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Lancet NCD health economics action 2

Tackling socioeconomic inequalities and non-communicable diseases in low-income and middle-income countries under the Sustainable Development agenda

Louis W Niessen, Diwakar Mohan, Jonathan Akuoku, Andrew J Mirelman, Sayem Ahmed, Tracey Koehlmoos, Antonio Trujillo, Jahangir Khan, David H Peters

Five Sustainable Development Goals (SDGs) are related to the reduction of health inequalities nationally and worldwide by aiming for poverty reduction, health and wellbeing for all, equitable education, gender equality, and reduction of inequalities within and across countries. The interaction between inequalities and health is complex: better economic and educational outcomes for households enhances health, low socioeconomic status leads to chronic ill health, and non-communicable diseases (NCDs) reduce income status of households. NCDs account for most causes of early death and disability worldwide, so it is alarming that strong scientific evidence suggests an increase in the clustering of non-communicable conditions with low socioeconomic status in low-income and middle-income countries since 2000, as was earlier observed in high-income settings. These include tobacco use, obesity, hypertension, cancer, and diabetes. Strong evidence from 231 studies overwhelmingly supports a positive association between low-income or low socioeconomic status, education, and NCDs. Only three studies differentiated [A: differentiated the associations?] by sex. Health is a key driver in the SDGs. Reduction of health inequalities and NCDs should become key in the promotion of the overall SDG agenda. A sustained reduction of general inequalities in income status, education, and gender within and between countries would enhance worldwide equality in health. To end poverty through elimination of its causes, NCD programmes should be included in the development agenda. National programmes should mitigate social and health shocks to protect the poor from events that worsen their susceptible socioeconomic condition and health status. Programmes related to universal health coverage of NCDs should specifically target susceptible populations and include elderly people and people who are most at risk, such as XX [A: please provide another example of a vulnerable population.]. Growing inequalities in access to resources for prevention and treatment need to be addressed through improved international regulations across jurisdictions that eliminate the legal and practical barriers in the implementation of non-communicable disease control.

Introduction

The UN and other international agencies advocate and seek integral approaches to the Sustainable Development Goals (SDGs),[1–8] which address existing global health inequalities through comprehensive, cross-sector strategies.[2,6,9–13] The formal targets set for the SDGs cover the economic, educational, environmental, and social pillars of sustainable development with a strong focus on equity across all goals at national and international levels.[4,6] Five SDGs set explicit targets that relate to the reduction of health inequalities both nationally and worldwide. These targets are poverty reduction, health and wellbeing for all, equitable education, gender equality, and reduction of inequalities within and between countries. The SDGs [A: this seems a circular argument. Do you mean that the five SDGs listed earlier cover 78/169 targets?] cover 78 of the 169 targets set,[4] indicating a new central role of health in development (figure 1). The role [A: the 'prioritisation'?] of health in the Millennium Development Goals was limited.[4,6,14]

The reduction of both poverty and health inequalities have become leading topics in the promotion of the SDGs.[2,4,6,12,14] [A: sentence deleted to reduce repetition with paragraph above.] For the first time, and through the

Key messages

- Health creates wealth, and health is a key contributor in achieving other Sustainable Development Goals; national and international programmes on sustainable development should address non-communicable diseases prevention and control
- Non-communicable diseases (NCDs) are neglected worldwide and expose people to health, social, and economic shocks; international and governmental programmes should protect the poor from NCDs and the worsening of their socioeconomic status
- Programmes related to universal health coverage need to address NCDs and should specifically target vulnerable populations, including middle-aged and elderly people, who are most at risk of NCDs
- Health inequalities due to NCDs within countries and between countries are increasing; international regulations and national jurisdictions should eliminate policies and practical barriers in the access to resources needed to implement universal health coverage and promote health equity

This is the second in a **Series** of five papers about economics and non-communicable diseases.

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Figures 4 and 5 cited before Figure 2?

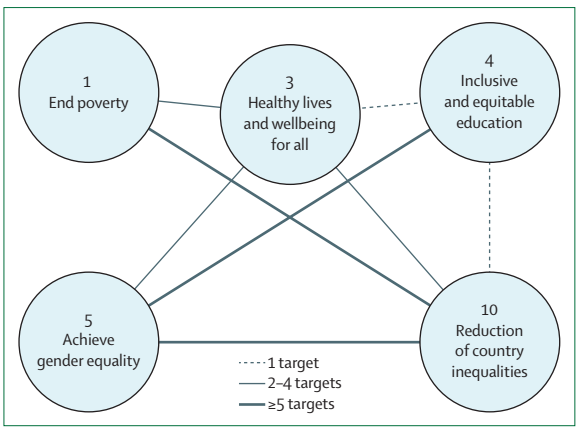

Figure 1: **Targets network of the five Sustainable Development Goals related to health equalities**
Adapted from LeBlanc (2015) by permission of XX.[4] **[A: We suggest that you use the original figure, but colour it so as to highlight the relationships between the targets/SDGs and health, greying out anything that's not one of the 78 targets. You will also need to seek permission from UN DESA to reproduce and modify the figure.]**

Panel 1: Qualitative evidence on socioeconomic status and non-communicable diseases

A limited number of studies report qualitative findings and focus on cancer or diabetes and complications. Chronic diseases in general are the focus of one study.

A study from Kenya[36] used focus group discussions and in-depth interviews to examine how acute events and chronic conditions would have financial consequences, and financial catastrophic expenditure after illness was measured. The investigators concluded that chronic diseases are a greater financial burden on the poor (as measured by expenditure per household) than acute care. As a result, many poor people forgo treatment.

