Health Inequalities

AN INTERDISCIPLINARY EXPLORATION OF SOCIOECONOMIC POSITION, HEALTH AND CAUSALITY

SYMPOSIUM REPORT

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Table of Contents

Foreword

Introduction.....1

Summary.....2

Report of the Symposium.....3

Annex A: Symposium Programme.....22

Annex B: Scientific Committee on Health Inequalities.....24

Foreword

Dear Reader

The following report summarises the scientific findings and discussions of the European Federation of Academies of Sciences and Humanities (ALLEA) and the Federation of European Academies of Medicine (FEAM) interdisciplinary symposium on health inequalities organised by the Royal Netherlands Academy of Arts and Science (KNAW) in May 2018 in Amsterdam. This symposium, which convened leading academics and other interested stakeholders, revealed that this topic calls for further multidisciplinary discussion if common policy recommendations are to be developed for regulators.

Initiated by the KNAW, the multidisciplinary project is guided by the work of an interdisciplinary Scientific Committee that comprises experts of ALLEA and FEAM. The tripartite initiative aims to facilitate an in-depth debate.

We wish you an interesting read.

Antonio Loprieno

President of ALLEA

George Griffin

President of FEAM

Health Inequalities – an interdisciplinary discussion of socioeconomic position, health and causality

Amsterdam, the Netherlands, 24 May 2018

1. Introduction

The association between socioeconomic position and health is one of the most widely reproduced findings in population health research. However, despite decades of research into health inequalities there is still no consensus on some of the basic issues. For example, different disciplines hold different views on the nature of the causal relationship between low socioeconomic status and health, and on the main mechanisms for mediating the relationship. There is still uncertainty about the extent to which the relationship reflects a causal effect of socioeconomic position on health, reverse causation of health on socioeconomic position or confounding by underlying factors that affect both socioeconomic position and health. This report provides a summary of a recent symposium bringing together key opinion leaders from various scientific backgrounds to explore evidence and perspectives on the issues raised in the project discussion paper[1] prepared by the ALLEA-FEAM Scientific Committee on health inequalities, which is chaired by KNAW. This symposium and the report are intended as starting points for further interdisciplinary discussion.

1 ALLEA-FEAM Scientific Committee on Health Inequalities, Discussion Paper *Health Inequalities – an interdisciplinary exploration of socioeconomic position, health and causality* (Amsterdam: The Royal Netherlands Academy of Arts and Sciences, 2018). Contents accessible via https://knaw.nl/discussionpaper-health-inequalities

2. Summary

All countries are still faced with substantial differences in health between socioeconomic groups within their population. These health differences are a major challenge for public policy but effective policy-making requires a proper understanding of what drives inequalities. There is uncertainty and controversy about the extent to which the relationship reflects causation (socioeconomic position influences health), reverse causation (health influences socioeconomic position) or confounding (by factors that affect both socioeconomic position and health).

This symposium draws on the tripartite partnership between ALLEA-FEAM-KNAW to share data, expertise and experience from across the biological, health and social sciences regarding the topic of health inequalities. A previously-circulated discussion paper has characterised key questions, identifying pivotal findings in the evidence base and contentious methodological points. This discussion paper has been used during the symposium as a substantial resource in defining issues and questions and provides momentum to catalyse further exploration of the published record to resolve uncertainties and disparities. The well-balanced and lively symposium invited perspectives by leading researchers with expertise in demographics, public health, economics, statistics, social sciences, genetics, and public policy to help to clarify the nature of health inequalities in relation to occupational class, education and income.

Although differing views remain on what is uncertain in the evidence base, all participants agreed that it is vital to use the best available evidence to inform public policy now while, at the same time, expressing the commitment to perform robust research to fill knowledge gaps. This symposium demonstrated an important international role for academies in stimulating inter-academy and inter-disciplinary dialogue, and with an objective to achieve broader awareness of the issues. The next phase of the project is also critically important to provide further analysis and insight about different methodological approaches and controversies in the published evidence (and criteria for evaluating the literature) and to strengthen the entry points for policy to intervene on health inequalities.

3. Report of the symposium

George Griffin (FEAM), chair of the morning session, opened the meeting by describing the objectives of this tripartite ALLEA-FEAM-KNAW partnership to share evidence, expertise and experience from across the biological and social sciences on health inequalities. This subject is not new but is still a problem for all countries, reflecting the challenges of ongoing social developments. Comparison of epidemiological evidence across the EU provides one of the major resources with which to dissect out determinants of regional and other differences, and test hypotheses, in evaluating health inequalities.

Wim van Saarloos (KNAW) welcomed participants on behalf of KNAW, describing the activities of the academy, thanking Johan Mackenbach for his central role in drafting the project discussion paper, and emphasising the importance of the continuing task to interpret and use the scientific evidence base to advise policy makers.

Bernard Charpentier (FEAM) introduced the activities of FEAM, including its role in contributing to inform the work of the European Commission through the SAPEA consortium and to engage with other biomedical groups through the FEAM Forum. FEAM was already active in working on various topics relevant to health inequalities. For example: vaccination (those least likely to be vaccinated are the most vulnerable to health inequalities, often because of socioeconomic disparities); personalised medicine (that might benefit only wealthier patients and, thereby, exacerbate health inequalities); and the priorities of the next Framework Programme (Horizon Europe), where it is expected that health will be an important focus for the increased research budget. FEAM is also interested in initiating work on the topic of forced migration, of continuing relevance to the issues for health inequalities.

Graham Caie (ALLEA) introduced the activities of ALLEA, whose academy members cover all science, including social sciences, and the humanities. The strength of this symposium lies in bringing together disciplines to explore methodologies and share data to clarify possible contributions to health inequalities, such as the quality of health care, environmental determinants, health behaviours and other social factors. The differing conclusions reached hitherto by different disciplines have made it difficult

for policy makers to act decisively. The aim of the present work – a good example of the power of academy collaboration – is to help equip decision makers and society to address the challenges.

