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Socioeconomic inequalities in physical and cognitive functioning: cross-sectional evidence from 37 cohorts across 28 countries in the ATHLOS project

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ABSTRACT

Background Physical and cognitive functioning in older age follows a socioeconomic gradient but it is unclear whether the strength of the association differs between populations. Using harmonised data from an international collaboration of cohort studies, we assessed socioeconomic inequalities in physical and cognitive functioning and explored if the extent of inequalities varied across countries based on their economic strength or wealth distribution.

Methods Harmonised data from 37 population-based cohorts in 28 countries were used, with an overall sample size of 126 765. Socioeconomic position of participants was indicated by education and household income. Physical functioning was assessed by self-reported mobility and activities of daily living; and cognitive functioning by memory and verbal fluency tests. Relative (RII) and slope (SII) index of inequality were calculated in each cohort, and their association with the source country's Gross Domestic Product (GDP) and Gini-index was assessed with correlation and cross-level interaction in multilevel models.

Results RII and SII values indicated consistently higher risk of low physical and cognitive functioning in participants with lower education or income across cohorts. Regarding RII, there were weak but statistically significant correlations and interactions with GDP and Gini-index, suggesting larger inequalities in countries with lower Gini-index and higher GDP. For SII, no such correlations were observed.

Conclusion This study confirms that socioeconomic inequalities in physical and cognitive functioning exist across different social contexts but the magnitude of these inequalities varies. Relative inequalities appear to be larger in higher-income countries but it remains to be seen whether such observation can be replicated.

BACKGROUND

Maintaining physical and cognitive functioning are important components of healthy ageing.[1] Most people experience a gradual decline in these functions as they get older, and as populations age, the growing prevalence of individuals living with severe limitations in their cognition or physical abilities has become a major public health concern globally.[2] It is estimated that more than 45% of those above the age of 60 years have moderate or severe disability worldwide, and this figure is even higher in low-income countries.[3]

Previous research suggests that ageing-related limitations in physical and cognitive functioning are strongly associated with socioeconomic characteristics of individuals.[4–6] People with higher education attainment, better jobs or higher income tend to have better physical or cognitive function compared with those in the lower levels of the socioeconomic spectrum. In addition to such cross-sectional associations, there is also some longitudinal evidence indicates that the speed of functional decline during ageing is faster in people with lower socioeconomic position (SEP).[7 8]

Despite the relatively extensive research in this topic, there are still important gaps in the evidence. Although the inverse relationship between SEP and cognitive/physical functioning has been observed in both high and low-income/middle-income countries, it is unknown whether the strength of the association and the extent of socioeconomic inequalities in these functional abilities are consistent across countries with different level of economic development or wealth distribution. This question may have important policy implications. If it is shown that economic advantage can lead to smaller disparities in ageing-related health outcomes within the population, such evidence would support investment in the general economic growth and efforts to distribute the financial resources more evenly.

The harmonised dataset created by the Ageing Trajectories of Health: Longitudinal Opportunities and Synergies (ATHLOS) consortium consists of data from diverse countries all over the world, ranging from low and middle to high income, and covering a wide spectrum on the income inequality scale.[9] Such data are well suited to examine the above question and potentially provide guidance on policies aiming to address social inequalities in healthy ageing.

The main aim of this analysis was to assess the relationship between socioeconomic indicators and low physical and cognitive functioning in different countries and cohorts included in the ATHLOS project, and to explore if the extent of these inequalities varied across countries with different economic strength or wealth distribution.

METHODS

Study sample

As part of the ATHLOS project, data from 17 population-based longitudinal studies were harmonised into one dataset. Detailed information on the project and the data harmonisation procedures are described elsewhere.[9]

The current analysis included the following nine studies, some of which with cohorts in multiple countries: the 10/66 Dementia Research Group Population-Based Cohort Study[10]; the Collaborative Research on Ageing in Europe[11]; the Study on Nutrition and Cardiovascular Risk in Spain (ENRICA) study of nutrition and cardiovascular risk in Spain[12]; English Longitudinal Study of Ageing (ELSA)[13 14]; the Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)[15]; the Longitudinal Ageing Study in India (LASI)[16]; the Mexican Health and Ageing Study (MHAS)[17]; the WHO Study on Global Ageing and Adult Health[18]; and the Survey of Health, Ageing and Retirement in Europe (SHARE).[19] These studies were chosen because data on specific indicators of both physical and cognitive functioning were available. Baseline (first wave) data were used in most included studies as this provided the largest sample size. In ENRICA, HAPIEE and MHAS studies, physical and cognitive functioning of participants was assessed in the second or third waves, therefore data from these subsequent waves were used. Regarding LASI, only pilot data were available. The nine studies altogether included subjects from 37 cohorts in 28 countries.