In a Sri Lankan study,[37] care-seeking was investigated in patients with diabetes from households at different income levels, using in-depth interviews. The investigators found that the related direct and indirect costs are a high economic burden for households, especially in rural areas. Households in this study also reported not being able to pay for disease treatment while diabetes-related complications increased.

In a Chinese study[38] about coping with childhood cancer, most families reported paying for all treatment costs out of pocket, whereas a few families had financial difficulties as a result. Similarly, in a study[39] involving palliative care from India, families stated that not only patients were obliged to give up work as a result of illness, but the caregivers also had to change work habits. Respondents stated that illness had forced them to sell assets, and children were obliged to miss school.

Investigators from Pakistan[40] explored the situation of families with a cancer diagnosis in the setting of needing to negotiate therapeutic options. Wealth was found to be an important determinant of choosing therapeutic options, with wealthier people going to allopathic doctors, and poor people accessing traditional medicine. Families struggled to pay costs and became impoverished.

formulation of the SDGs and the 78 cross-sector targets (figure 1), the UN has explicitly recognised the broad socioeconomic determinants of health and wellbeing[9,15,16] and the strong interdependencies between socioeconomic development and health.[10,13,15–17] Reduction of health inequalities improves socioeconomic outcomes for households, whereas reduction of socioeconomic inequalities enhances health at the population and household level.[4,6,9,12,13,16]

Non-communicable diseases (NCDs) contribute to more than two-thirds of deaths worldwide. Four-fifths of NCDs occur in low-income and middle-income countries (LMICs), and a third of deaths from NCDs affect people younger than 60 years.[18–21] As the share of premature death and disability caused by NCDs is increasing, the potential to exacerbate global health inequities is also augmenting.[18,20] The observed inequalities in health status, access to care and medicines, and in health financing reflect the accumulation of unequal lifetime exposures as well as unequal access and quality of health systems between populations. This situation exists for antenatal care and across the life span, to increased **[A: "and increases"?]** health risks associated with socioeconomic status and reduced access to timely public health measures, individual prevention, and health-care services.[22,23] Access and coverage to prevention and treatment programmes to control NCDs have become essential in the attainment of universal health **[A: OK?]** coverage and, as such, are fundamental to implementation of the SDGs.[13,24–27] Here we examine the interaction between health and wellbeing and the SDGs. We position health as a primary driver among the SDGs and identify the four SDGs on poverty reduction, equitable education, gender equality, and reduction of inequalities within and between countries as key in the attainment of health and wellbeing for all **[A: we have removed the citation to figure 1 from here because it is unnecessary.]**.

The relationship between socioeconomic status and ill health

Low-income groups living in high-income countries are much more likely to have a higher chronic disease burden than higher income groups **[A: in those same countries?]**.[17,23,28–30] Little systematic evidence exists to support this relationship in low-income and middle-income countries (LMICs). Obesity is becoming increasingly common in LMICs and is affecting women and the poor in particular.[17,31–33] Wagstaff[17] describes how people living in poverty are restricted in their ability to practise healthy behaviours that promote health and how they are predisposed to chronic diseases and late (and hence more advanced) diagnosis. The reverse pathway is also plausible, as chronic illnesses might lead to poverty because of direct and indirect expenditures and loss of productivity.[13,27] Levesque and colleagues[34] showed that the poor commonly do not have the ability to pay for the treatment of NCDs. Events related to chronic diseases might cause impoverishment through wage loss, missed schooling, or through catastrophic expenditures in relation to chronic illness.[17,32,34] Prolonged treatment and continuous use of health services often involve costly diagnostic procedures and treatment. During the economically productive years, continued

disability and repeated acute illness related to chronic disease might hamper household productivity, especially in the absence of social safety nets. These mechanisms complete a vicious cycle of unhealthy behaviours and exposures in the low-income groups that increase the risk of NCDs and other diseases and, in turn, lead to more poverty, increasing disparities, and illness.[17,24]

By contrast with the abundance of evidence from high-income countries, studies on the association between socioeconomic status and NCDs in LMICs are relatively scarce. In this Series paper, we examine the relationships between socioeconomic inequalities and NCDs in LMICs and their evolution over time. We describe the scientific literature about the relationships between socioeconomic status and NCDs, summarise the characteristics of these relationships over time, and present the strengths of the evidence. We identify the documented linkages between the SDGs (figure 1) and contribute to the international and national development agenda to build broad health services and a public health agenda that promote health in the context of poverty, gender, education, inequalities, and wellbeing.[4,21]

Socioeconomic status and NCDs: the scientific evidence

We focus on the scientific studies with strong study designs that produce the best available evidence on the temporal, probable, causal relationship between socioeconomic status and NCDs. This relationship is impossible to study in studies with weak designs, such as cross-sectional surveys. The quality of the studies identified in this Series paper varies and makes a quality assessment necessary. We used the system of quality assessment developed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) working group because it distinguishes clearly between quality of the evidence and the strength of the conclusions and recommendations.[35] The GRADE system has been widely used and accepted by a representative group of methodology developers.[35] It also gives explicit, comprehensive criteria for downgrading or upgrading quality of evidence relative to other studies. This interpretation process leads to a classification of strong and weak conclusions to present to a wider audience such as policy makers and the general public. The identified qualitative studies are limited [A: in number? Or in scope?], and findings are reported in relation to cancer and diabetes with complications and chronic conditions (panel 1). The quantitative information on the correlation between socioeconomic status and NCDs is diffuse, changes over time, and provides heterogeneous results from weak, cross-sectional studies, whereas the high-grade evidence (by GRADE criteria; appendix) consistently shows a positive relationship [A: we have removed call-outs to figures 4 and 5 here because figures 2 and 3 must be cited first. Let me know if the order of the figures is wrong]. There is a large diversity between study variables and definitions used (appendix), which makes a formal meta-analysis impossible [A: we have removed the call-out to table 2 here because contents are described in better detail below].