Johan Mackenbach (Erasmus Medical Centre, the Netherlands) presented "Health inequalities, an overview of unresolved scientific issues", covering the evidence base and issues raised in the discussion paper. Evidence from the Netherlands, for example, over the period 2011-2014 shows that longer longevity is associated with increasing income (despite the Netherlands being a relatively egalitarian society). Similarly, disability-free life expectancy and self-assessed good health show substantial gradients with rising income. Evidence from the comparison of other EU countries is consistent in demonstrating that mortality in both women and men is higher in those with lower education or lower occupational class. The disparity between low and high education status is seen for a wide range of causes of death: infectious diseases (including TB), but also non-communicable diseases, road traffic accidents and homicide, for example. Inequalities in mortality have widened in most EU countries for both men and women during the period 1970-2010; although the differences are less in the south than central Europe, the same relative pattern is seen everywhere. Disability (2010 data) across the EU is also less in those with higher education or occupational class.

Historically, it had been assumed that problems of health inequalities would decline with the rise of health and social welfare provision, but the problem was re-emphasised in the 1980s by the UK Black Report[2] and other reports (including in the Netherlands) indicating that mortality was still substantially higher in lower socioeconomic groups. This rediscovery of the problem led to various international and national policy initiatives, e.g. the WHO goals to reduce health inequalities and EU research programmes, but it remained uncertain as to what would help to reduce inequalities. Recently, inclusion of additional scientific disciplines and methodological refinements has provided new research insights but some of the emerging findings have seemingly contrasted with the earlier epidemiological conclusions. There is now significant controversy based on competing claims about the linkage of economic inequality and health, and about the relative contribution made by various risk factors, e.g. smoking or low personal control in the workplace.

2 UK Department of Health and Social Security, *The Black Report* (1980). Currently only accessible via the Socialist Health Association website: https://www.sochealth.co.uk/national-health-service/public-health-and-wellbeing/poverty-and-inequality/the-black-report-1980/

The discussion paper of the ALLEA-FEAM-KNAW multidisciplinary committee proposes that the stage has been reached that requires re-examination of the evidence base and reconsideration of ideas about health inequalities. Three principal questions have been posed:

Q1 Is there a causal effect of socioeconomic position on health?

Q2 What mediates the effect of socioeconomic position on health?

Q3 What is the effect of policies and interventions on inequalities in health?

Qs 1 and 2 have been reviewed in the project discussion paper, Q3 is likely to become a key part of future activities of the project, that will provide further analysis on the methodological approaches, evidence base, and entry points for policy. The discussion paper covers core areas relating to socioeconomic position and health that include:

» Causation (socioeconomic position influences health) versus selection (reverse causation, health influences socioeconomic position): with a consensus that reverse causation can occur in addition to causation, but no consensus on the relative importance of causation and reverse causation. Taking a life course perspective, causation and reverse causation may strengthen each other in a vicious cycle.

» The influence of confounding: with a consensus that confounding may occur, e.g. by personal (genetic) attributes, but no consensus on the relative importance of confounding factors nor on how confounding should be conceptualised. From the life course perspective, it is important to disentangle childhood socioeconomic conditions from confounding (including parenting) but it is unclear how to do so.

» Health inequalities are the outcome of complex underlying processes that are difficult to capture empirically. Most of the evidence comes from observational studies because experiments are not practical, or ethical. Cross-sectional associations are potentially biased by reverse causation, and even longitudinal associations may be biased by previous health status and personal characteristics that are independent of socioeconomic conditions. Many of the new quasi-experimental techniques used for establishing causality are unable to capture the full effects of social inequality over the life course because they focus on only a small part of the exposure to socioeconomic conditions.

» Nonetheless, while acknowledging the life course weakness, the best evidence may now often come from

quasi-experimental studies. These studies have concluded: (i) For education status, there are causal effects on health, reverse causation is less important, but there is a risk of confounding by personal attributes; (ii) For occupational class, reverse causation is important, there is a risk of confounding by personal attributes, but no evidence from quasi-experimental studies for causal effects; (iii) For income, reverse causation is important, there is a risk of confounding by personal attributes, little evidence for a causal effect on adult health but some for childhood health.

» Mediation analysis aims to uncover and estimate the indirect effects of socioeconomic position through exposure to more direct health determinants. A mediator, which is on the causal pathway, is not the same as a confounder, which is not. Conventionally, mediation analysis was performed by the "difference method" but unbiased results can only be obtained under limited conditions, e.g. if there is no confounding between socioeconomic position and mediator or between mediator and health outcome. Newer, more complex methods of mediation analysis are beginning to provide results that differ from those generated from conventional methods. Therefore, the existing evidence needs to be re-assessed and used with caution.

Thus, it can be concluded from the discussion paper from the first phase of the project that there is still considerable uncertainty about the answers to the key Qs 1 and 2. New research methods are generating new evidence but its value requires more assessment, accompanied by interdisciplinary dialogue on the methodological issues.

In general discussion following Prof Mackenbach's contribution, there was further emphasis on the importance of the life course perspective (and the value of longitudinal cohort research studies) in clarifying the influences of education and income. A question was also asked that then pervaded the whole symposium, "do we need to understand in order to act?" That is, even if we are not sure about the detail of causal mechanisms underlying associations of health inequalities with education and income, pragmatism would still recommend intervention to improve education provision, for example. Discussants agreed that it is reasonable to seek to strike a balance in recognising uncertainty and informing policy, but how much uncertainty is acceptable? What is vital is to use the best available evidence to inform public policy options while, at the same time, progressing research to fill knowledge gaps. It is essential to communicate to policy makers where

there is already sufficient consensus to act.

Eric Brunner (University College London, UK) presented "Explanations of health inequalities emerging from the Whitehall study"[3], taking as his starting point the UK political reaction to the Black report. This reaction had expressed disappointment that health inequalities had not disappeared following the inception of the NHS, recognising that a broader range of interventions were required, but that resources were limited. Since then, UK data for the period 1990-2016 show substantial increases in life expectancy for both women and men but this positive trend is now dissipating, associated with onset of austerity in 2008 – but what is the nature of the association?

