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How are lifestyle factors associated with socioeconomic differences in health care costs? Evidence from full population data in the Netherlands

Willem I.J. de Boer, Louise H. Dekker, Ruud H. Koning, Gerjan J. Navis, Jochen O. Mierau

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ABSTRACT

Introduction: There is a strong socioeconomic gradient in health care costs. However, little is known about the role of lifestyle factors in the association between health care costs and socioeconomic status (SES). This study investigates variation in the association between lifestyle indicators and health care costs between and within neighborhoods with similar SES.

Method: Using 2016 whole-population data for all 790 neighborhoods of the Netherlands, we estimated the association between neighborhood average health care cost performance (i.e., health care costs adjusted for population age and gender) and neighborhood socioeconomic status (NSES) and four lifestyle indicators - smoking, alcohol consumption, exercise and sport club membership. Additionally, using regression analysis, we explored the multivariate relationship between average health care cost performance, NSES and lifestyle indicators.

Results: Neighborhoods with proportionally fewer smokers and more sport club members had significantly lower average health care costs. Remarkably, neighborhoods with more people who complied with the recommended maximum alcohol consumption had significantly higher health care costs. These findings were consistent within and between neighborhoods with different SES levels. Neighborhoods with more compliance with exercise guidelines had lower health care costs. However, this relationship was inconsistent across different NSES levels, with the largest cost reductions found in the most deprived neighborhoods.

Conclusion: Our findings suggest that prevention policies aimed at reducing the number of smokers and increasing sport club membership may reduce health care costs across all NSES groups, while increasing compliance with physical exercise norms may be effective mainly in low SES neighborhoods.

1. Introduction

A large body of epidemiological and population health research addresses relationships between neighborhood characteristics and a myriad of health and economic outcomes (Duncan and Kawachi, 2018; Chetty et al., 2016). As such, neighborhood socioeconomic status (NSES) has been associated with adverse health outcomes, including chronic disease (Howard et al., 2016; Pickett and Pearl, 2001; Diez Roux, 2001), mortality (Kim et al., 2018; Brown et al., 2013) and poor self-rated health and quality of life (Rocha et al., 2017). These associations are often cited to explain why health care expenditures are disproportionately high in neighborhoods with particular characteristics (de Boer et al., 2019).

However, while the socioeconomic gradient in health is one of the most consistent findings in epidemiological research (Bilal et al., 2019; Stringhini et al., 2017), a recent study found great variation in health care costs between neighborhoods with similar socioeconomic characteristics (de Boer et al., 2019). With global health expenditures on the rise (World Health Organization, 2017), this finding warrants further exploration, as a better understanding of the complex relationship between NSES and health care expenditures may reveal pathways for future cost savings.

Health behaviors are a very plausible mediator of social inequalities in health. Factors such as physical activity, alcohol consumption and

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especially smoking are strongly socially patterned, while being simultaneously related to health outcomes (Lantz et al., 1998; Petrovic et al., 2018). Research shows that socially disadvantaged individuals are more likely to exhibit behaviors detrimental to their health. This could be due, for example, to material and financial constraints, a lesser appreciation of the benefits of health behaviors for longevity and difficulties in absorbing health promotion messages (Stringhini et al., 2011; Wardle and Steptoe, 2003; Pampel et al., 2010).

Nevertheless, the social patterning of neighborhoods is not uniform (Diez Roux and Mair, 2010). The complexities of these patterns may yield opportunities for intervention (Diez Roux and Mair, 2010). They also leave room to hypothesize a different role of lifestyle in influencing the effects of NSES on health care costs has not been examined.

The objective of the current study is to investigate variation in the association between lifestyle factors and health care costs both between and within neighborhoods with similar socioeconomic statuses. For this research we used whole-population data for the Netherlands. The research focuses on several lifestyle indicators: smoking, alcohol consumption and physical activity. The negative effects of smoking and alcohol consumption have been extensively demonstrated (Evans and Stoddart, 2017; Sturm, 2002). For physical activity the relationship with health and health care costs seems to be more complex, varying by type and context of physical activity. Research shows that occupational physical activity may have opposite health effects compared to leisure time physical activity (Holtermann et al., 2012). In addition, Andersen et al. demonstrated that among all physically active individuals, those who participated in a sport experienced 50% less mortality than those who did not participate in a sport (Andersen et al., 2000). The current research therefore includes two lifestyle indicators for physical activity: a general indicator for compliance with the Dutch guideline for sufficient physical exercise and a more specific indicator for sport club membership.