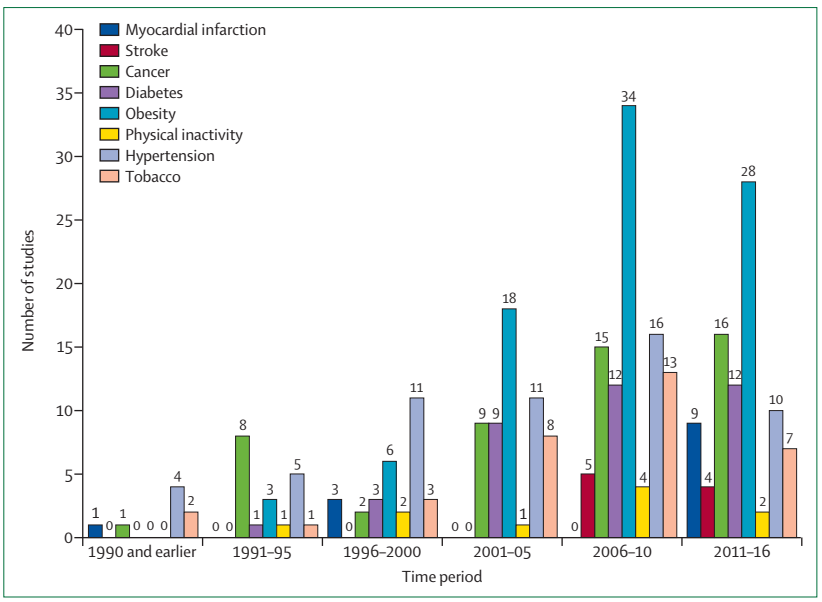

Figure 2: **Distribution of studies on poverty and non-communicable diseases or risk factors studied over time**

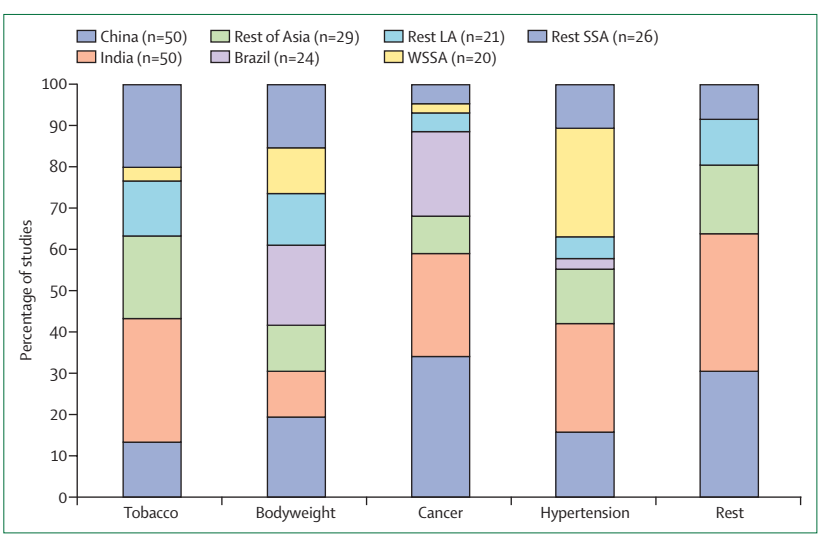

Figure 3: **Regional distribution of studies with four [A: should this say "five"?] most reported conditions [A: what do Rest, Rest LA, Rest SSA, and WSSA stand for?]**

11 studies, published between 2000 and 2015 [A: please provide exact dates of the search], focus on the chronic disease to poverty pathway [A: please list the publication details of these 11 studies so we can add them to your reference list. Also, since the Series will be published in 2018, have any relevant studies been published since 2015? If so, please include.].[27] One of these studies was part of a larger cohort study[41] and produced an

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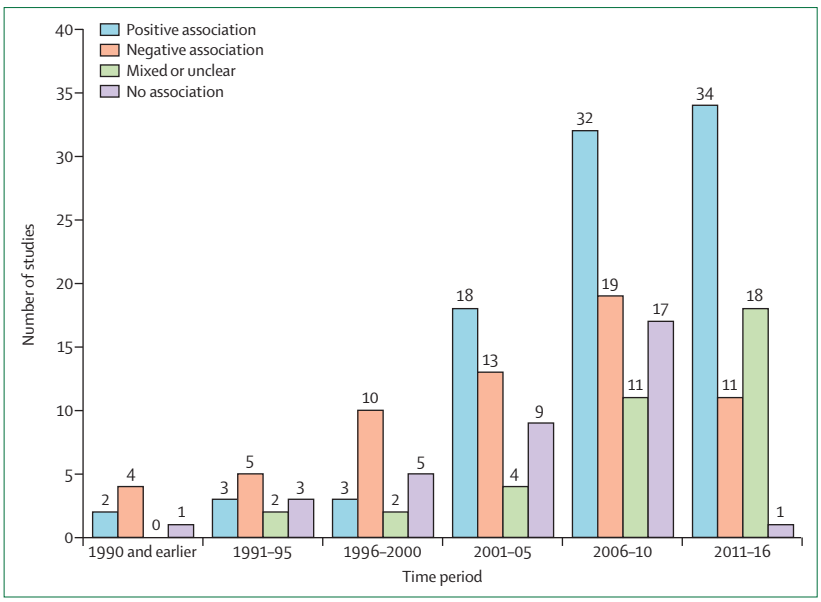

Figure 4: **Distribution of quantitative studies by type of association between non-communicable diseases and risk factors and poverty, over time** [A: Is this title OK?]