In the long-term, pioneering Whitehall studies of the civil service, the research approach, using the Bradford Hill criteria [4] for causality, capitalised on the hierarchy of occupations found in government employment – at the top, characterised by power and privilege, at the bottom characterised by lower education and status, but throughout a common principle of job and pension security. Analysis over a 25-year period showed a stepwise increment in cardiovascular disease and total mortality according to occupational class, mortality increasing from the highest to lowest occupational grades, even when adjusted for confounders such as smoking. Supportive data from the UK census 1971-1991 also demonstrated a growing inequality in cardiovascular mortality between social classes despite a reduction in total such mortality over this period. The Whitehall studies additionally revealed occupational class social inequalities in health-related functions (physical and mental health) and in recovery from poor function. Among the insights on causality elicited from the Whitehall studies were:

» Clear evidence that adult socioeconomic position affects cardiovascular function and some evidence of small effects of reverse causation – health in childhood does affect adult socioeconomic status.

» Social mobility reduces health inequalities.

3 M.G. Marmot, George Davey Smith, Stephen Stansfeld, Chandra Patel, Fiona North, Jenny Head, Ian White, Eric Brunner and Amanda Feeney, *Health inequalities among British civil servants: the Whitehall II study* (London: The Lancet, 1991). Contents accessible via https://ac.els-cdn.com/014067369193068K/1-s2.0-014067369193068K-main.pdf?_tid=a1e403a8-1cab-449b-bb13-e7c90aea794c&acdnat=1540387231_1943c6fb5d0c7777b24c142aee206ebd

4 Robyn M. Lucas and Anthony J. McMichael, *Association or causation: evaluating links between "environment and disease"* (Canberra: Public Health Classics, 2005). Detailed listing of criteria and respective description accessible via http://www.who.int/bulletin/volumes/83/10/792.pdf

- The hierarchy of health effects is not confounded, except for correlated measures of socioeconomic position.
- There is dose-responsiveness within the hierarchy (one of the original Bradford Hill criteria for demonstrating causality).

With regard to mechanisms, in the first Whitehall study multiple logistic regression analysis applied to the cohort could not explain the major part of the cardiovascular mortality in terms of conventional risk factors. However, there are methodological weaknesses in forming this conclusion and other factors, e.g. genetics, early nutrition, were not measured. More recent assessment, taking into account thinking about "cause of the causes" and characterising direct and indirect pathways operating via biological and behavioural risk factors, can now account for about 60% of the mortality gradient across the hierarchy of occupations. The remaining gap can be attributed in part to missing data, problems of self-assessment, and changes in exposure over time. Clarifying life course pathways is, again, essential.

Understanding what mediates the socioeconomic gradient in health has been advanced by introduction of the psychosocial hypothesis (appertaining to psychological resources, beliefs and emotions) that now links "low job control" and "effort-reward imbalance" with the incidence of heart disease. Stress at work can be connected to cardiovascular disease through the neuroendocrine axis (brain hypothalamus-pituitary gland-adrenal gland corticosteroid secretion-multiple effects, including on glucose metabolism). Metabolic endocrine markers, consistent with the metabolic syndrome, depend on rank in the occupational hierarchy and research on other primate species has confirmed that low social status is associated with high circulating levels of corticosteroids.

Prof Brunner concluded by emphasising the relevance for policy translation objectives. Despite uncertainties in the evidence, the broad objectives embedded in the UK 2010 strategic review of health inequalities[5] remain highly relevant:

- Give every child the best start in life
- Maximise capabilities for all
- Provide for fair employment conditions
- Provide for healthy standard of living
- Support communities

5 Clare Bambra, Kerry Joyce and Alan Maryon-Davis, *Strategic Review of Health Inequalities in England post-2010 (Marmot Review): Task Group 8: priority public health conditions: final report* (London: University College London, Department of Epidemiology and Public Health, the Global Health Equity Group, 2010). Full report accessible via https://www.researchgate.net/publication/41231868_Strategic_review_of_health_inequalitiesin_England_post-2010_Marmot_Review_Task_Group_8_priority_public_health_conditions_final_report

» Ensure the preventive role of health services.

In general discussion, it was agreed that the Whitehall and other longitudinal cohort studies were a continuing rich resource for insight in tackling Qs 1 and 2 of the project discussion paper. For example, is birth weight a predictor of subsequent events? There is a link between lower birth weight and lower job grade that reflects health selection in some way. This association raises important issues for social policy, e.g. for improving nutrition during pregnancy and on how to break the intergenerational cycle of deprivation.

Jay Kaufman (McGill University, Canada) discussed in detail statistical aspects of discerning patterns in estimating relationships in "Methodological issues in explaining health inequalities". The adjustment tradition in statistical models of collected observational data attempts to characterise the relationship between variables that may otherwise confuse the explanation of the observation. That is, making causal inferences from passively observed data requires not only structural identification but also significant data under various scenarios, with consistency assumptions. There are three main structural threats to validity:

(i) Confounding bias – most causal inference methods assume no unmeasured confounders. Quasi-experimental methods, as preferred by economists, use structural assumptions to achieve identification even in the presence of some unmeasured confounding.

(ii) Selection bias – including cohort selection bias in life course design studies.

(iii) Information bias – e.g. measurement error, misclassification.

Understanding these biases is important in clarifying the issues raised in the project discussion paper. When trying to answer Q1, the problem is that a binary answer is of little value. The validity of causal interpretation is threatened by systematic and random error but also by the imprecision in specifying (and estimating) the intervention of interest. When trying to answer Q2 on mechanisms, coherent adjustment strategies are founded on the premise of well-defined exposures but there is methodological challenge in trying to define and integrate exposure, e.g. the whole of an individual's experience of education. However, if the objective is qualitative rather than quantitative inferences, then the methodology used may not need to be so vigorous and it is possible, for example, to assess the impact of policy to reduce poverty by using evidence from initiatives in other countries.