Participants with missing data on the outcome variables (cognitive or physical functioning) were excluded in all studies (n=9588), and those with missing education (n=13 805) or income (n=2289) were excluded from the analysis when educational or income inequalities were assessed, respectively. Data on income were not available in the HAPIEE and ENRICA studies, therefore these studies were included only in the analysis on education. The overall sample size for the analyses with the two socioeconomic indicators (education and income) were 126 765 and 114 228, respectively. The analytical sample size for individual cohorts ranged from 965 to 10 971.

Outcome assessment

Physical functioning of study participants was assessed by five activities of daily living and mobility (walking, using the toilet, bathing or showering, eating and getting dressed). Individuals who reported any difficulties in any of the five activities were considered as having low physical functioning. These items include fundamental activities necessary to manage basic everyday physiological needs, therefore, difficulties in any of them indicate moderate to severe limitations in physical functioning.[20] Similar to other variables in the harmonised ATHLOS dataset, original data on these items went through extensive harmonisation procedure that, in most cases, converted multicategorical to binary variables.[9]

Cognitive functioning was measured using the following three objective tests in all participating studies: immediate word recall, delayed word recall and verbal fluency. As the first two indicate verbal memory and learning, and verbal fluency measures language and executive function, these tests provide information on at least two key domains of a person's cognitive abilities.[21] Individuals whose cognitive test score was in the lowest 25% within their specific cohort for any of the three tests were considered as having low cognitive functioning.

The internal consistency of the above described composite measures of physical and cognitive functioning is shown in online supplemental table S1. Cronbach's alpha for physical and cognitive functioning was 74% and 59%, respectively. Although this suggests less than ideal consistency for cognitive functioning, as the value is dependent on the number of items included in the score, it is not unexpected with only three components.[22] Additionally, these three items have been used to assess limitations in cognitive functioning in several previous studies.[23] The predictive validity of both scores was assessed in relation to grip strength, mortality and a more comprehensive list of questions on physical functioning and cognitive tests in the ELSA study. The results indicated acceptable validity (online supplemental table S2).

Measures of socioeconomic inequalities

Educational attainment and household income were used as indicators of participant's SEP. Participants in each study were categorised into three groups based on the level of their highest education (primary or less, secondary, tertiary) and into quintiles according to their income.

In order to estimate the relative and absolute differences in physical and cognitive functioning between individuals with low and high education or income we calculated the relative index of inequality (RII) and slope index of inequality (SII). These indices take into account the proportion of people in the different categories of education and income, and they show the relative (RII) and absolute (SII) risk of low functioning in the lowest vs the highest categories, irrespectively of the number of categories or their distribution across the sample.[24 25] RII and SII were calculated in each cohort separately and their values were adjusted for age and sex.

Assessment of differences in magnitude of inequalities among countries

As indicators of the specific countries' economic strength and wealth distribution, we used World Bank data on their GDP (Purchasing Power Parity; PPP) and Gini index, respectively.[26 27] For each country, those values were used which corresponded to the specific year (or the closest year with available data) when the data collection of the study carried out in that particular country took place. As Gini-index in Cuba and Puerto Rico were not available from the World Bank, this information on these countries was retrieved from other sources (online supplemental table S3).

To estimate whether RII and SII varies by countries with different GDP or Gini-index, we calculated Spearman's correlation coefficients and cross-level interaction coefficients with multilevel logistic regression models. The ecological correlation was assessed between the RII/SII values and GDP/Gini-index of the respective countries across the 37 cohorts. The second step used multilevel models to examine whether the associations between education or income and low physical or cognitive functioning were significantly modified by GDP or Gini-index; the interaction terms and their significance level were estimated in both random intercept and random slope models.