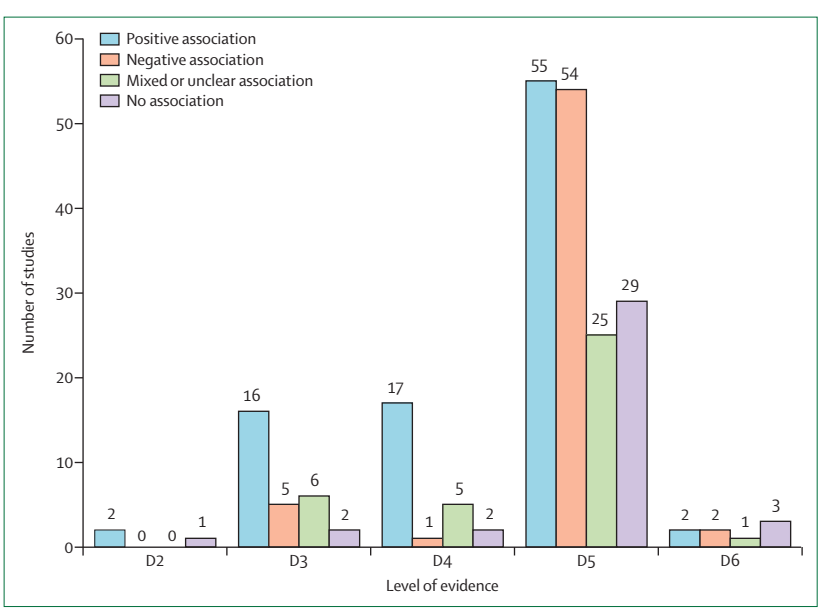

Figure 5: **Distribution of quantitative studies by reported direction of association between chronic diseases and risk factors with poverty, by strength of evidence**

Evidence grading criteria and evidence rating scales are available in the appendix. D1=randomised controlled trials. D2=non-randomised controlled trials. D3=uncontrolled interventions, before–after trials, and time-series studies. D4=case-control studies and cross-sectional studies with two groups or more. D5=cross-sectional studies. D6=descriptive studies.

intermediate level of evidence (D3 level; uncontrolled before-after or time series studies), whereas the other studies were based on weaker cross-sectional designs (seven D5-level studies [A: please provide the references to these seven studies please]) or are purely descriptive (two D6-level studies [A: please provide the references to these two studies please]).

[A: please ensure that publication details for the papers discussed in this section (ie, not the 231 papers) are included in your reference list. Please indicate the papers you would like to cite (and where), and I will update the reference list.] The largest body of evidence suggests an effect of poverty on chronic disease occurrence (including risk exposures, occurrence of clinical diseases, and complications of disease) based on cross-sectional designs. 160 (69%) of 231 studies can be classified as producing weak-level evidence. Three studies, involving a nested case-control study,[3] [A: is this the correct reference?] produce high-level (D2) evidence, 28 studies produce similar high-level evidence (D3; uncontrolled before-after, case-cohort studies, or times series study), and 26 studies produced evidence of slightly lower quality (D4; case-control studies). The remaining six studies produced D6 level of evidence. Findings from the D2-level study[3] showed mixed or unclear association between poverty and chronic disease, whereas 15 of the 23 D3-level studies (uncontrolled studies) showed a positive association, and 17 of the 32 D4-level studies showed a positive association. Studies with D5-level evidence showed a mix of associations (a positive association in 55 of 161 studies). We classified studies as mixed or unclear when they showed associations in different directions between different strata (eg, men and women) or among different measures of poverty (eg, education and wealth).

Epidemiology of socioeconomic status and chronic conditions

We identified a substantial body of evidence in 231 articles (; figure 3; figure 4; figure 5; appendix). About half of the studies were from Asia (50 studies in India and 50 studies in China), and a substantial number of reports were from Brazil (figure 3). An increasing trend in publications by calendar year (appendix) was accompanied by a a steep increase and a more systematic use of poverty measures from 2005 to 2015 [A: please update to include studies from 2016 and 2017], as summarised in panel 2. The quantitative information on the association between poverty and disease is rather diffuse, has changed over time, and is characterised by a variable quality by standard evidence criteria (figure 4; figure 5; appendix).[56,57] A formal meta-analysis is impossible because variables and definitions are considerably heterogeneous.[35] The distribution of studies by condition over time is shown in figure 2, and the differences in distribution of studies by region and condition are shown in figure 3. Many diverse studies on cancer and hypertension have been done in Asia, whereas very few [A: correct? Or have none been done?] have been done in Latin America. The number of studies on diabetes and obesity has increased in the past decade [A: Could you specify whether this was worldwide or from specific parts of the world? Can you also be specific

about years (eg, since 2005)? Again, this needs to be updated to include the past 2 years.].

Identified dimensions of socioeconomic status

Wealth indicators, including household and individual income, asset-based measures, and consumption measures, and educational attainment were the most frequently measured dimensions of poverty, used in more than half of the published reports (panel 2). Household income, usually adjusted for household size, has often been assessed through proxy measures such as self-reporting on household assets or expenditures. Education can be measured and analysed by the number of years of schooling and the presence or absence of professional, college, or technical education. Other common dimensions of socioeconomic status were occupation and place of residence. Occupation is usually classified on the basis of the necessary skills or the hierarchy in society. These two dimensions (wealth and education) are often used alone or in conjunction with wealth to calculate composite indices. Place of residence has been used as a proxy for socioeconomic status when differences exist, as in rural versus urban living or for people living in neighbourhoods with differing levels of socioeconomic development.