There are different decomposition options to analyse the total effect of socioeconomic position on health in generating mechanistic inferences. These options are outlined in some detail in the project discussion paper and can be classified as Controlled direct effect, Controlled indirect effect and Natural direct or Pure direct effect. There is controversy among researchers on how and when to use these options; part of the controversy relates to policy relevance insofar as Natural/Pure direct effect methodology cannot be subjected to experimental observations and linked to policy. The assessment problems mean that it is difficult to interpret the validity of mediation from data in the literature without understanding which of the decomposition options have been employed. This has significant implications for the project discussion paper, e.g. none of the mediation analysis approaches listed in Box 3.2 of the discussion paper[6] actually solve the identification problem if there are unmeasured cofounders.

There has been considerable progress made over the last decade in addressing the methodological issues but Prof Kaufman advises that there has been too much emphasis on Pure direct effects in the recent literature because, although the approach has attractive (decomposition) properties, it is weak on policy implications. The Controlled direct effect may be preferred.

For the future, it is important first, to continue aiming to characterise the real-world context (with well-defined interventions), secondly, to be open about estimates of effects in terms of their magnitude and imprecision, and thirdly, to sustain the research efforts, because the outcomes are of societal importance.

During general discussion, Prof Kaufman was invited to extend his response on the value of Qs 1 and 2:

» Is Q1 unanswerable, unless an intervention is specified? Prof Kaufman – Q1 is vaguely phrased. Qualitatively, socioeconomic position can be said to be a cause of health inequalities and the policy goals listed by Prof Brunner remain valid, but if the aim is to quantify risk then an intervention must be specified.

» In answering Q2, do you have doubts about the new techniques? Prof Kaufman – generally, modern methods have improved, e.g. in understanding non-linearity. Under some circumstances the various methods agree closely but some of

6 ALLEA-FEAM Scientific Committee on Health Inequalities, Discussion Paper *Health Inequalities – an interdisciplinary exploration of socioeconomic position, health and causality* (Amsterdam: The Royal Netherlands Academy of Arts and Sciences, 2018), 27. Contents accessible via https://knaw.nl/discussionpaper-health-inequalities

the traditional methodologies used in the social sciences are fragile in some circumstances.

These points were elaborated further in the subsequent Panel discussion.

The chair of the afternoon session, Johan Mackenbach, described how contributors had been invited to present their views on two particular points: does variation in education cause health inequalities, and does low income/socioeconomic status cause health inequalities?

Eddy van Doorslaer (Erasmus University Rotterdam, the Netherlands) reviewed "Does low income cause ill-health? An economist's perspective". While the answer to the question (yes) might seem obvious, the relationship is not so clear if controlled for confounders. This presentation draws on a comprehensive review published in 2015, guided by economic theory, updated by more recent evidence. The general conclusions from the 2015 review can be summarised:

» Does health inequality affect income inequality (reverse causality)? Yes.

» Does income inequality affect adult health inequality? Not proven, but there may be a stronger relationship longer-term.

» Does income inequality affect population health? No.

» Early life conditions, including parental income, do matter for child health.

» The health of the poor is more vulnerable to income shocks.

» There are stronger effects in low- and middle-income countries.

The second point above, the focus of the symposium, is difficult to examine in high income countries because of the presence of social security safety nets and because random permanent income shocks are rare. Nonetheless, even if not causal, health goals may still be used to justify redistribution of income.

Does higher income/wealth cause better health? The answer expected from economic theory on investment and consumption benefits is yes (because the rich demand more health and can afford market prices, although they can also afford harmful behaviour), but the empirical evidence is not so clear. Because there is little scope for experimentation, quasi-experimental methods are invoked (using "natural experiments" such as German unification), together with the search for impacts of exogenous variation in wealth (e.g. lottery wins).

A major study provides additional insight since the time of the 2015 review: using Swedish data on players of the national lottery (the majority of the population in Sweden) to estimate the impact of random income shocks on adult health and child development. The results of

this study of relatively permanent income shift show:

» No significant effect of wealth on mortality.

» No measurable effect on child health or development (except for increased risk of hospitalisation and decreased risk of obesity).

» A small reduction in adult use of mental health drugs.

» No signs of an effect growing with time or of stronger effect at lower initial levels of wealth.

The researchers concluded that, in affluent countries with extensive social security safety nets, causal effects of wealth are not the main source for wealth-mortality gradients nor of variations in child development. Prof van Doorslaer reinforced this with his own overall conclusion that there is no strong evidence for impact of income on health in high income countries and that the expectation of greater effects at the bottom end of income distribution was not confirmed. Thus, any contribution of wealth on health may be minor.

Margaret Whitehead (University of Liverpool, UK) in her contribution "Does low income cause ill-health? A public health perspective" started by observing that the project discussion paper took a rather simplistic view about the perspectives and assumptions of public health scientists. In actuality, their positions may be more complex and are based on evidence, not assumptions. The analytical framework of mechanisms generating social inequalities in health can be discussed in terms of differential exposure, differential vulnerability and differential consequences. The pathways reviewed in the project discussion paper – causation, reverse causation and multiple interactions - are not mutually exclusive.

By contrast with the evidence adduced by Prof van Doorslaer, there is a large body of other contemporary evidence reaching other conclusions. This includes:

» *Child health* A systematic review in 2017 "does money affect children's outcomes?" draws on randomised clinical trials, quasi-experimental and longitudinal studies. This review concludes that income has causal effects on a wide range of outcomes including child physical health and development, cognitive and social achievement. Low income was not found to be a proxy for other factors such as education. Two potential mechanisms were proffered for the impact: (i) Investment model – via parents' ability to invest in goods and services that promote a child's healthy development; and (ii) Family stress model – low income affects parents'

mental health and influences their behaviour. Recent evidence from the UK Millennium Cohort Study (2017)[7], analysing the time of first transition into income poverty, discloses increased child and maternal mental health risk (the latter influencing the former). Other work finds a dose-response relationship of poverty with child mental health risk, and longitudinal studies show that children from less advantaged backgrounds had higher risk of premature death in adulthood.