Hence, our research investigates to what extent these four lifestyle indicators – smoking, alcohol consumption, getting sufficient exercise and sport club membership – influence average health care costs and variation in those costs within, as well as between, neighborhoods with similar socioeconomic statuses.

### 2. Methods

#### 2.1. Data

Data on health care costs were provided by Vektis, an information center for Dutch health insurers (Vektis, 2016). Dutch law requires health insurers to provide detailed health care data to Vektis, which compiles this information and makes it available for research and public health policy. Here we investigate all health care costs that fall under the Health Insurance Act. This comprises all basic health care, including primary, hospital, pharmaceutical, mental health, dental and paramedical care (Vektis, 2016). All inhabitants of the Netherlands are required by law to purchase health insurance consistent with the Health Insurance Act; therefore these data cover almost the entire population of the Netherlands (i.e., 99.8%).

We used 2016 data at the neighborhood, or 3-digit postal code area. Each such neighborhood contains an average of about 21,000 persons. For each neighborhood, health care costs were available by gender and by age (0, 1, 2, etc. up to 89, with 90 years and older in one age category).

The dependent variable for our analysis was average health care cost performance (AHCP), defined as the difference between the observed average health care cost and expected average health care cost. We calculated the expected health care cost by multiplying the national average cost by the neighborhood’s population size (the number of insured years), for each of the 182 (91 × 2) age and gender combinations. A positive value for AHCP indicates that the actual health care cost was higher than the expected cost based on the specific age/gender distribution of that neighborhood.

As independent variables, we considered the socioeconomic status for each neighborhood (NSES), as well as the four lifestyle indicators. The Netherlands Institute for Social Research (SCP) provided data on the socioeconomic status (SES) of all 4-digit postal code areas of the Netherlands (Sozialer Planam, 2019), based on income, education and occupation of the inhabitants. The SES data is constructed as a z-score with a normal distribution. It has a mean of zero, and ranges from −3.5 to 2.2, with higher values indicating more affluent neighborhoods. For our research, we aggregated the existing 4-digit postal code data into 3-digit postal code NSES values by calculating weighted (by population size) averages (Sozialer Planam, 2018).

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Explanation</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHCP</td>
<td>Average health care cost performance (in euros)</td>
<td>−84.14</td>
<td>244.05</td>
<td>−1446.06</td>
<td>684.96</td>
</tr>
<tr>
<td>Sex</td>
<td>Females (%)</td>
<td>50.1</td>
<td>2.0</td>
<td>28.2</td>
<td>58.6</td>
</tr>
<tr>
<td>Age</td>
<td>Average age</td>
<td>42.2</td>
<td>2.9</td>
<td>22.7</td>
<td>58.4</td>
</tr>
<tr>
<td>NSES</td>
<td>Neighborhood socioeconomic status</td>
<td>0.0</td>
<td>0.8</td>
<td>−3.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Smoking</td>
<td>Individuals not smoking (%)</td>
<td>79.9</td>
<td>3.2</td>
<td>65</td>
<td>86</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Individuals complying with the alcohol norm (%)</td>
<td>39.6</td>
<td>5.4</td>
<td>26</td>
<td>66</td>
</tr>
<tr>
<td>Exercise</td>
<td>Individuals complying with healthy exercise guidelines (%)</td>
<td>49.8</td>
<td>4.5</td>
<td>35</td>
<td>66</td>
</tr>
<tr>
<td>Sport club membership</td>
<td>Individuals who are sport club members (%)</td>
<td>25.8</td>
<td>6.1</td>
<td>8</td>
<td>49</td>
</tr>
</tbody>
</table>

### Table 2

Correlations between cost performance, NSES and four lifestyle indicators.