All statistical analyses were carried out using STATA V.15 statistical software (StataCorp).

RESULTS

Age and sex distribution of individuals and the proportion of participants with low physical and cognitive functioning in the included cohorts are shown in table 1. The mean age ranged from 47.2 to 76.3 years, and all cohorts included both males and females. The age-standardised and sex-standardised prevalence of reported difficulties in physical functioning ranged between 7.8% and 79.1%, and the proportion of people identified as having relatively low cognitive functioning ranged from 33.7% to 56.5% across cohorts.

Figures 1 and 2 show the RII (95% CI) regarding low cognitive and physical functioning by education and income across the 37 cohorts. In all figures the cohorts were ranked by the country

Table 1 Key characteristics of the cohorts included in the analysis

Study	Wave	Country	n	Age		Sex	Prevalence of low physical functioning*		Prevalence of low cognitive functioning†	
				Mean	SD	% female	%	95% CI	%	95% CI
1066	First	Cuba	2771	75.2	7.0	65.2	17.1	16.3 to 17.9	37.4	35.6 to 39.2
		Dominican Rep.	1985	75.2	7.5	65.8	19.1	18.2 to 20.1	36.5	34.4 to 38.7
		India	1977	71.9	5.9	56.0	32.5	31.6 to 33.4	53.7	50.5 to 54.9
		Puerto Rico	1991	76.3	7.3	67.3	18.9	17.8 to 19.9	37.1	35.0 to 39.3
		China	2160	73.2	6.1	56.3	8.1	7.4 to 8.8	37.8	35.8 to 39.9
		Mexico	1995	74.3	6.6	63.2	13.7	12.8 to 14.6	40.3	38.1 to 42.4
		Peru	1909	74.8	7.3	61.5	12.9	12.0 to 13.8	33.7	31.6 to 35.9
		Venezuela	1885	72.3	6.7	63.5	16.6	15.6 to 17.6	42.7	40.5 to 45.0
COURAGE	First	Finland	1774	58.6	15.8	56.9	27.2	25.0 to 29.3	38.3	36.1 to 40.6
		Poland	3940	57.0	17.9	60.2	55.4	53.8 to 57.1	40.1	38.6 to 41.7
		Spain	4555	59.7	15.9	54.6	32.9	31.6 to 34.3	41.1	39.7 to 42.6
ELSA	First	UK	10 720	63.9	10.9	54.5	31.5	30.7 to 32.4	43.7	42.8 to 44.6
ENRICA‡	Second	Spain	2051	71.8	6.3	52.2	18.0	16.3 to 19.7	41.1	38.9 to 43.2
HAPIEE‡	Second	Czech Republic	4191	58.3	7.2	54.0	14.4	13.2 to 15.6	53.5	52.0 to 55.0
		Russia	5369	58.0	6.9	57.9	27.6	25.8 to 29.4	50.9	49.5 to 52.2
		Poland	5588	57.7	6.9	51.9	16.4	15.5 to 17.4	48.7	47.4 to 50.0
		Lithuania	6854	60.9	7.5	54.7	28.0	27.2 to 28.8	56.5	55.4 to 57.7
LASI	Pilot	India	1603	55.0	11.9	56.1	15.3	13.0 to 17.6	41.5	39.2 to 44.0
MHAS	Third	Mexico	5350	68.5	9.6	65.1	48.2	46.1 to 50.2	43.2	41.9 to 44.6
SAGE	First	China	10 971	58.3	11.5	47.7	31.0	30.0 to 32.0	38.8	37.9 to 39.8
		Ghana	2487	55.2	12.8	37.6	67.0	65.1 to 68.9	34.2	32.4 to 36.1
		India	6014	47.2	16.9	49.8	79.1	77.8 to 80.3	35.5	34.3 to 36.7
		Mexico	2048	61.8	14.2	60.9	58.5	56.2 to 60.8	51.1	48.9 to 53.2
		Russia	4079	62.4	13.0	64.3	65.6	64.3 to 67.0	47.2	45.6 to 48.8
		South Africa	2584	59.2	12.0	59.4	55.4	53.5 to 57.4	40.1	38.2 to 42.0
SHARE	First	Israel	2522	63.2	9.9	56.3	15.6	14.2 to 16.9	37.8	36.0 to 39.7
		Austria	1572	64.6	9.9	58.6	10.6	9.1 to 12.0	44.0	41.6 to 46.5
		Belgium	3769	63.7	10.6	54.5	15.0	13.7 to 16.2	38.0	36.4 to 39.5
		Denmark	1675	63.2	11.1	55.2	12.3	10.8 to 13.8	40.5	38.1 to 42.9
		France	3009	63.8	11.2	57.1	14.8	13.6 to 16.0	37.5	35.7 to 39.2
		Germany	2929	63.5	9.7	54.1	12.3	11.1 to 13.4	46.0	44.2 to 47.8
		Greece	2808	62.4	11.1	56.8	12.4	11.3 to 13.6	39.6	37.8 to 41.1
		Italy	2539	64.0	9.4	55.8	14.8	13.5 to 16.1	48.7	46.8 to 50.7
		The Netherlands	2842	62.7	10.1	54.3	12.5	10.8 to 14.2	40.8	39.0 to 42.6
		Spain	2330	65.8	10.8	58.5	17.2	15.8 to 18.6	45.2	43.2 to 47.2
		Sweden	2954	64.3	10.3	53.8	9.7	8.7 to 10.7	35.3	33.6 to 37.1
		Switzerland	965	63.8	11.2	54.1	7.8	6.2 to 9.5	43.0	39.9 to 46.2