» *Adult health* A systematic review in 2015 on "does money in adulthood affect adult outcomes?" provides strong evidence that additional resources reduce mental health problems, with the effect pronounced in lower socioeconomic groups. A recent US study on negative wealth shocks in middle-aged and older adults finds significant mental health toll and increased all-cause mortality over 20-years follow-up.

» *Does ill health cause low income (reverse causation)?* People with disability are at greater risk of living in or near poverty. But there are large differences between countries and the effect is context/policy dependent. Meta-analysis in 2015 shows that poor health in adolescence is associated with poorer education and employment in adulthood, with the evidence stronger for mental health conditions. Thus, public investment in health may improve life chances. Having to pay for health care is particularly impoverishing but there is a lack of EU evidence on this point.

Prof Whitehead summarised that, from a public health perspective, there is strong contemporary evidence (supported by the historical record) for a causal effect of income on health, especially in children and adult mental health conditions, with some evidence also for a reverse causal effect. Research is focusing on mechanisms and pathways but it is important for the scientific community to emphasise the implications for policy now. For example, reducing income poverty would have important effects on children and there is also need for better social protection for those affected by disability and chronic illness.

The differences presented by Profs van Doorslaer and Whitehead were explored further in subsequent Panel discussion.

David Hill (University of Edinburgh, UK)

7 The Millennium Cohort Study (MCS) is a multi-disciplinary research project following the lives of around 19,000 children born in the UK in 2000-01. Its principal investigator is Prof Emla Fitzsimons of the Centre for Longitudinal Studies at the University College London. More information is available https://www.cls.ioe.ac.uk/page.aspx?-sitesectionid=851 Survey data is accessible on UK Data Service page https://beta.ukdataservice.ac.uk/datacatalogue/series/series?id=2000031

reviewed "Does low education cause ill-health? A geneticist's perspective". More broadly, do genetic effects confound the relationship between socioeconomic status and health? That is, people with certain genetic risk factors may be more susceptible to the negative health effects of socioeconomic disadvantage. His starting point was that socioeconomic status is partially heritable. The assessment of whether genotypic similarity predicts phenotypic similarity expressed, for example, in terms of number of years of education completed, can be explored by methods based on behavioural genetics (twin studies) and molecular genetics (DNA analysis of unrelated subjects). Behavioural genetics research suggests 40% heritability (perhaps an overestimate because of the shared environment for twins) whereas molecular genetics suggests 20% heritability (an underestimate because of missing analysis of parts of the genome). Attempts to reconcile these findings were made using resources from Generation Scotland and conclude in estimating about 40% for education heritability.

Further investigation of the phenotype was made using data from the UK Biobank[8] with two measures of socioeconomic status – Deprivation index (postcode-based) and Household income index. At least 11% of the variation in household income and 21% of variation in social deprivation can be attributed to genetic status: although the collective genetic effect may be substantial, the effects of individual loci are small. A substantial positive genetic correlation between deprivation and household income was identified, as were large positive genetic correlations between both measures of SES, with education and intelligence, indicating that the genetic aetiology of SES, education, and intelligence overlaps highly. However, when measures SES, and education are compared with health variables negative genetic correlations are found for traits such as coronary artery disease, obesity, smoking and Alzheimer's disease, whereas positive genetic correlations are found for self-rated health and subjective wellbeing. This indicates that the genetic variants linked with an increase in education and SES are also linked to a reduction in the risk of disease and an increase in self-perceived health and wellbeing.

Methods to evaluate the causal effects of education on health that can avoid the confounding genetic effects include discordant twin studies that is same genes, different education provision: those with higher level of education had an extra 3 years of life at age 60 by comparison with their twin. However, this evidence is limited because twins represent a special population and there is relatively little variation in education between pairs. Other methods to evaluate

8 https://www.ukbiobank.ac.uk/

causation include natural experiments, e.g. resulting from policy changes determining years of education provided, and Mendelian randomisation.

Dr Hill concluded that socioeconomic status is a heritable phenotype, genetic effects are shared between socioeconomic status and health, and there are likely causal effects between education and health outcomes.

In general discussion, it was noted that it is difficult to quantify the total effect attributed to the genetic influences of education that act on health traits, but as shown in by the genetic correlations, it is not zero. Polygenic risk scores can be used to predict phenotypic variance in health traits using the genetic effects linked to education, but this technique will only capture a subset of the total effect on health attributable to genetic effects linked to variance in education. With larger sample sizes it will be possible to derive polygenic risk scores with better predictive power, however these are still unlikely to capture all genetic effects.

During the general discussion it was also noted that genetic influences depend on the environment such that a wider array of environmental differences will typically result in a smaller net genetic impact. The opposite is also true, genetic effects will make a greater contribution to individual differences in education as environmental opportunities for education become more equal, however it is important to note that if the environment is more equal, there will be a smaller range of individual differences to explain. The contribution of genetics to the intergenerational transmission of socioeconomic status is an important continuing topic for research and the issues received further attention in Panel discussion.

Olle Lundberg (Centre for Health Equity Studies, Sweden) contributed "Does low education cause ill-health? A sociologist's perspective." Education as a multi-dimensional resource is important for the individual in imparting knowledge and skills, supporting neuro-cognitive development and providing value for the labour market. Health is shaped over the life course and education has a central role. Key relationships are portrayed in the Figure taken from the presentation by Prof Lundberg (see next page).

These 5 relationships can be further characterised for the individual:

(a) Education providing neurocognitive development, knowledge and skills, including those of communication. The evidence from the literature shows for example that schooling contributes to increased IQ and shapes brain mechanisms underlying improved cognitively demanding tasks (identifying the right Posterior Parietal Cortex from functional imaging studies).