<table>
<thead>
<tr>
<th></th>
<th>AHCP</th>
<th>NSES</th>
<th>Smoking</th>
<th>Alcohol consumption</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSES</td>
<td>−0.598***</td>
<td>1</td>
<td>−0.568***</td>
<td>0.620***</td>
<td>1</td>
</tr>
<tr>
<td>Smoking</td>
<td>−0.568***</td>
<td>0.355***</td>
<td>−0.340***</td>
<td>−0.462***</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>0.420**</td>
<td>−0.355***</td>
<td>−0.340***</td>
<td>1</td>
<td>0.364***</td>
</tr>
<tr>
<td>Exercise</td>
<td>−0.266***</td>
<td>0.329**</td>
<td>0.116**</td>
<td>−0.639***</td>
<td>1</td>
</tr>
<tr>
<td>Sport club member</td>
<td>−0.573***</td>
<td>0.588***</td>
<td>0.685***</td>
<td>−0.639***</td>
<td>0.364***</td>
</tr>
</tbody>
</table>

* p < 0.01.

** p < 0.001.
### Table 3
Regression results on average health care costs performance (dependent variable) for NSES and 4 lifestyle indicators.

<table>
<thead>
<tr>
<th>Smoker</th>
<th>Alcohol consumption</th>
<th>Exercise</th>
<th>Sport club member</th>
<th>NSES</th>
<th>NSES * lifestyle factor</th>
<th>Lifestyle factor</th>
<th>NSES - lifestyle factor</th>
<th>Constant</th>
<th>R²</th>
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<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Alcohol consumption</td>
<td>Exercise</td>
<td>Sport club member</td>
<td>NSES</td>
<td>NSES * lifestyle factor</td>
<td>Lifestyle factor</td>
<td>NSES - lifestyle factor</td>
<td>Constant</td>
<td>R²</td>
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<tr>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
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<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
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<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
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</table>

The following four lifestyle indicators were used in this research, with all being measured at the neighborhood level:

- **Smoking.** The percentage of people aged 19 and older who answered “no” to the question, “Do you ever smoke?” In this definition for current smoking status, the electronic cigarette was excluded. Data on e-cigarette use was not available at the neighborhood level, as it was not part of the survey we used.

- **Alcohol consumption.** The percentage of people aged 19 and older who complied with the 2016 Dutch recommendation to consume no more than one glass of alcohol on average per day.

- **Exercise.** The percentage of people aged 19 and older who complied with the 2016 Healthy Exercise Guideline. This recommends that a person should do at least enough moderately intensive physical exercise to consume 200 kcal on a daily basis. The amount, frequency and intensity of the recommended exercise differ by age groups.

- **Sport club membership.** The percentage of the population that was a member of a sport club.

The first three lifestyle variables were derived from Statistics Netherlands (CBS) in cooperation with the Netherlands Institute for Public Health and the Environment (RIVM) and Municipal Health Services Netherlands (GGD). The CBS, RIVM and GGD conduct a population-wide, biannual survey of health and lifestyle (“Gezondheidsmonitor”; N = 457,000 in 2016) (CBS, RIVM, GGD, 2016). From the findings of that survey, RIVM estimates these indicators for local areas (i.e., sub-neighborhoods) using a small-domain estimator model (van de Kassteele et al., 2017). For our analysis, we aggregated local area data for 2016 to the neighborhood level.

The Dutch National Olympic Committee (Nederlands Olympisch Comité * Nederlandse Sport Federatie; hereafter: NOC*NSF) provided the percentage of sport club members for each neighborhood (also at the 3-digit postal code level). NOC*NSF collects information on sport club membership, including members’ home addresses, through the national sport federations. These data include all federations recognized by and associated with the NOC*NSF, except the sport fishing association. NOC*NSF divides the number of sport club members by the neighborhood population size to get the percentage of sport club members in each neighborhood.

In the Netherlands, some 60% of the population participates in a sport weekly, with almost half of sport participants being members of a sport club (NOC*NSF, 2018). Although being a member of a sport club does not itself imply physical activity, it is a leisure time indicator that is associated with being physically active and adhering to a healthy lifestyle (Telford et al., 2016).