*Reported difficulties in any of the following functions: walking, using the toilet, bathing or showering, eating and getting dressed (age and sex standardised values).
†Test results were in the lowest 25% within the cohort for any of the following tests: immediate word recall, delayed word recall, verbal fluency.
‡HAPIEE and ENRICA studies were included in the analysis for educational inequalities but not for income inequalities.
COURAGE, Collaborative Research on Ageing in Europe; ELSA, English Longitudinal Study of Ageing; HAPIEE, Health, Alcohol and Psychosocial factors in Eastern Europe; LASI, Longitudinal Ageing Study in India; MHAS, Mexican Health and Ageing Study; SAGE, Study on Global Ageing and Adult Health; SHARE, Survey of Health, Ageing and Retirement in Europe.

specific GDP in the year of the data collection. RII was found to be higher than one in nearly all cohorts for both cognitive and physical functioning, for both education and income. These results suggest that individuals with lower levels of education or lower income are more likely to experience low cognitive and physical functioning compared with those with higher SEP. Although the direction of the observed socioeconomic inequalities in these functional abilities were consistent across countries with different economic strength or wealth distribution, there was a large heterogeneity in RII between cohorts, which suggests that the magnitude of social inequalities differ internationally. In fact, the heterogeneity in RII seems to follow, to some extent, a pattern, with larger inequalities seen in countries with higher GDP. However, the uncertainty around the point estimates, particularly for physical functioning, was also larger in many of the wealthier countries.

In addition to the visual inspection of the figures, the positive trends between RII and GDP, as well as the inverse trends