Composite measures have been used increasingly in the past 5 years. Measures that identify disadvantaged social groups, such as the Human Development Index (HDI)[42] and the Kuppuswamy's Socio-Economic Status Scale,[58] were seen mostly in studies after 2005. Ethnicity and social groups are other ways in which the poverty levels of the population have been measured. All studies reviewed assessed the dimensions of socioeconomic status through self-reporting.

The qualitative studies are summarised in panel 1. These studies covered a limited number of chronic conditions, yet provide rich descriptions of how families become indebted because of non-communicable disease or cope with it [A: with debt?]. The coping strategies included health-seeking behaviour and maintaining livelihoods despite NCDs.

Socioeconomic status and NCDs: strength of evidence

Our findings are predominantly based on quantitative estimates from 227 of 231 studies, one using both types of studies [A: please clarify. One study using both types of studies?], as summarised in panel 1. The quantitative studies were subjected to an adapted evidence-grading scheme[57] from the scientific literature.[56] Most of the evidence is on the pathway from socioeconomic status to NCDs, whereas 11 studies focus on the chronic disease to poverty pathway. Cross-sectional study designs are used in 164 (71%) of 231 studies. Many of the cross-sectional studies are population-based surveys using the WHO STEPS method.[59–62] Study designs have become more sophisticated with time: case-control studies, cohort studies, and time series make up 16% of the identified studies. Early quantitative studies show the mix [A: the mixed?] association between socioeconomic status and NCDs, by quality of evidence (figure 4; figure 5). The increasing trend in observations of a positive association between socioeconomic status and NCDs since 2000 is shown in figure 4. The early studies identifying a negative association were published before 2000, and the trend in reporting a negative association has decreased in the past decade, and the high-level evidence (most of which was produced in studies after 2000) shows a consistent positive relationship between socioeconomic status and NCDs (figure 4).

Population selection bias

The associations between poverty and chronic conditions depend on the sampling framework showing possible selection bias in the studies. A positive association was found between poverty and NCDs or their risk factors in 57 (36%) of the 157 studies [A: correct absolute number of studies?] that sampled data from a general population. Likewise, a positive association between poverty and NCDs or their risk factors was found in 19 (68%) of the 28 studies [A: correct absolute number of studies?] involving representative samples of health-service users (appendix).

***Panel 2*: Definitions of poverty status, chronic diseases, and association measures**

Measures of poverty

Education and income are the two most common dimensions of poverty. These poverty measures have all been self-reported, either at the individual or household level. Education is usually reported as number of school years completed or as the highest qualification attained. The local Human Development Index is reported in a study from Brazil,[42] and Abegunde and Stanciole[43] reported health-care expenditures, non-health-care expenditures, labour income, transfers income, and workdays lost by household members in Russia.

Measures of chronic disease

19 studies include cancer (all types) and stroke as diseases and include body-mass index (BMI) and hypertension as risk factors. Two studies do not state any specific disease but measure presence of disease[42] and mortality from disease.[44] Two studies on stroke report late outcomes after stroke (ie, disability after stroke, according to the modified Rankin Scale[45] and 3 year survival[46]). Cancer outcomes are mainly reported in terms of fatality.[47–50] Treatment outcomes are investigated in one study,[42] disease incidence in a second study,[51] and quality of life 1 year after surgery in a third study [A: reference?]. Clinical outcomes in all studies are based on in-service records. In the three studies on risk factors, BMI, and hypertension, the risk factors in their populations were measured directly.[52–54] The one study[43] on the chronic disease to poverty pathway relies on self-reports from people with a chronic condition.

Measures of the poverty–disease association

Odds ratios,[45,48] relative risk measures,[44,47,54,55] and hazard ratios[46] were the most common measures. In two cohort studies from Mumbai,[49,50] age-standardised relative survival (calculated as the ratio of the observed survival to expected survival in a group of people in the general population similar to the diseased group with similar age distribution) was used to indicate the excess risk of dying from the disease. For studies looking at risk factors, prevalence is the measure used as the outcome variable.[52,53] In the Brazilian study[42] on outcomes after leukaemia, investigators looked at a variety of measures, including complete remission rate, overall survival rate, and leukaemia-free survival rate.

