**Target journal BMJ**

**Original Research Article**

**Title: Association between active transport and acute myocardial infarction: Cross sectional ecological study using national registry and Census data**

Robin Lovelace

Mark Green

Sarah Walpole\*

Should include at least one other MINAP academic group person (I suggest Prof Adam Timmis, Chair of MAG), and a Farr Institute / MINAP senior (head of Farr Prof Harry Hemingway)

Marlous Hall

Chris Gale

\*Corresponding author:

TBC - ?Robin or Chris as first and last author??

sarah.walpole@hyms.ac.uk

+44 7517 243 783

**Abstract**

**Objective:** To investigate the association between active transport and the prevalence of acute myocardial infarction in England.

**Design:** Cross sectional ecological study using UK Census data (year-year), Public Health England data (year-year) and Myocardial Ischaemia National Audit Project data (2010-2013).

**Setting:** XXXX middle layer super output areas in England.

**Participants:** XXXX active transporters.

**Main outcome measures:** Incidence of hospitalised acute myocardial infarction (n=XXXX).

**Results:**

**Conclusions:** Active transport was associated with [to be inserted].As this was an ecological study we cannot prove causation between active transport and acute myocardial infarction. Findings should only be interpreted at the middle super output area

[**Trial registration:**] needs to be done

**What this paper adds**

Section 1: What is already known on the subject

* Coronary heart disease is the leading cause of death worldwide. It accounts for approximately 73,000 deaths in the United Kingdom annually, the vast majority from acute myocardial infarction.
* Physical activity reduces risk factors for coronary heart disease at the individual level; whereas motorised transport contributes to air pollution, which is a risk factor for heart disease.

Section 2: What this study adds

* Active transport is associated with increased self-reported physical activity (correlation between PHE and Census).
* At the regional level, there is a significant inverse association between active transport and incidence of acute myocardial infarction. This association remains after accounting for variation in socioeconomic status, smoking prevalence and …

**Introduction**

Coronary heart disease (CHD) is the leading cause of death worldwide, and its incidence is rapidly rising in low and middle income countries.1 CHD and its associated treatment account for approximately 12% of healthcare costs in Europe and Canada,2 and 17% in the USA.23 In England, CHD accounts for approximately 73,000 deaths each year, the vast majority from acute myocardial infarction (AMI).

Behavioural characteristics are important in understanding the prevalence of CHD, with physical inactivity a key risk factor.4–7 Only 40% of men and 28% of women in England achieve recommendations of 30 minutes of physical activity at least five days a week, according to self-reported exercise levels which may underestimate the extent of the problem of inactivity.8

Active transport is the use of physical activity, most commonly walking or cycling, to commute.8,10 Compared to recreational physical activity, active transport offers greater potential to incorporate physical activity into daily routines. Moreover, participants who engage in any active transport have improved cardiovascular risk profiles including lower body mass index, mean waist circumference and likelihood of hypertension and diabetes

Although recent studies suggest a dose-response relationship between active transport and markers of cardiovascular fitness,16 there is a paucity of population based data about the association between active transport and cardiovascular events. A prospective study of two cohorts (of xxx and xxx participants) in the East of England found a correlation between increased amount of time spent in active transport and lower risk of death due to AMI in a first cohort, but no association in a second cohort where more detailed data on physical activity were included.

In the absence of comprehensive population based studies, our objectives were first to study the association between active transport and AMI, second explore the extent to which the components of active transport, cycling and walking were associated with AMI, and third to investigate whether associations were contingent on a time lag effect between the dates of exposure to active transport and indecent AMI.

**Methods**

*Data sources*

We extracted all cases of AMI admitted to hospital between 2010 and 2013 in England from the Myocardial Ischaemia National Audit Project (MINAP), a national prospective clinical register containing detailed information about quality of care and clinical outcomes of patients with AMI. The diagnosis of AMI was based on guidelines from the European Society of Cardiology, American College of Cardiology, and American Heart Association. Further details of MINAP have been published previously

PHE data

Census data

*Geographic units*

Counts of AMI were aggregated to 6791 Middle Super Output Area (MSOA) of England. MSOAs are administrative zones with a mean population size of 7787, created for the dissemination of data.19 We used MSOAs as the focus of analysis to keep the spatial scale small enough to maximise detail, whilst being large enough to capture sufficient counts of AMI to would produce stable estimates. We pooled annual data together for similar purposes and use data between 2010 and 2013.