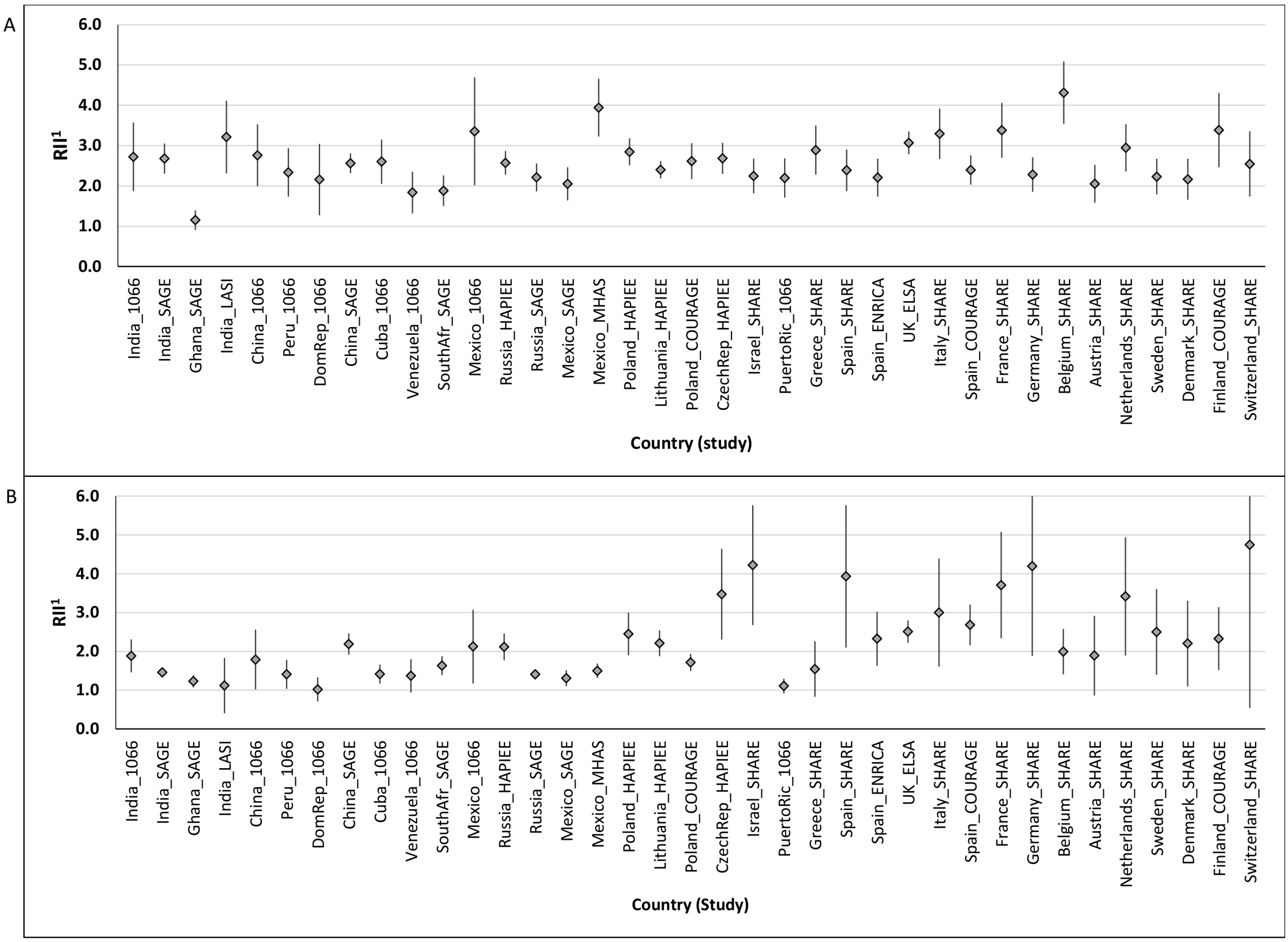

Figure 1 Relative index of educational inequalities (RII) (95% CI) in (A) cognitive and (B) physical functioning across the 37 cohorts (cohorts are ranked according to their source country's GDP). [1]RII adjusted for age and sex.

between RII and Gini-index, were also confirmed by Spearman's correlation coefficients and by testing for cross-level interaction in multilevel models (table 2). Although the correlations were weaker for cognitive functioning, their direction was the same for both outcomes. Multilevel models with random slope indicated that the strength of the association between education and both physical and cognitive functioning significantly differed between cohorts based on their respective country's Gini-index, while the effect modification by GDP reached statistical significance only for educational inequalities in physical functioning. Regarding income inequalities, the interaction with GDP was statistically significant for physical functioning, and non-significant trends were observed for the other tests.

When we restricted the analytical sample to people aged above 60 the overall trends remained similar to the main analysis but the correlations became somewhat weaker and most examined interactions did not reach statistical significance in the random slope models (online supplemental table S4).

Results remained similar when data from SHARE, the study which provided the majority of data for high-income countries, was excluded, and also when education and income were mutually adjusted for each other (online supplemental tables S5 and S6).

In terms of SII, which indicates absolute inequalities, the results showed generally higher risk of low physical and cognitive functioning in individuals with lower education or income (online supplemental figures S1–S4). However, despite the relatively large heterogeneity across cohorts, we found no consistent pattern of correlation between SII and GDP or Gini-index (online supplemental table S7).