	Study design	Exposure variable	Outcome variable	Association measure	Magnitude of association measure
Chen et al (2015)[63]	Cohort	Residence, socioeconomic deprivation, education, occupation, annual income	Mortality	Multivariate adjusted HR for elementary school versus higher education	HR 1·88 (95% CI 1·05–3·36)
Elwell-Sutton et al (2013)[64]	Cohort	Income, education, occupation	Hypertension, diabetes	Concentration Index; Healthy Inequity Index; multivariate analysis	Independent contribution of low-income status in Concentration Index and Healthy Inequity Index (SE at p<0·05 level)
Fagundes, Rocha et al (2006)[42]	Cohort	Direct measurement of HDI of place of living	Direct measurement of treatment outcomes from records, use of Hidac, complete remission rate, survival rate, leukaemia-free survival rate	Relative risk for HDI <0·660	Relative risk: use of Hidac 0·130 (p<0·01); complete remission rate 0·523; survival 1·472; leukaemia-free survival 3·659 (p<0·01)
Forde et al (2012)[65]	Matched control prospective cohort study	Education, household income	Obesity	OR for obesity in multivariate analysis	OR 1·27 (95% CI 1·03–1·57); p=0·03
Ginsburg et al (2013)[66]	Cohort	Residential mobility, maternal education, asset wealth index	Obesity	Socioeconomic status in multivariate analysis	Beta-coefficient 0.42 (SE 0·13) for women; not significant for men
Hou et al (2008)[53]	Cohort	Self-reported monthly household income and educational level based on years of school	Direct measurement of BMI and blood pressure; standardised prevalence for overweight and obesity	OR	OR (compared with low educated women): medium-educated women 0·64 (95% CI 0·52–0·79); highly educated women 0·50 (0·36–0·68)
Khan et al (2015)[41]	Dynamic cohort	Self-reported monthly household income and educational level based on years of school; asset score	Death from chronic disease, by verbal autopsy	OR and Concentration Index	OR [A: for lower-quintile income group?] compared to higher-quintile group: 1·26 (95% CI 0·92–1·69)
Li and Yu (2002)[47]	Cohort (case-cohort design)	Self-reported annual income	Death due to lung cancer	Rate ratio	Rate ratio compared to high average year income: middle-income 2·1 (95% CI 0·94–4·67); low-income 6·22 (1·87–20·7)
Liu and Zhu (2014)[67]	Case-control study; time series	Household income	Diabetes	Beta coefficient in multivariate analysis	Beta coefficient: 6·3% decrease in annual income for people with diabetes as compared with people who do not have diabetes
Liu et al (2007)[45]	Cohort	Self-reported educational levels from illiteracy through university	Self-reported post-stroke disability according to modified Rankin Scale	OR	OR for lower educational level 0·686 (95% CI 0·570–0·825)
Sauvaget et al (2008)[54]	Cohort	Self-reported educational level, occupation, and standard of living	Direct measurement of BMI	χ^2 for trend in multivariate adjusted relative risk for various BMI categories in low, middle, and high socioeconomic status	p value for trend: low socioeconomic status 0·008; middle socioeconomic status 0·0097; high socioeconomic status 0·1402
Xu et al (1996)[48]	Nested case control	Self-reported educational levels from illiteracy through university and income per person	Direct measurement of recorded death from cancer	OR	OR for income: <¥15 per person 1 (reference [A1]); ¥15–19·9 per person 1·2 (95% CI 0·8–1·8); ¥20–26·9 per person 1·6 (1·1–2·2); ¥27–39·9 per person 1·8 (1·2–2·6); >¥40 per person 1·7 (1·2–2·5); OR for education: no education 1 (reference [A1]); primary school 1·1 (0·8–1·6); junior middle school 1 (0·7–1·6); high school 0·8 (0·5–1·3); college 0·8 (0·5–1·5)
Yu et al (1993)[51]	Cohort	Self-reported educational level (highest level attended) and income (total income of household)	Record reviewof oesophageal cancer incidence	Age-adjusted and sex-adjusted relative risks	Relative risk: for any education 0·82 (95% CI 0·71–0·94); any income 1·05 (0·94–1·18)

(Table 1 continues on next page)

Strong evidence: clustering of socioeconomic status and NCDs

A temporal relationship between chronic disease and poverty can be investigated in studies with strong designs. Studies with strong designs in this Series paper include mainly cohort studies and one nested case-control study. Data from one of these studies[43] on the pathway from chronic disease to poverty shows a positive association in one study group, whereas of the other 19 studies examining the poverty to chronic disease pathway, a positive association was found in 15 studies, mixed or unclear associations were found in five studies (a positive association was found in one of these studies), and a negative association was found in one study [A: please provide the publication details so we can include it in your reference list] (table 1; table 2).

To accommodate the heterogeneity in study outcome measures and still arrive at a summary outcome, we used the excess risk ratio as a general, unadjusted, crude comparative measure as for the studies with strong

	Study design	Exposure variable	Outcome variable	Association measure	Magnitude of association measure
(Continued from previous page)					
Zhou et al (2006)[46]	Cohort	Self-reported taxable gross income per month, educational levels from illiteracy through university	Record review of death within 3 years of stroke	Age-adjusted and sex-adjusted adjusted HR	HR for education: illiteracy 0·96 (95% CI 0·46–2·00); primary school 1·25 (0·57–2·72); junior high school 0·77 (0·34–1·74); senior high school 1·05 (0·41–2·71); technical training 1·99 (0·71–5·61); university degree 1 (reference [A1]); HR for occupation: unemployed 6·27 (2·97–13·21); manual worker 5·23 (2·88–9·49); non-manual worker 1 (reference [A1]); HR for income: ¥0 5·37 (3·19–9·03); <¥1000 2·22 (1·36–3·63); ≥¥1000 1 (reference [A1])
Koch et al (2010)[44]	Cohort	Self-reported annual household income and educational levels from years of schooling	All-cause adult mortality, including those mortality from chronic diseases	Adjusted relative risk of death	Adjusted relative risk for education (p<0·01): elementary 1 (reference [A1]); high school 0·67 (0·53–0·85); college 0·30 (0·17–0·53); <¥4200 annual income 1(reference [A1]); ¥4200–6000 annual income 0·86 (0·69–1·06); ¥6000–10 000 annual income 1·11 (0·88–1·40); >¥10 000 annual income 1·05 (0·84–1·31)
Yang et al (2010)[68]	Cohort	Self-reported annual household income and educational levels from years of schooling	QOL scores 1 year after surgery	Beta coefficient from multiple regression analysis	3·135 increase in QOL score from low to high socioeconomic level (p<0·01)

HR=hazard ratio. HDI=Human Development Index. QOL=quality of life. BMI=body-mass index. OR=odds ratio. *Significant at p<0·05 [A: where is this symbol used?].[A1: correct?]