Exposure

Our primary exposure was the proportion of individuals in each MSOA who commuted to work using active forms of transport. We included two variables: the proportion who cycled and the proportion who walked. Data were collected from the 2011 United Kingdom Census which includes self-reported information about an individual’s main mode of transport to work and their time spent commuting to work. Studies of adults who actively commute to work shows that active commuting is usually done in addition to recreational physical activity, thus increasing overall physical activity.20,21 [Active commuting as a good proxy for total physical activity – reference.]

Case mix variables

To account for possible confounding from socioeconomic status, we used the population weighted estimates of the 2015 English Indices of Multiple Deprivation (IMD) for MSOAs which were developed by Public Health England. IMD is a multidimensional measure of deprivation capturing covering seven domains of deprivation including income, employment, health deprivation and disability, education skills and training, barriers to housing and services, crime and the living environment.

*Statistical analysis*

[insert descriptive statistics here]

To model the incidence of AMI within each area, a Bayesian negative binomial regression model was used, based on the Integrated Nested Laplace Approximation (INLA) method.23,24 The model was adjusted using the following confounding variables: [insert all confounders here]. The expected number of AMI admissions, based on demographic structure, was included in the model as an offset to account for variability in the total population and its composition per MSOA. We used indirect standardisation to calculate our estimates based on 10 year age bands by sex. Population data were gathered from ONS mid-year population estimates.

To account for the spatial structure of observations, we used the Besag-York-Molliè model22 which is a standard model for estimating ecological associations with an explicit spatial element. This model allows us to utilise information from nearby areas under the assumption that these are likely to be more similar than areas further apart, thereby reducing uncertainty and minimising influence from outliers.23

[Insert something here about how we estimated lag effects.]

All analyses were undertaken using R [ref) and the analytical code can be found here:

*Ethical approval*

The National Institute for Cardiovascular Outcomes Research, which includes the MINAP database, has support under section 251 of the National Health Service Act of 2006 to use patient information for medical research without informed consent. National Health Service ethical approval for this study was not required under current research governance arrangements as all data used was non-identifiable and pseudonymised. A favourable ethical approval was provided by the University of Leeds (ref…).

*Patient involvement*

No patients were involved in setting the research question or the outcome measures, and nor were they involved in the design and implementation of the study. We plan to involve patients in dissemination of the study results by inviting patients and their families to the study information session hosted at the MRC Medical Bioinformatics Centre at the University of Leeds.

**Results**

* Descriptives–
* Active transport – cycling… walking…
* AMI rates
* Case mix rates
* Geographical descriptives
* Temporal descriptives
* Then go to standardised rates, then inferences then associations

Table 1 [pilot analysis, not on full data set – full analysis in progress] presents the results from a Bayesian negative binomial regression model analysing the incidence of myocardial infarction for all persons. There was a significant negative association between cycling prevalence and MI before and after adjustment for other variables. A one percent increase in the percentage of people who cycle to work in an area is associated with a decrease of 1.4% fewer cases of MI. The model was less certain on the direction of the association for the percentage of people who walk within a MSOA with overlap of the 95% Credible Intervals (the effect size was also tiny). While the posterior mean appears small, a one unit increase in the IMD score reflects a small increase in the level of deprivation. For example, the range of IMD values for MSOAs is 1.82 to 82.49. Therefore our results would suggest a fairly large effect size. The 95% credible intervals are also narrow suggesting a good level of certainty on the estimate.

Tables 2 and 3 present the analyses stratified by sex however there is little difference to the overall results presented in Table 1. [OR – stratifying the analysis by sex did not provide any statistically significant difference in results (and not include the tables, or maybe not even say this), may be relevant to stratify by age, especially given that commuting usually stops around 60.]