DISCUSSION

Main findings

In this study, we assessed educational and income inequalities in physical and cognitive functioning in 37 cohorts, harmonised by the ATHLOS project. The results showed that the relative and absolute risk of low functional abilities was higher in individuals with lower education or income compared with those at the higher end of the socioeconomic scale. Although the direction of the association was mostly consistent across countries with varying economic strength and wealth distribution, the magnitude showed considerable differences. Regarding relative inequalities, we found a trend suggesting that countries with higher GDP or lower Gini-index may have steeper socioeconomic gradient in both physical and cognitive functioning. This trend was particularly apparent when socioeconomic inequalities were assessed by education. As opposed to relative inequalities, we found no consistent correlations between inequalities on the absolute scale and either GDP or Gini-index.

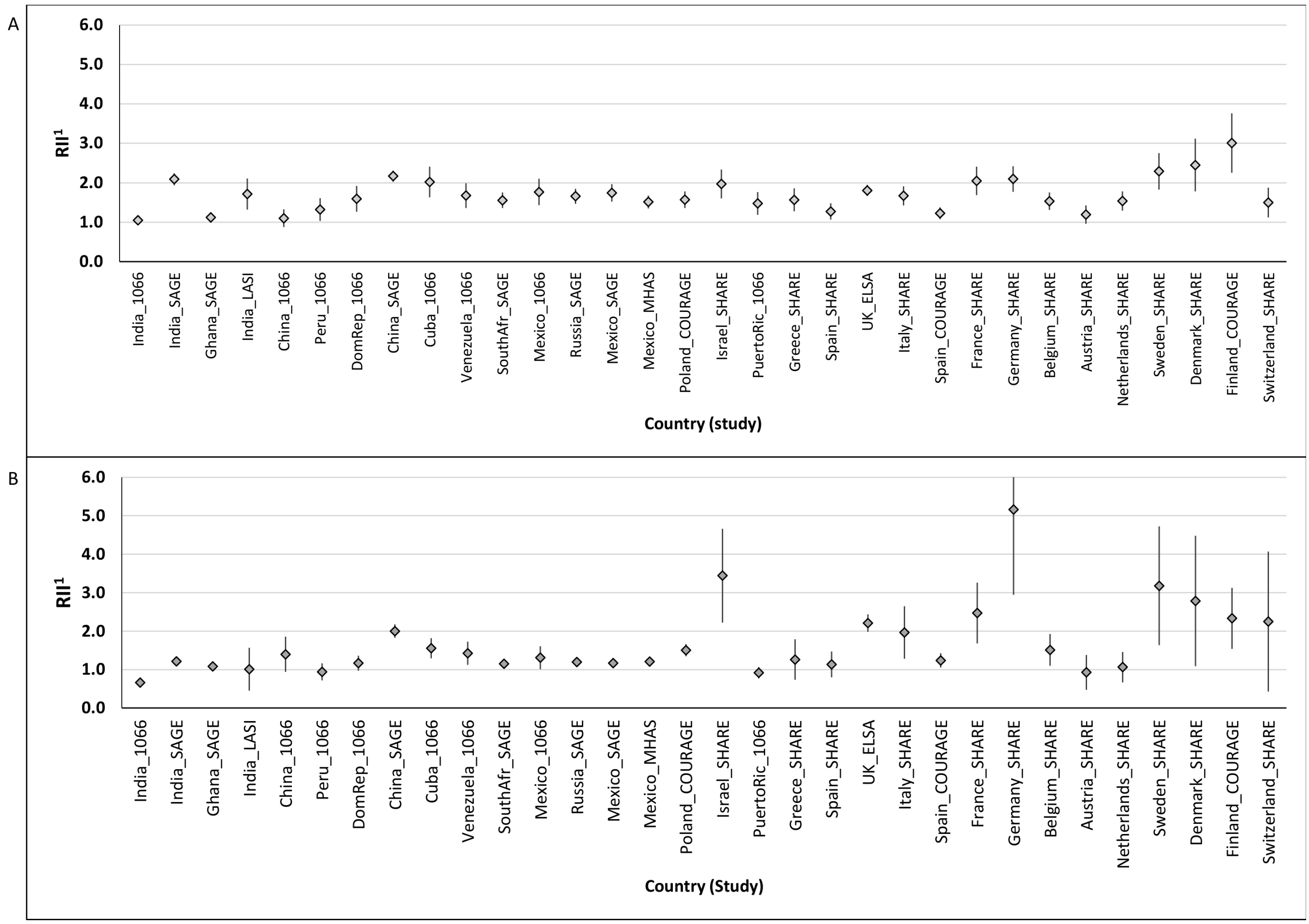

Figure 2 Relative index of income inequalities (RII) (95% CI) in (A) cognitive and (B) physical functioning across the 37 cohorts (cohorts are ranked according to their source country's GDP). [1]RII adjusted for age and sex.