Table 1: **Characteristics of high-grade evidence follow-up studies on chronic disease and poverty**

evidence (table 2). We defined this ratio as the unadjusted ratio between the measure for chronic condition and the socioeconomic measure, calculated for the lowest and highest socioeconomic status category value, for any given health variable. The unadjusted crude excess risk ratios are shown by study sample size in table 2. Given the limitations of this approach, almost all studies show a positive relationship between poverty and chronic disease. In the study[54] with the largest sample size, the excess risk ratio between chronic disease mortality and body-mass index and mortality is relatively small but positive, whereas the study[46] with the largest excess risk ratio (between income and chronic disease survival) has a much smaller sample size. This indicates the presence of confounders in this type of analysis. A more formal meta-analysis is not possible because of the very different measures used, the lack of reported uncertainty ranges, and the variety in multiple confounders. It is striking that the excess risk ratios range from –0·17 for a weak association (but including other positive outcomes in the same study) to 0·97 (a strong positive association). Education measurements were included in 12 studies, and socioeconomic measures were included in 11 studies.

In summary, although this excess ratio for socioeconomic status is largely indicative, we found a consistent, positive relationship between socioeconomic status and NCDs that probably varies in order of magnitude because of different confounders in each of the individual studies.

Conclusions

In most studies with strong design, a positive relationship is found between socioeconomic status and chronic conditions in LMICs, which confirms that the epidemiology of poverty and NCDs in LMICs now converges with the abundance of study findings from high-income countries.[29,30,70,71]

In general, up to the year 2000 (but also in the following years), the scientific literature on LMICs provided mixed information and reflected changing country conditions worldwide. However, there is a general lack of robustness in the scientific literature because of weak and often inconclusive study findings that are limited by the cross-sectional nature of the evidence. Since 2000, study quality has been improving with an increasing number of longitudinal designs. Studies with a strong design include one nested case-control study and 16 cohort studies. Case-control studies are most feasible in resource-constrained settings, and obesity and hypertension seem to be the most obvious and feasible conditions to study because they are easy to measure.

With this first comprehensive review, we succeeded in identifying studies even without a primary objective related to socioeconomic status and NCDs. Some limitations exist because we excluded scientific literature that was not written in English. We did not expect the findings from those studies to influence our conclusions. We included many articles from national-level Indian journals that did not present high-level evidence on the relationship between poverty and chronic disease. We excluded articles in Portuguese, Russian, Polish, and Chinese.

Definitions of the terms related to socioeconomic status and disease conditions varied widely. Many poverty measures are relative concepts, changing over time, and could address household or individual characteristics. Only one study[52] addresses both community and individual levels [A: "addresses socioeconomic status and disease conditions at both the community and individual levels"?],

	Risk in poor groups	Risk in non-poor groups	Excess risk ratio*	Study sample size
Khan et al (2015)[41]$ [A1]	Incidence of death from chronic disease in the lower-quintile income group	Incidence of death from chronic disease in the higher-quintile income group	0·2231	>100 000
Sauvaget et al (2008)[54]	Incidence rate of death per person-years of follow-up in the low-socioeconomic status category	Incidence rate of death per person-years of follow-up in the high-socioeconomic status category	0·1858	75 868
Elwell-Sutton et al (2013)[64]	Probability of not getting hypertension treatment in lowest education group#[A2]	Probability of not getting hypertension treatment in highest education group	0·268	30 499
Yu et al (1993)[51]	Age-adjusted and sex-adjusted relative risk of oesophageal cancer incidence in category of no income	Age-adjusted and sex-adjusted relative risk of oesophageal cancer incidence in category of any education	0·18	12 693
Yu et al (1993)[14]	Age-adjusted and sex-adjusted relative risk of oesophageal cancer incidence in category of no education	Age-adjusted and sex-adjusted relative risk of oesophageal cancer incidence in category of any income	–0·05	12 693
Koch et al (2010)[44]	Adjusted relative risk of death for elementary education	Adjusted relative risk of death for college education	0·7	11 600
Koch et al (2010)[44]	Adjusted relative risk of death for annual household income <US$4200	Adjusted relative risk of death for annual household income >US$10 000	–0·05	11 600
Yeole et al (2000)[49]	Observed 5 year probability of death due to head and neck cancer in no education category	Observed 5 year probability of death due to head and neck cancer in education >12 years category	0·13199	6311
Chen et al (2015)[69]	Incidence of death after stroke in highest socioeconomic deprivation group	Incidence of death after stroke in lowest socioeconomic deprivation group	0·6048	2978
Hou et al (2008)[53]	Odds of being overweight or obese in low-educated women category	Odds of being overweight or obese in highly educated women category	0·57409	2924
Hou et al (2008)[53]	Odds of being overweight or obese in women with income <¥1000 category	Odds of being overweight or obese in woment with income >¥3000 category	0·3497	2924
Hou et al (2008)[53]	Odds of being overweight or obese in low-educated men category	Odds of being overweight or obese in highly educated men category	0·16925	2164
Hou et al (2008)[53]	Odds of being overweight or obese in men with income <¥1000 category	Odds of being overweight/obese in in men with income >¥3000 category	–0·1698	2164
Xu et al (1996)[48]	Odds of lung cancer incidence in income <¥15 per person category	Odds of lung cancer incidence in income >¥40 per person category	–0·0898	1862
Xu et al (1996)[48]	Odds of lung cancer incidence in no education category	Odds of lung cancer incidence in college education category	0·63598	1862
Xu et al (1996)[48]	Odds of stomach cancer incidence in no education category	Odds of stomach cancer incidence in college education category	0·83281	1862
Yeole et al (2001)[64]	Observed 5 year probability of death due to colorectal cancer for no education category	Observed 5 year probability of death due to colorectal cancer for >12 years education category	0·00765	1767
Forde et al (2012)[65]	Odds ratio intervention on BMI in group with primary education and lowest household income	Odds ratio intervention on BMI in group with secondary education and lowest household income	0·26829	1273
Zhou et al (2006)[46]	Odds of death after stroke in illiteracy category	Odds of death after stroke in university degree education category	0·91954	806
Zhou et al (2006)[46]	Odds of death after stroke in ¥0 income category	Odds of death after stroke in >¥1000 income category	0·97196	806
Liu et al (2007)[45]	Odds of poor outcome after stroke in illiteracy category	Odds of poor outcome after stroke in university education category	0·83889	434
Li and Yu (2002)[47]	Odds of death due to lung cancer in low average year income category	Odds of death due to lung cancer in high average year income category	0·82639	316
Fagundes et al (2006)[42]	Odds ratio for survival after leukaemia treatment in HDI <0·660 category	Odds ratio for survival after leukaemia treatment in HDI >0·660 category	0·32065	123