To make the results more intuitive, we used positive coding for the lifestyle variables; that is, higher values indicate healthier lifestyles. Our hypothesis is that a healthier lifestyle leads to lower health care costs. We thus expected each positively coded lifestyle indicator to be negatively related to ACHP. We analyzed data for 2016, the most recent year for which data was available for all variables.

#### 2.2. Analysis

To analyze the role of lifestyle factors in the socioeconomic gradient of neighborhood health care costs, we first calculated Pearson correlations between the dependent variable and all independent variables. Next, we measured the associations with average cost performance (ACHP) for NSES and the lifestyle indicators, using four ordinary least squares regression models. The first model looks at the univariate relationship between ACHP and NSES. The second model estimates the relationship between ACHP and each of the lifestyle variables separately. The third model estimates a multivariate association between ACHP and NSES together with a lifestyle indicator. To test whether NSES and the lifestyle indicators have independent effects on ACHP, the
fourth model expands on the third model, including an additional interaction effect between NSES and the lifestyle indicator. The econometric methodology of these models is further explained in a Supplementary document. Finally, we produced margins plots showing the marginal relationships between NSES and average health care cost performance for each lifestyle indicator. This is a visual depiction of the interactions in the final model. These margin plots include 95% confidence intervals.

3. Results

Table 1 shows the summary statistics for all variables at the neighborhood level. The statistics are unweighted. As a result, the mean of the average health care cost performance is not equal to zero (the weighted mean does equal zero). For completeness, the statistics for sex and age were added, since these variables were used to calculate the average health care cost performance for each neighborhood.

Table 2 shows the correlations between average health care cost performance, NSES and the four lifestyle indicators. We observe a significant negative association between NSES and health care cost performance ($p < 0.001$). All but one of the lifestyle indicators shows a significant negative correlation with average health care cost performance. Only alcohol consumption has a positive (and significant) correlation with AHCP. Looking at the associations with NSES, smoking, exercise and sport club membership all have positive correlations with AHCP, while alcohol consumption has a significant negative correlation with NSES. Among the lifestyle indicators, sport club membership shows a strong (absolute value $> 0.6$) and positive correlation with smoking, while also having a strong negative correlation with alcohol consumption.

Table 3 presents the results of the models regressing AHCP on NSES and the lifestyle indicators. The first column shows the outcomes of the first model, with only NSES. Next, the outcomes of the second, third and fourth models are presented, separately for each lifestyle indicator. The outcome of the first model demonstrates a significant negative association between AHCP and NSES. This confirms the finding from the correlation matrix (see Table 2). Similarly, from the second models it is clear that all lifestyle variables are significantly associated with AHCP. For smoking, exercise and sport club membership a significant negative association was found between a healthy lifestyle and average health care cost performance. The coefficient for smoking is highest: neighborhoods with 1 percentage point more non-smokers had €38.51 lower healthcare cost performance per person on average. At the national level in the Netherlands, reducing the number of smokers by 1 percentage point could lead to an annual health care cost savings of some €650 million. This amount is equivalent to 1.6% of all insured health care. Similarly, in neighborhoods with a 1 percentage point higher sport club membership and where residents got enough exercise, the health care cost performance per person was, respectively, €24.81 and €14.25 lower. This corresponds to a potential annual health care cost reduction of some €420 million (1.0%) for sport club membership and €240 million (0.6%) for exercise. However, for alcohol consumption the coefficient is positive; that is, neighborhoods with a 1 percentage point higher compliance with the alcohol norm had on average €16.18

Fig. 1. Margin plots showing the interaction effect of a lifestyle indicator on the relationship of NSES with average health care cost performance, for four lifestyle indicators, with confidence intervals (2016). Note: Values on the horizontal axes represent the lifestyle factor. Those on the vertical axes represent the marginal effect of NSES on AHCP; that is, the effect of moving up one standard deviation on the NSES scale on average health care cost performance. The dotted horizontal lines represent the effect of NSES on AHCP without the interaction effect.
higher health care cost performance per person.