**Table 2: Person and sex-specific analysis of predictors of heart attack admissions for all ages for Local Authorities (2010-2013).**

*Note: Each model was adjusted for level of deprivation, prevalence of overweight and obesity, levels of physical activity and smoking. Model included an age- and sex-specific offset which was the expected count of admissions to control for age and sex differences between Local Authorities.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 3: Age specific Poisson regression examining predictors of heart attack admissions for Local Authorities (2010-2013)** | | | | | | | |
|  | | Males | | | Females | | |
| IRR | Lower CI | Upper CI | IRR | Lower CI | Upper CI |
| 16-24 | % Cycle | 0.853 | 0.754 | 0.955 | 1.122 | 0.856 | 1.358 |
| % Walk | 0.991 | 0.949 | 1.033 | 0.935 | 0.853 | 1.017 |
| 25-34 | % Cycle | 0.923 | 0.894 | 0.951 | 0.938 | 0.831 | 1.040 |
| % Walk | 0.962 | 0.944 | 0.980 | 0.981 | 0.945 | 1.016 |
| 35-44 | % Cycle | 0.941 | 0.931 | 0.951 | 0.949 | 0.919 | 0.979 |
| % Walk | 0.957 | 0.947 | 0.967 | 0.950 | 0.934 | 0.966 |
| 45-54 | % Cycle | 0.945 | 0.939 | 0.951 | 0.909 | 0.893 | 0.925 |
| % Walk | 0.937 | 0.930 | 0.943 | 0.951 | 0.941 | 0.960 |
| 55-64 | % Cycle | 0.926 | 0.920 | 0.933 | 0.935 | 0.923 | 0.946 |
| % Walk | 0.928 | 0.922 | 0.934 | 0.949 | 0.942 | 0.956 |
| *Note: Each age-specific model was adjusted for level of deprivation, prevalence of overweight and obesity, levels of physical activity and smoking* | | | | | | | |

Note: IRR = incidence rate ratio, CI = credible interval

**Discussion**

This is the first ecological study using high quality, high geographical resolution data to correlate MI incidence with active transport across a developed country. The findings show an association between increased active transport and myocardial infarction.

The findings show association, not causation,

Walking and cycling different, as evidenced in… lit review, prospective study… 17

Deprivation was important since previous research has shown that in countries in the fourth stage of epidemiological transition (where diagnosis and treatment of ischaemic heart disease is available)26 lower socioeconomic status27–29 and perceived lower socioeconomic status30 are associated with higher incidence of cardiovascular disease.

As this is an ecological study, conclusions about causation cannot be drawn directly from the results.

The results can be no more accurate than the data from which they are derived. The MI data are from a full national data base, but are limited to those events that are hospitalised – deaths occurring before hospital are not included. The diagnostic criteria for myocardial infarction are objective and clear, although it is notable that they are not 100% sensitive or specific. It is also relevant that multiple factors contribute to MI risk, and despite controlling for sociodemographic factors, the explanatory variable active travel is not the only possible reasons for variation in MI rates.

Active travel data from the UK census are comprehensive in their coverage of MSOAs in the UK. A limitation is that active transport to work is used as a proxy for all active transport, and variation in the time spent in other physical activity is not accounted for. Furthermore, the intensity of physical activity during active commuting cannot be accounted or controlled for.

The active travel data are dependent on the accuracy of reporting of respondents to the mandatory UK Census. Nocon et al. found that studies using questionnaire data tended to identify a lower reduction in cardiovascular risk associated with physical activity; this may reflect a tendency for participants to over-report duration of physical activity.

Although we employ data which are at a higher geographical resolution than previous studies, there is nonetheless reduced potential to understand causality and implications of this study for individuals. Because this is an ecological study, it cannot identify causation between the two primary variables of interest. The introduction of methods to explore time lag enables investigation of possible causality, but no firm evidence of causality.

While many potential confounding factors are included in this analysis, a number of other factors are known to influence MI rates and are not assessed, for example, genetic factors and air pollution.

The platform used to carry out this study enables transparency of methods used and facilitates peer review and development of methodology and evidence base… ??