Interpretation of results

Our result regarding the inverse link between socioeconomic indicators of education/income and low cognitive and physical functioning is consistent with previous evidence.[4–8] It confirms that the direction of the association is the same in most populations worldwide, irrespectively of the country or region where people live.

To our knowledge, this is the first study that explored the differences in the magnitude of these inequalities across countries with different macroeconomic context, and the suggestion of a trend of larger relative inequalities with increasing GDP and declining Gini-index has not been reported before. There are a number of potential explanations as to why socioeconomic inequalities in physical and cognitive functioning, on a relative scale, might be more pronounced in economically more developed countries and in those with more equal wealth distribution.

First, this observation may be due to a numerical artefact. It has been shown that both absolute and relative inequality measures have mathematical ceilings and the magnitude of inequality correlates with the overall level (prevalence) of the

Table 2 Correlation of the relative index of inequality (RII) with GDP and Gini-index, and results of cross-level interaction analysis in multilevel models

	RII		Spearman's correlation		Cross-level interaction			
					Random intercept model		Random slope model	
Country-level indicator	Socioeconomic indicator	Functional outcome	Coeff.	P value	Coeff.	P value	Coeff.	Pvalue
Gini-index	Education	Cognitive function	−0.31	0.065	−0.92	<0.001	−0.98	0.006
		Physical function	−0.62	<0.001	−0.87	<0.001	−0.95	0.004
	Income	Cognitive function	−0.23	0.202	−0.27	<0.001	−0.31	0.057
		Physical function	−0.41	0.020	−0.40	<0.001	−0.38	0.097
GDP	Education	Cognitive function	0.12	0.463	2.9×10^{-6}	<0.001	2.9×10^{-6}	0.158
		Physical function	0.67	<0.001	3.3×10^{-6}	<0.001	4.3×10^{-6}	0.031
	Income	Cognitive function	0.23	0.210	2.2×10^{-7}	0.463	1.5×10^{-6}	0.100
		Physical function	0.49	0.005	1.7×10^{-6}	<0.001	2.5×10^{-6}	0.044

outcome.[28] As relative inequalities tend to be larger in populations with lower rates of outcomes, this may to some extent explain the pattern observed in our data. In fact, when we recalculated partial correlations between RII and Gini-index and GDP after adjusting for the prevalence of low physical and cognitive functioning in each cohort, we found that the correlations were weaker compared with our main results (online supplemental table S8). However, the direction of the findings remained the same and some of the coefficients remained statistically significant. These results suggest that although this mathematical artefact has a role in the observed trends, it may not provide the full explanation for the pattern.

Second, it is possible that in countries such as Ghana, India, Peru, as well as other countries of Africa, Asia and Latin America, education and income are less important determinants of functional abilities than in the economically stronger and more stable European states. For example, comorbidity of communicable and non-communicable diseases might explain more of the variation in both physical and cognitive functions in countries where such diseases are more common or the adequate treatment is less accessible.[29] Considering the strong associations of chronic diseases with physical and cognitive functioning, including chronic conditions as covariates in future analyses would be important. This approach would be particularly important for the older age groups where the prevalence of chronic diseases, such as CVD, cancer or diabetes is higher. Unfortunately, relevant data were not available in the ATHLOS dataset.

Finally, country-specific estimates of GDP or Gini coefficient may not be representative for the specific cohorts included in these analyses. One would expect, however, that this would introduce random misclassification which would lead to underestimation of the association between inequality indices and macroeconomic indicators.