The third model includes both NSES and the lifestyle indicators as covariates. The signs of all coefficients in the third model are similar to those found in the first and second models. The associations between smoking and sport club membership with health care cost performance are negative and significant ($p < 0.001$). However, combined with NSES, the association of exercise with AHCP is not significant ($p = 0.147$). Alcohol consumption again has a significant positive coefficient.

The fourth model presents interaction terms for NSES and the lifestyle indicators. A significant interaction term means that the effect of NSES on AHCP differs for neighborhoods with different levels of the lifestyle indicator. In other words, the marginal effect of the lifestyle indicator differs for neighborhoods with different levels of NSES. For the lifestyle indicators smoking, alcohol consumption and sport club membership, individual coefficients for NSES and the lifestyle indicators are, again, significant. However, the interaction effects are not significant, which suggests that NSES and each lifestyle indicator has an independent effect on AHCP. Only for exercise, the interaction term is significant ($p < 0.001$) and positive (+4.35). This implies that the association between AHCP and NSES was greater in neighborhoods where more people complied with the minimum exercise guideline.

Fig. 1 shows the interaction effect of the lifestyle indicators on the relationship between NSES and AHCP, with confidence intervals. Additionally, the dashed lines show the effects of NSES on AHCP independent of the lifestyle indicators (as in the third model). The figures show a downward slope for smoking and an upward slope for alcohol consumption, exercise and sport club membership. An upwards slope indicates that neighborhoods with a healthier lifestyle would profit less—i.e., have a smaller drop in average health care cost performance—from moving up the socioeconomic ladder than neighborhoods with less healthy lifestyles. For exercise, in neighborhoods with a low level of compliance with the exercise guideline the marginal effect of NSES on AHCP is below the dashed line, as is the confidence interval. This means that the marginal effect of NSES on AHCP is significant for exercise. In other words, an improvement of NSES in neighborhoods with low adherence to the exercise norm would reduce AHCP more than in neighborhoods where compliance with the exercise norm is high. For all other lifestyle indicators, the confidence interval includes the original estimate of the NSES at all levels of the lifestyle indicator. Hence, for these lifestyle indicators, the marginal effect of NSES on AHCP is not significant. An alternative but equivalent interpretation of the foregoing results is that increasing the rate of compliance with the exercise norm would reduce health care costs more in low SES neighborhoods than in high SES neighborhoods (see Fig. S1 in Supplement).

4. Discussion

The outcomes of our research confirm that health care costs are negatively associated with smoking (Xu et al., 2015) and insufficient physical activity (Pratt et al., 2000). While other research shows that lifestyle factors and socioeconomic characteristics are independently related to, for example, perceived health (Molarius et al., 2006) and health outcomes (Lantz et al., 1998; Petrovic et al., 2018), our findings show a similar association for average health care cost, particularly for smoking and sport club membership. Remarkably, this finding does not hold for getting sufficient exercise. This indicates that health effects may indeed vary for different types of physical activity. We did find that lifestyle effects sometimes differ for different NSES levels. Earlier research suggests that the health effects of exercise can be different depending on whether physical activity occurs during work or in leisure time, and whether it is in the context of practicing a sport (Andersen et al., 2000). Unfortunately for the current study, no neighborhood-level data were available detailing types of physical activity.

We found that greater compliance with the alcohol norm was associated with higher average neighborhood health care costs. This contradicts other research which points to many adverse health effects of (excessive) alcohol consumption (Bouchery et al., 2011; Wood et al., 2018). Indeed, evidence is ambivalent about the health effects of moderate alcohol consumption (Bouchery et al., 2011; Fernandez-Sola, 2015). Our findings in this regard support the hypothesis that moderate alcohol consumption can have health benefits, such as lower incidence of cardiovascular events and mortality (Fernandez-Sola, 2015). Other research suggests that the prevalence of excessive drinking may not be related to educational level (van Oers et al., 1999). Often, deprived neighborhoods have higher proportions of current drinkers (i.e., those presently consuming an alcoholic beverage), while also having lower weekly alcohol consumption rates (Brenner et al., 2015). In the Netherlands, statistics show that while lower educated men under the age of 65 consume most alcohol, alcohol use among women is highest for the highest educated group, for all age groups (Rijksinstituut voor Volksgezondheid en Milieu, 2017). Future research investigating the remarkable relationship between alcohol consumption and health care costs that we found would be very welcome, including looking at the effects of using different thresholds for “excessive” drinking.