Depending on results… about significance, etc…

Findings from epidemiological studies are supported by physiological studies demonstrating that physical activity reduces the risk of overweight, hypertension and cardiovascular risk.

Explore mediating factors at population level… There is evidence that the benefits of active travel may be more beneficial to some socio-demographic groups than others. For example, an RCT involving overweight men (n=60) and women (n=71) all aged 61-79 years found that about 40 minutes of cycling, an average of 2.5 times per week resulted in an average 10.6 and 5.5 mmHg reduction in blood pressure, and XX and XX reduction in body mass index in the groups respectively (Morita and Okita 2013). At the population level active travel is found to have more health benefits in urban residents than rural residents (Millet et al 2013). (Laverty et al – more uptake of walking in black ethnicity participants) A cross sectional study of 344 10-year old children in USA at two time periods, six years apart suggests that the association between active transport and cardiovascular risk holds seen in adults is also present in children (Anderson et al 2011).

This study strengthens the evidence base on the association between active transport and cardiovascular disease risk, and specifically cardiovascular death. The findings are useful to policy makers because they are at the societal level. The results show areas where risk of MI is relatively high and active transport low, and could inform targeting of population level interventions

*Acknowledgements*

We gratefully acknowledge the contribution of all hospitals and healthcare professionals who participate in the MINAP registry. We acknowledge the MINAP Academic Group and the National Institute for Cardiovascular Outcomes Research (NICOR) for providing the data and their contribution to this research.

*Competing interest declaration:*

*All authors have completed the Unified Competing Interest form at* [*www.icmje.org/coi\_disclosure.pdf*](http://www.icmje.org/coi_disclosure.pdf)*(available on request from the corresponding author) and declare that (1) [initials of relevant authors] have support from [name of company] for the submitted work; (2) [initials of relevant authors] have [no or specified] relationships with [name of companies] that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) [initials of relevant authors] have no [or specified] non-financial interests that may be relevant to the submitted work.*

*Funding:*

No funding was used to complete this study – all research was carried out by the researchers in their own time.

*Other declarations:*

All authors had full access to the data and can take responsibility for the integrity of the data and the accuracy of the data analysis; the lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

*[The research methods and process can be seen on [github].. along with data??.. ]*

**References**

1. Newton, J. N. *et al.* Changes in health in England, with analysis by English regions and areas of deprivation, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* **386,** 2257–2274 (2015).

2. Tarride, J.-E. *et al.* A review of the cost of cardiovascular disease. *Can. J. Cardiol.* **25,** e195-202 (2009).

3. Heidenreich, P. A. *et al.* Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. *Circulation* **123,** 933–944 (2011).

4. Lee, I.-M. *et al.* Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* **380,** 219–229 (2012).

5. Nocon, M. *et al.* Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. *Eur. J. Cardiovasc. Prev. Rehabil.* **15,** 239–246 (2008).

6. Sattelmair, J. *et al.* Dose Response Between Physical Activity and Risk of Coronary Heart Disease: A Meta-Analysis. *Circulation* **124,** 789–795 (2011).

7. Sofi, F., Capalbo, A., Cesari, F., Abbate, R. & Gensini, G. F. Physical activity during leisure time and primary prevention of coronary heart disease: an updated meta-analysis of cohort studies. *Eur. J. Cardiovasc. Prev. Rehabil.* **15,** 247–257 (2008).

8. Department of Health. *Start Active , Stay Active*. (2011). at <https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/216370/dh\_128210.pdf>

9. World Health Assembly. *WHO Global Action plan for the Prevention and Control of Non-communicable Diseases. A/RES/66/2*. (2013). doi:10.1007/BF03038934

10. Department of Transport. *What is Active Transport ?* (2011). at <http://beactive.wa.gov.au/assets/files/Fact sheets/What is Active Transport.pdf>

11. Woodcock, J. *et al.* Public health benefits of strategies to reduce greenhouse-gas emissions: urban land transport. *Lancet* **374,** 1930–1943 (2009).