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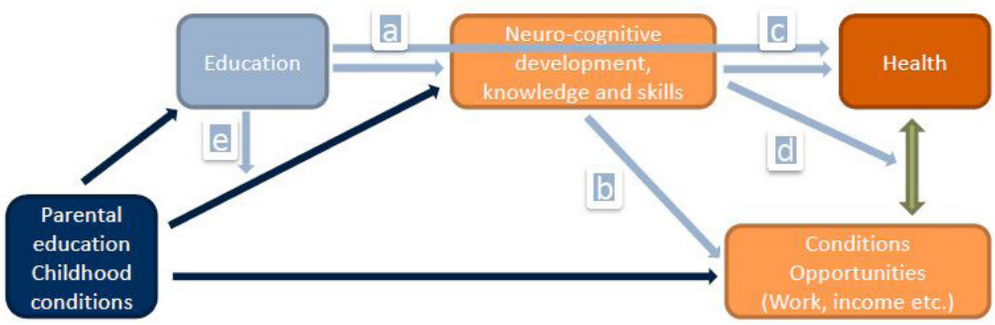
Education and health in context



(b) Cognitive functions, skills and knowledge affect conditions later in life. More education is linked to a range of favourable outcomes, e.g. employment, which are linked to better health.

(c) Cognitive function, skills and knowledge are also directly linked with health. For example, "learned effectiveness" such as problem-solving abilities and changed behaviours influence better health.

(d) Education can modify the health consequences of different conditions. For example, by improving the ability to handle problems and life stressors: education-linked inequalities in mortality are larger at lower levels of income.

(e) Education can compensate for different childhood conditions. For example, early child development and into adulthood is greatly affected by parents' education and there are stronger effects of starting child care early among lower income families.

At a societal level, expansion of education (pre-school, school and higher education) is most likely to contribute to better population health but has not reduced health inequalities. Those with lower education status are better educated than previously (a better absolute resource) but they are not necessarily better relative to others. Given these conclusions about the value of education, an important point raised in discussion related to the age at which pre-schooling should be started in the light of the evidence that full neuronal complement is achieved by the age of 3 years.

Domantas Jasilionis (Vytautas Magnus University, Lithuania and Max Planck Institute for Demographics, Germany) presented "Health inequalities in Eastern Europe – do they have the same explanation?" reviewing evidence from five decades of persisting east-west life expectancy divide in Europe. In the first decades after the 1960s, life expectancy declined for males in Eastern Europe; since the 1990s, the disparity has increased between Russia/Belarus and the rest of Eastern Europe. Since the mid-2000s, life expectancy has increased in all countries but the east-west gap remains large.

Life expectancy is higher for more highly educated males and females and the life expectancy gap between those with higher and lower levels of education is bigger in Eastern Europe. In detailed comparison of Lithuania and Sweden, this difference is seen at all ages and with bigger impact of exogenous factors in Lithuania. Other evidence examined the effects of education level on health inequality according to different welfare regimens and the effect of other risk factors (such as overweight, smoking and alcohol) in helping to explain inequality disparities between countries. From this analysis of evidence, there is still a paradox in that traditional risk factors cannot fully explain the east-west gap in socioeconomic inequalities. Moreover, the bigger longevity disparities in the east may not be accompanied by equivalent disparities in other health outcomes. Part of the explanation may reside in an effect of selective survival for lower socioeconomic groups in the east. The differences emerging from the specific Lithuania-Sweden comparison may be attributable to factors discussed in previous presentations, e.g. psychosocial stress and the lower physical ability to respond to stressors, low job control and effort-reward imbalance.

In conclusion, Eastern Europe can be defined as an increasingly diverse region but there is lack of reliable data for some countries. There is need for more research on the determinants of inequalities, particularly in current political contexts and with regard to understanding and ensuring benefits of EU membership.

Giuseppe Costa (University of Turin, Italy) considered "Policy implications of explanations of health inequalities", reviewing evidence from three case studies on health inequalities: at the city level (priority setting in Turin), national level (horizon scanning in Italy) and EU level (Member State representatives of Ministries of Health). The outputs from these case studies help to illustrate the various barriers in engaging with policy makers: using evidence to deal with responses such as "it's not our concern, we don't know what to do, we don't know how to do it, we can't afford to do it."

Moreover, although both incidence and progression are highly relevant to the understanding of health inequalities, the project discussion paper deals mainly with incidence whereas stakeholders are often strongly concerned about progression.

In reinforcing points made by previous speakers, Prof Costa characterised the elements for an explanatory framework linking social position and health in terms of: social vulnerability (and its effect on reverse causation), mediation (where explanation in terms of direct mediators such as psychosocial stress can still be controversial), health vulnerability, and local context as a moderator. Constructing and understanding the explanatory framework is important to clarify the implications for the various policy priorities:

(i) For raising awareness of health inequalities as the first step in policy setting, understanding causality does not matter but there is need for a marker for social benchmarking.

(ii) Developing redistributive policies and evaluating any inadvertent health consequences requires health-sensitive tailoring of interventions but, again, understanding of causality may not be crucial unless the proposed policy option has contrasting consequences for policy-intended and health-unintended effects.

(iii) Actions on reducing differential exposure and health vulnerability in response to risk factors/mediators, e.g. prevention across different settings within the broad context of universal health coverage.

(iv) Actions on the local context, that is improving the capacity to achieve the best health outcomes when there is local disadvantage.

For the three case studies described, city (Turin) stakeholders prioritised policy actions (iii) and (iv); national (Italy) discussants prioritised (iii) for health care provision; EU discussants took the broadest perspective, emphasising health equity in all policies, health care in vulnerable groups and provision of healthy environments.

The Panel discussion commenced with Prof Mackenbach's observation that the meeting had made significant progress in identifying areas of agreement and disagreement and illustrated the importance of continuing to encourage exchange between disciplines. What more detail could be added to prepare for the next steps of the project? Several points were advanced to catalyse the further discussion:

» Is the question as to whether low socioeconomic position causes ill health (Q1 in the discussion paper) unanswerable? Prof Kaufman

reiterated his view that it is not meaningful to answer yes/no to Q1. The answer would be less ambiguous and more helpful in informing policy if the question were made more specific, capturing sociological detail in describing intervention (e.g. education). Prof Brunner added that methodologies can be improved to clarify the relationship between socioeconomic position and health but research approaches on causation and on addressing inequality must both continue in parallel and support the policy development process.