Although we observed somewhat weaker correlation between RII and GDP and Gini-index when the sample was restricted to participants above the age of 60 years, this is consistent with previous evidence that suggests that socioeconomic gradients in health are less steep in older age groups, possibly in part due to survival bias.[30]

In contrast to relative inequalities, no association of GDP or Gini coefficient was observed for absolute inequalities. As absolute inequalities may be more important for public health policy than relative inequality, the ubiquity of the social gradient emphasises the importance of individual social factors as a crucial determinant of health.

Overall, however, our results do not support the view that general economic prosperity would be linked with smaller social inequalities in ageing-related functional abilities, although it is likely to affect the overall prevalence of ageing outcomes. Nonetheless, investing in economic growth and policies that aim to distribute wealth more equally remain key elements of the recommendations to improve population health in any country.

Limitations and strengths

A number of limitations need to be taken into account when interpreting our results. First of all, although all cohorts included in the analysis are recruited their participants from general older populations, they are not necessarily nationally representative samples. Most studies restricted their sample to a specific age range, and, for example, in the HAPIEE study, participants were included only from urban areas. The response rates also varied widely (from 53% to 96%).[9] Differences in sampling frames might also explain the variation in the prevalence and social gradient of impaired functioning (estimated by RII and SII) between cohorts, even within one country (ie, Mexico, China, India).

In order to include as many cohorts as possible in the analysis, we used only a limited range of self-reported questions and cognitive tests to assess the physical and cognitive functioning of participants. Although these measurements were not ideal, their internal consistency and predictive validity was adequate to justify their suitability for the study of social gradients in ageing outcomes across populations. Nevertheless, differences in reliability and validity of these instruments between cohorts may also contribute to the observed variation of RII and SII values within one country.

Finally, we cannot entirely exclude the possibility that differences in data quality and cultural factors affecting the data collection procedures might also contribute to the observed correlations between RII and GDP and Gini index.[31] For example, it is possible that in wealthier countries participants may provide more accurate information on their income, and in some cultures people might be more willing to admit their functional limitations than in others. The consequent lower level of misclassification can potentially lead to higher risk estimates and higher RII values. Nonetheless, the fact that the results remained largely the same after excluding participants from the SHARE study provides some evidence against this explanation.

Our study also has important strengths. This is the first time when socioeconomic inequalities in physical and cognitive functioning were explored in a global scale, using data from 28 different countries, including low, middle and high-income states. The extensive and systematic harmonisation of the primary data made it possible to obtain truly comparable estimates for the examined socioeconomic inequalities, and therefore, we were able to assess their association with country-level economic indicators.

What is already known on this subject

The available evidence suggests that physical and cognitive functioning are associated with socioeconomic characteristics of individuals in a way that people with higher education attainment, better jobs or higher income tend to have better physical or cognitive function compared with those in the lower levels of the socioeconomic spectrum. However, most previous studies examined only one or few cohorts at a time, and cross-country comparisons in this research are scarce. In particular, the question whether the strengths of the association between socioeconomic position and physical or cognitive functioning differs among low, middle and high-income countries has not been explored to date.

What this study adds

Using harmonised data from 37 cohorts in 28 countries, this study confirmed that the inverse link between SEP and low physical and cognitive functioning is universal across geographical settings. Additionally, the analysis also suggested that the extent of relative (but not absolute) socioeconomic inequalities are greater in countries with higher GDP and lower income inequalities, compared with economically weaker states with more unequal wealth distribution.

CONCLUSION

In conclusion, despite the large variation in social conditions of participating cohorts, we found a virtually universal pattern whereby lower socioeconomic status was associated with increased levels of impaired cognitive and physical functions. Some of the relative inequalities appeared larger in cohorts from higher-income countries but the interpretation of this international pattern is not clear.

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Contributors DS, MM and MB developed the original idea and designed the analytical approach. AMP, Y-TW and WL made substantial contributions to the analytical design and the interpretation of results. AS-N organised the data harmonisation procedures, and JMH was responsible for the management of the ATHLOS project. All authors contributed to the writing of the manuscript and approved the final version of the text.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All included studies were carried out in line with principles embodied in the Declaration of Helsinki and have been approved by the relevant local research ethics committees.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available on reasonable request. Documentation and metadata of the ATHLOS harmonisation process can be accessed at: https://github.com/athlosproject/athlos-project.github.io; https://athlos.pssjd.org. The original cohort data are publicly available or can be accessed via contacting the study management teams on reasonable request.

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