[A1: what does this $ symbol mean?] [A2: what does this # symbol mean?] BMI=body-mass index. HDI=Human Development Index. *Excess risk ratio=(risk in poor – risk in non-poor)/risk among poor. Values for the excess risk ratio range from –1 to 1, with –1 denoting all risk among the non-poor and 1 denoting all risk for poor (Abegunde and Stanciole [2008],[43] Yang et al [2010],[68] Chen and Meltzer [2008],[52] and Ginsburg et al [2013][66] are excluded because variables were continuous).

Table 2: **High-grade follow-up studies by health risk, poverty status, and excess risk ratio, ranked by sample size**

and no study addresses social or economic capital measures.

We also could not differentiate our findings by population strata (eg, gender or rural and urban differentials) that might modify the relationship between health conditions and socioeconomic status. Additional limitations are small sample sizes and the lack of addressing potential collinearity because of education, wealth, and occupation. Additionally, access to treatment was not assessed although this was an important factor. The excess risk ratios in table 2 do not consider heterogeneity. Excess risk computations as a crude, descriptive, associative measure of an existing relationship between socioeconomic status and NCDs was seen as

justifiable and consistent. Further explorations of this relationship should include characteristics of existing health systems to understand how health systems can affect disparities in NCDs.

Relevance

We presented systematically collected evidence on socioeconomic status in NCDs in LMICs to stimulate further efforts in setting international and national agendas. These joint agendas should contribute to changes in health and education programmes and research of social safety nets and pro-poor health-financing mechanisms.

The increase in number of studies coincided with the increase in available resources for development and increases in education levels in most countries, especially in India, China, and Brazil. Fast economic development and rapid urbanisation are occurring in Asia, South America, and, to a lesser extent, in Africa. China, India, and Brazil share this rapid epidemiological transition and the resulting double burden.[53,72,73] These countries might move further through a health transition, accompanied by greater urbanisation and lifestyle changes.[74] The poor, with shorter life expectancies and bearing the brunt of undernutrition, malnutrition, childhood **[A: childhood diseases?]**, and pregnancy-related conditions, are likely to be most affected by NCDs.

Our review of the peer-reviewed scientific literature has led to a better understanding of the negative effects of socioeconomic status on NCDs in LMICs. Known mechanisms and interventional programmes to interrupt the harmful effects **[A: of socioeconomic status?]** are within the domains of poverty alleviation, social security systems, general educational programme development, global public health, health financing, health education, and health promotion, but also within the domains of prevention activities in relation to physical activity, food quality and intake, and other life style factors **[A: edited for additional clarity – OK?]**. Investigators must differentiate between effects on people who are already poor or ill to better understand self-reinforcing effects. Broad intervention studies, including those involving social safety nets, health financing, specific health-systems innovations, and broad strategies to tackle NCDs, should better address their distributional effects in addition to overall average outcomes and effects on target populations. This identifies further evaluation research and strategies that contribute to more general and international health-development approaches and to a public health and health-services agenda that promotes health and wellbeing in the broader context of poverty reduction, equitable education, gender equality, and reduction of national and international inequalities.[21]

Towards comprehensive national SDG policies

The collective body of research from longitudinal studies in which investigators try to understand the link between socioeconomic status and NCDs in LMICs provides high-grade evidence in support of positive associations between low social and economic status and NCDs. Under **[A: "Within"?]** the SDGs,[21] to end poverty in LMICs through elimination of its causes, NCDs programmes should be included in the development agenda. International development efforts and national governments should mitigate social and health shocks to protect the poor from major events **[A: please consider being more specific with wording here. What sort of events?]**, worsening their already disadvantaged socioeconomic conditions and their susceptible health status. SDG programmes related to universal health coverage of NCDs should target susceptible populations, which include middle-aged and elderly people who are most at risk of NCDs. Further effort should be made toward capturing groups that are likely to be further disadvantaged, such as women and people living in rural areas. The inequalities in access to health resources need to be addressed through international regulations and through regulations within national jurisdictions and health systems. These should eliminate the legal and practical barriers in the implementation of universal health coverage of NCDs in all countries. The sustained reduction of inequalities in poverty, education, gender, and health, both in and between countries, will promote worldwide equality in health and wellbeing and further enhance both socioeconomic and human development.

Contributors

LWN wrote the first and the final versions of the Series paper, supervised the paper, did the article selection and data extraction, and guided and supervised the overall completion process of the paper. DHP had the original idea of the study, wrote the study proposal, and contributed to the writing of the Series paper. TK contributed to the design of the Series paper and participated in the updates of the paper. DM, JA, AJM, SA, and JK did the article review and contributed to the writing of the Series paper in all its stages. AJ contributed to the design of the Series paper, assessed the extraction results focusing on methods and analytics, and contributed to the paper in all its stages.

Declaration of interests

We declare no competing interests.

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