» Is there a risk that genetic contributions confound previous analysis of the Whitehall and other longitudinal studies? Prof Brunner replied that height had been used as a genetic proxy in the Whitehall study but it is accepted that this is a weak proxy. There is still relatively little information on how genetics might affect the magnitude of the socioeconomic gradient (this issue is also discussed later with regard to education).

» Focusing on low income and health: to what extent do the conclusions by Profs van Doorslaer and Whitehead disagree? For example, is there agreement that any effects of low income on adults are mainly on mental health? Both Profs van Doorslaer and Whitehead confirmed that there is disagreement, partly because of the difficulty of generalising from evidence in specific studies ("social inequity at large") and because of the multiplicity of different mechanisms in different contexts, that may not yet be fully captured in the discussion paper. The conflicts in interpreting evidence are highly relevant to policy development, e.g. does money matter for child health? It is apparent that the economics and public health communities are using different literature bases, are judging them differently in terms of criteria for credibility and discounting different studies. Areas of contention must be resolved and it was agreed that a second phase of the project could usefully do more to exchange views on the different criteria for evaluating quality in evidence. Panel discussion reiterated other relevant points, including: (i) It is important not to be partisan about causalities because reverse causation also requires political action; (ii) It is not just income inequality that matters but how resource is redistributed to protect the most vulnerable (e.g. in focusing on social security and education systems); and (iii) Relative income position is more important than absolute income.

» Focusing on education and health: although there is probably less disagreement that education has a causal effect on health, part of the education-attributed influence is probably confounded by those genetic factors leading to both better education and better health. Nonetheless, an education effect is likely still present even if it were possible to adjust for genetic factors, underscoring the necessity of continuing to attend to education provision. Might it be counter-productive to focus on genetics in this field, because of the risk that it can be taken to imply that the poor are genetically different? Dr Hill advised that genetics should not be ignored but clarified – it would be more dangerous to ignore genetic effects if they contribute to health inequalities. Prof Kaufman agreed that genetic effects should not be ignored but the policy objective must be to create an environment (e.g. good schooling) where genetic effects are minimised.

» Given the complexity of the analysis and the high degree of inter-relationship (including potential synergy) between different factors, is it useful to consider them one-by-one? Prof Kaufman noted that the usual statistical modelling approach is indeed to isolate each factor, holding everything else constant, but the real world does not operate like that. Therefore, all available research approaches, including observational data, must be used.

In his **concluding remarks**, Prof Caie reaffirmed previous points made by Profs Charpentier, Griffin and Mackenbach: the demonstrable value of this symposium reflects an important international role for academies in stimulating inter-academy and inter-disciplinary dialogue, drawing on evidence from different approaches to understanding and tackling health inequalities, from different countries, and with an objective to raise broader awareness of key issues. This event can be regarded as completing a first phase of the project; while input from all ALLEA and FEAM academies may be sought in future as to continue interdisciplinary analysis and provide European policy makers with unambiguous messages for policy recommendations. Citing the last words of Mary Queen of Scots "In this end is my beginning."

Annex A

ALLEA-FEAM-KNAW Symposium Programme

Health inequalities: An interdisciplinary discussion of socioeconomic position, health and causality

Hosted by KNAW

Date: 24 May 2018, 9.30 a.m. – 5.00 p.m.

Venue: De Nieuwe Liefde, Da Costakade 102, Amsterdam, the Netherlands

Chairs: George Griffin, FEAM (morning); Johan Mackenbach, KNAW (afternoon)

9.00 a.m. Registration

9.30 a.m. Wim van Saarloos, KNAW; Bernard Charpentier, FEAM; Graham Caie, ALLEA – *Opening, welcome*

10.00 a.m. Johan Mackenbach, KNAW/Erasmus Medical Center, The Netherlands – *Health Inequalities, an overview of unresolved scientific issues*

10.30 a.m. Eric Brunner, University College London, United Kingdom – *Explanations of health inequalities emerging from the Whitehall study*

11.30 a.m. Jay Kaufman, McGill University, Canada – *Methodological issues in explaining health inequalities*

12.30 p.m. Lunch

1.30 p.m. Eddy van Doorslaer, Erasmus University Rotterdam, The Netherlands – *Does low income cause ill-health? An economist's perspective*

1.55 p.m. Margaret Whitehead, University of Liverpool, United Kingdom – *Does low income cause ill-health? A public health perspective*

2.20 p.m. David Hill, University of Edinburgh, United Kingdom – *Does low education cause ill-health? A geneticist's perspective*

2.45 p.m. Olle Lundberg, Centre for Health Equity Studies, Sweden – *Does low education cause ill-health? A sociologist's perspective*

3.10 p.m. Domantas Jasilionis, Vytautas Magnus University, Lithuania & Max Planck Institute for Demographic Research, Germany – *Health inequalities in Eastern Europe – Do they have the same explanation?*

3.35 p.m. Break

3.50 p.m. Giuseppe Costa, University of Turin, Italy – *Policy implications of explanations of health inequalities*

4.05 p.m. *Panel discussion*

4.50 p.m. Graham Caie, ALLEA – *The role of academies, closing remarks*

Annex B

ALLEA-FEAM Scientific Committee on Health Inequalities

Professor **Johan Mackenbach**, *Chair*

» Professor of Public Health, Erasmus Medical Center, Rotterdam, The Netherlands

» Royal Netherlands Academy of Arts and Sciences (KNAW)

Professor **Giuseppe Costa**

» Professor of Public Health, Dept. Clinical and Biological Sciences, University of Turin, Italy

Dr **Domantas Jasilionis**

» Max Planck Institute for Demographic Research, Rostock, Germany

» Center for Demographic Research, Vytautas Magnus University, Kaunas, Lithuania

Professor **Brian Nolan**

» Professor of Social Policy, Institute for New Economic Thinking, Nuffield College, University of Oxford

» Royal Irish Academy

Professor **Johannes Siegrist**

» Professor of Work Stress Research, Institute for Medical Sociology, Heinrich-Heine-University Düsseldorf, Germany