Our analysis had several limitations. First of all, while we used rich, whole-population data, our data included only health care costs covered under the Dutch Health Insurance Act. Although this coverage is broad, including all basic health care, it may nonetheless have missed some direct and indirect health-related expenses stemming from, for example, general practitioner care, hospital care and pharmaceuticals. Secondly, in our study we analyzed lifestyle indicators for smoking, alcohol consumption and physical activity, but we omitted a fourth potentially important lifestyle factor: nutrition. Unfortunately, no data on nutrition was available at the neighborhood level. As a healthy diet can have positive health effects, future studies may wish to take diet into account (Dekker et al., 2017; Lenoir-Wijnkoop et al., 2013).

Thirdly, because our study focused on the neighborhood level, the findings may not be fully transferable to policies and interventions aimed at the individual level. However, research shows that neighborhood characteristics can affect the physical health of individuals (Loh et al., 2016). Therefore, because of the unique characteristics of the Dutch health care system and Dutch society (e.g., the country’s rather egalitarian socioeconomic structure and large sport club membership), the outcomes of this research may not be fully generalizable to other countries. However, because of the scope of this research, we believe that the findings provide valuable insights, as would similar investigations in other countries. Additionally, because we used a cross-sectional approach, the socioeconomic gradients in health care costs that we found represent associations, and are not necessarily indicative of causal relationships between NSES, lifestyle factors and health care costs. Future research could look in more detail at the effects of NSES and lifestyle factors on specific types of health care costs.

5. Conclusion

From our correlations and regression analyses, we can conclude that, at the neighborhood level, a higher percentage of non-smokers, persons getting enough exercise and sport club members are all associated with significantly lower health care costs. Accounting for age and gender, but not differences in NSES, neighborhoods with 1 percentage point less smokers, more sport club members and getting enough exercise had on average €39, €25 and €14 less annual health care costs per person, respectively. Surprisingly, neighborhoods with a higher compliance with the alcohol norm also had significantly higher health care costs. One percentage point less alcohol users was associated with €16 higher average costs. Moreover, our regression analysis showed that the associations for smoking, sport club membership and alcohol consumption were both additional to (consistent coefficient signs in models 3 and 4) and independent of (no significant interaction coefficient in models 4) a neighborhood’s socioeconomic status. Hence, the lifestyle indicators smoking and sport club membership seem to be complementary to NSES in explaining variations between...
Our findings suggest that policies aiming at increasing the number of non-smokers and sport club members would be beneficial in reducing health care costs for all neighborhood socioeconomic levels. Increasing the percentage of persons getting enough exercise in general may only be effective in low socioeconomic status neighborhoods. Physical activity policies would be advised to focus on increasing exercise particularly via sport club membership and perhaps also through other leisure time activities, such as by removing or diminishing (financial) barriers to participate in such activities for low income groups. In the Netherlands, local policies aimed at increasing youth sport club membership seem to be successful in reducing socioeconomic differences in sport club participation. Future research could focus on other lifestyle factors, such as nutrition, as well as on the differential effects of several types of physical activity, including physical activity in the context of work or as a means of transportation (e.g., commuting by foot or by bicycle) and practicing a sport outside the context of a sport club. To investigate the causal relationship between lifestyle factors, socioeconomic characteristics and health care costs, future research could furthermore look at individual data or take a longitudinal approach.

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There were no sources of funding for this research.

**Declaration of competing interest**

Ruud Koning is supervisory board member of health insurer Unive Noord-Nederland. Jochen Mierau participates in projects funded by health insurers Menzis and De Friesland Zorgverzekeraars. Louise Dekker participates in projects funded by health insurer De Friesland Zorgverzekeraars. No health insurer was directly involved in this research. Noord-Nederland. Jochen Mierau participates in projects funded by health insurers Menzis and De Friesland Zorgverzekeraars. Louise Dekker participates in projects funded by health insurer De Friesland Zorgverzekeraars. No health insurer was directly involved in this research.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.105929.

**References**