12. Lu, S. R., Su, J., Xiang, Q. Y., Zhang, F. Y. & Wu, M. Active transport and health outcomes: Findings from a population study in jiangsu, China. *J. Environ. Public Health* **2013,** (2013).

13. Laverty, A. A., Mindell, J. S., Webb, E. A. & Millett, C. Active Travel to Work and Cardiovascular Risk Factors in the United Kingdom. *Am. J. Prev. Med.* **45,** 282–288 (2013).

14. Millett, C. *et al.* Associations between Active Travel to Work and Overweight, Hypertension, and Diabetes in India: A Cross-Sectional Study. *PLoS Med.* **10,** (2013).

15. Flint, E. & Cummins, S. Active commuting and obesity in mid-life: Cross-sectional, observational evidence from UK Biobank. *Lancet Diabetes Endocrinol.* **4,** 420–435 (2016).

16. Furie, G. L. & Desai, M. M. Active Transportation and Cardiovascular Disease Risk Factors in U.S. Adults. *Am. J. Prev. Med.* **43,** 621–628 (2012).

17. Hoevenaar-Blom, M. P., Wanda Wendel-Vos, G. C., Spijkerman, A. M. W., Kromhout, D. & Monique Verschuren, W. M. Cycling and sports, but not walking, are associated with 10-year cardiovascular disease incidence: the MORGEN Study. *Eur. J. Cardiovasc. Prev. Rehabil.* 1 (2010). doi:10.1097/HJR.0b013e32833bfc87

18. Sahlqvist, S. *et al.* The association of cycling with all-cause, cardiovascular and cancer mortality: findings from the population-based EPIC-Norfolk cohort. *BMJ Open* **3,** e003797 (2013).

19. ONS. *2011 Census: Population and Household Estimates for Small Areas in England and Wales*. (2011). at <http://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/2011censuspopulationandhouseholdestimatesforsmallareasinenglandandwales/2012-11-23>

20. Sahlqvist, S., Song, Y. & Ogilvie, D. Is active travel associated with greater physical activity? The contribution of commuting and non-commuting active travel to total physical activity in adults. *Prev. Med. (Baltim).* **55,** 206–211 (2012).

21. Wanner, M., Götschi, T., Martin-Diener, E., Kahlmeier, S. & Martin, B. W. Active Transport, Physical Activity, and Body Weight in Adults. *Am. J. Prev. Med.* **42,** 493–502 (2012).

22. Besag, J., York, J. & Molli, A. Bayesian image restoration, with two applications in spatial statistics. *Ann. Inst. Stat. Math.* **43,** 1–20 (1991).

23. Blangiardo, M. & Cameletti, M. *Spatial and Spatio-temporal Bayesian Models with R - INLA*. (Wiley, 2015).

24. Rue, H., Martino, S. & Chopin, N. Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. *J. R. Stat. Soc. Ser. B (Statistical Methodol.* **71,** 319–392 (2009).

25. Matthews, C. E. *et al.* Influence of exercise, walking, cycling, and overall nonexercise physical activity on mortality in Chinese women. *Am. J. Epidemiol.* **165,** 1343–1350 (2007).

26. Yusuf, S., Reddy, S., Ounpuu, S. & Anand, S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* **104,** 2746–2753 (2001).

27. Mackenbach, J., Cavelaars, A. E. J. M., Kunst, A. E. J. M. & Groenhof, F. Socioeconomic inequalities in cardiovascular disease mortality. An international study. *Eur. Heart J.* **21,** 1141–1151 (2000).

28. Mackenbach, J. P. *et al.* Socioeconomic Inequalities in Health in 22 European Countries. *N. Engl. J. Med.* **358,** 2468–2481 (2008).

29. Kaplan, G. A. & Keil, J. E. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation* **88,** 1973–1998 (1993).

30. Tang, K. L., Rashid, R., Godley, J. & Ghali, W. A. Association between subjective social status and cardiovascular disease and cardiovascular risk factors: a systematic review and meta-analysis. *BMJ Open* **6,** e010137 (2016).

**Figure legends**

**Figure 1….**

**Tables**

[double-spaced]