» Heidelberg Academy of Sciences and Humanities

Professor **Alfred Spira**

» Professor of Public Health and Epidemiology, Université Paris Sud, France

» French Academy of Medicine

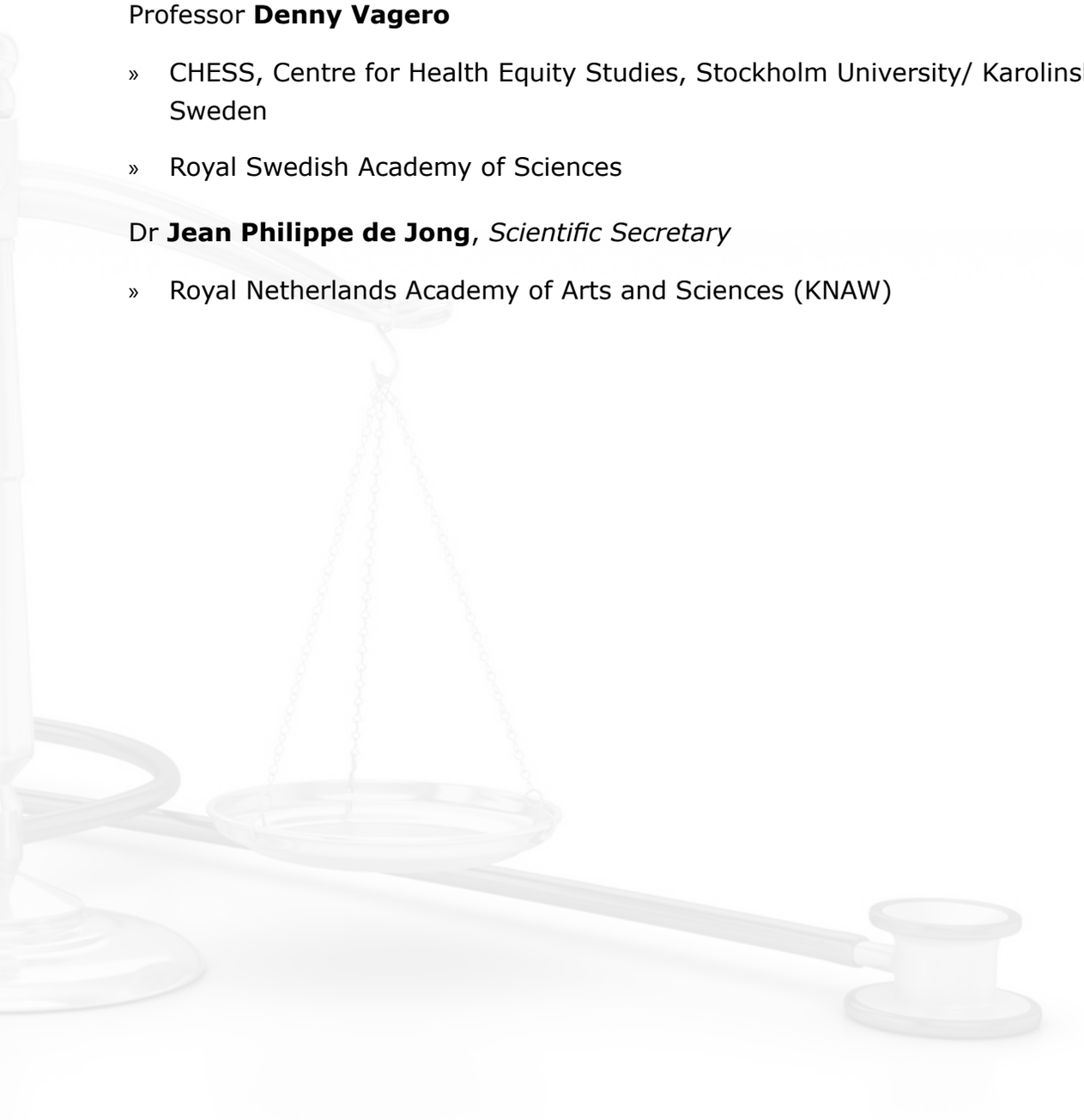
Professor **Denny Vagero**

» CHESS, Centre for Health Equity Studies, Stockholm University/ Karolinska Institutet, Sweden

» Royal Swedish Academy of Sciences

Dr **Jean Philippe de Jong**, *Scientific Secretary*

» Royal Netherlands Academy of Arts and Sciences (KNAW)



About ALLEA, the European Federation of Academies of Sciences and Humanities

ALLEA, the European Federation of Academies of Sciences and Humanities, was founded in 1994 and currently brings together almost 60 academies in more than 40 countries from the Council of Europe region. Member Academies operate as learned societies, think tanks and research performing organisations. They are self-governing communities of leaders of scholarly enquiry across all fields of the natural sciences, the social sciences and the humanities. ALLEA therefore provides access to an unparalleled human resource of intellectual excellence, experience and expertise.

About FEAM, the Federation of European Academies of Medicine

FEAM is the European umbrella group of national Academies of Medicine and Medical Sections of Academies of Sciences. FEAM's mission is to promote cooperation between national Academies of Medicine and Medical Sections of Academies of Sciences in Europe; to provide them with a platform to formulate their collective voice on matters concerning human and animal medicine, biomedical research, education, and health with a European dimension; and to extend to the European authorities the advisory role that they exercise in their own countries on these matters.

About KNAW, the Royal Netherlands Academy of Arts and Sciences

The Royal Netherlands Academy of Arts and Sciences was founded in 1808 as an advisory body to the Dutch Government. The Academy derives its authority from the quality of its members, who represent the full spectrum of scientific and scholarly endeavour and are selected on the basis of their achievements. It is also responsible for fifteen internationally renowned institutes whose research and collections put them in the vanguard of Dutch science and scholarship. As the forum, conscience, and voice of the arts and sciences in the Netherlands, the Academy promotes quality in science and scholarship and strives to ensure that Dutch scholars and scientists contribute to cultural, social and economic progress.

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