.988–1.275	0.076	
Low	1.404	1.230–1.603	0.000	1.388	1.215–1.585	0.000	
% low educated in neighbourhood	1.052	1.007–1.100	0.024	1.050	1.004–1.098	0.032	
Cold and draught in the house				1.138	1.028–1.260	0.013	

All models were adjusted for age, gender and chronic conditions at baseline.

Table 5
Mediation analyses for all-cause mortality exploring the role of 'Smoking' (n = 9984).

	Model without mediator			Model with mediator			Change in point estimate
	HR	95%CI	p	HR	95%CI	p	
Population density (10 persons/hectare)	1.029	1.007–1.051	0.008	1.025	1.003–1.047	0.025	− 0.004
Educational level							
High	1.000			1.000			
Medium high	1.082	0.939–1.248	0.277	1.070	0.928–1.235	0.350	
Medium low	1.122	0.989–1.274	0.074	1.100	0.969–1.249	0.142	
Low	1.404	1.231–1.601	0.000	1.305	1.144–1.489	0.000	
% low educated in neighbourhood	1.052	1.007–1.100	0.024	1.048	1.002–1.096	0.039	
Smoking				1.927	1.784–2.081	0.000	

All models were adjusted for age, gender and chronic conditions at baseline.

density and mortality. It is possible that not the population density itself but the way this density is achieved (e.g. design and the construction of higher density housing) is more important for these stressors (Giles-Corti et al., 2012). Finally, the slight attenuation of the association between population density and mortality after smoking was taken into account may indicate that denser urban areas trigger smoking behaviour, potentially due to a higher density of tobacco outlets or as a way of coping with urban stressors (Finan et al., 2018; Pearce et al., 2012). This indication of mediation was not observed for alcohol consumption although similar pathways were expected (Fone et al., 2016). More research into positive and negative consequences of higher population density that could affect health of urban residents is needed to further our understanding on how urban population density affects health.

4.2. Limitations

A main strength of this study is that we linked a large prospective cohort of over 10,000 individuals with more than 23 years of follow-up to cause-specific mortality registry data. However, some limitations should also be considered. First, studies investigating the relation between neighbourhood characteristics and health are expected to be context-dependent. This study was carried out in a medium sized, compact university city in the Netherlands (with a population of n = 190,000 in 1991) and this may limit the generalizability to other cities, especially outside of Europe where cities are in general build differently historically and spatially (e.g. with more urban sprawl).

Second, population density and potential mediators were only measured once. By doing so, we assume that these measurements are adequate indicators of prolonged exposure during follow-up. This assumption however, may have been violated in two ways: 1) individuals may have moved during follow-up, and 2) changes in exposure and mediators are not taken into account. The first violation is probably most important, because migration to different neighbourhoods may have resulted in exposure misclassification, and participants with worse health may have moved to more densely populated neighbourhoods (and vice versa). Especially if migration occurred early during follow-up, misclassification poses a threat to the validity of the observed results. Van Lenthe and colleagues (Van Lenthe et al., 2007) have previously examined migration patterns among GLOBE-participants and found that 39% of the respondents had moved after 10 years of follow-up (although some within the same neighbourhood), particularly participants aged 25–34 years and single and divorced participants. Because mortality mainly occurs among older persons, we expect this to have little impact on our findings. The second violation may have occurred if population density or mediating risk factors changed during follow-up, even for participants that did not migrate. Previous research in the GLOBE-study has shown that the association between health behaviour and mortality is stronger when multiple measurements of health behaviour are used compared to one measurement (Oude Groeniger et al., 2017). We may therefore underestimate the role of health behaviour. In addition, it is unlikely that large changes occurred in population density and perceived urban stressors, because that would imply significant changes made to either the houses or neighbourhoods of this already very dense city.

Third, information was only available on perceived stressors. Perceived stressors however, may not accurately capture the stress-related exposures of individuals living in more densely populated neighbourhoods. We may have excluded other important stress-related factors that could explain the observed association between population density and mortality. In addition, differences in perceived stressors may not capture actual differences in stressors between individuals living in more and less densely populated neighbourhoods, because people grow accustomed to their individual situation and gradually adept their frame of reference to that specific situation (Diener et al., 2006).

Fourth, we were unable to account for potential spatial auto-correlation due to data limitations. By ignoring the spatial dependency, we may have slightly underestimated uncertainty surrounding our point estimates.

Finally, in order to adjust for socioeconomic position only measures of education were used, because of a lack of data on income or other socioeconomic factors for the full sample. Educational level has been

Table 6
Mediation analyses for all-cause mortality exploring the role of 'No active transport' (n = 9360).

	Model without mediator			Model with mediator			Change in point estimate
	HR	95%CI	p	HR	95%CI	p	
Population density (10 persons/hectare)	1.029	1.007–1.053	0.011	1.031	1.008–1.055	0.007	+ 0.002
Educational level							
High	1.000			1.000			
Medium high	1.087	0.939–1.259	0.264	1.091	0.942–1.263	0.246	
Medium low	1.106	0.970–1.261	0.133	1.106	0.970–1.262	0.131	
Low	1.377	1.201–1.579	0.000	1.373	1.197–1.574	0.000	
% low educated in neighbourhood	1.051	1.003–1.101	0.037	1.054	1.006–1.105	0.027	
No active transport				1.211	1.105–1.328	0.000	

All models were adjusted for age, gender and chronic conditions at baseline.

shown to be a good indicator of SEP for individual socioeconomic position in The Netherlands (Van Berkel-Van Schaik and Tax, 1990) and most strongly relates to mortality. We did have access to average neighbourhood income for 76 out of 86 neighbourhoods (n = 9947). Additional analysis including average neighbourhood income in this subset of the sample showed no effect on the observed results (see Online Material). Furthermore, large population densities can also be achieved by crowding, which is often suggested as an indicator of SEP. However, additional analysis including a measure of crowding (average number of persons per room in the household) did not change the results of this study (see Online Material). Although we believe that we adjusted for socioeconomic position adequately, some residual confounding cannot be excluded.

4.3. Conclusion and implications

This study showed that in a compact densely populated city in The Netherlands, increased population density was modestly associated with a higher risk of mortality. Although the health-enhancing impact of more walking and cycling among individuals living in more densely populated neighbourhoods compensated part of this effect, overall, higher density remained associated with a higher risk of mortality. The Netherlands is generally seen as an example of a country with a good infrastructure for walking and cycling. Making cities more compact, but neglecting the importance of a good infrastructure, may increase the negative impact of higher population density on health. Equally important, our findings provide an important nuance to recent studies that have advocated the need for 'compact cities' (Giles-Corti et al., 2016; Sallis et al., 2016; Stevenson et al., 2016): the positive effect of increased population density on health may reach a tipping point, after which it has a damaging effect on health or the negative consequences no longer outweigh the positive ones. More research is needed to identify the risk factors within these overly dense neighbourhoods, which will become increasingly important due to the continued growth of urban populations across the globe. In conclusion, in compact dense cities, even with good infrastructure for walking and cycling, high population density may negatively impact mortality.

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