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The wealth of nations and the dissemination of cardiovascular research☆☆

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ABSTRACT

Background: This study aimed at understanding whether investigators from less wealthy countries were at a disadvantage in disseminating their research, after accounting for potential differences in research quality and infrastructure.

Methods and Results: In this bibliometric analysis a representative random selection of 10% ($n = 1002$ studies) of all abstracts submitted to the European Society of Cardiology (ESC) congress 2006 was followed for publication and citation from September 2006 to December 2011. The main variable of interest was the per-capita gross domestic product (GDP) of the country of the principal investigator. Using multivariable models that adjusted for socioeconomic indicators and previously identified markers of research quality, we examined the relationship between per-capita GDP and three study endpoints: Acceptance at the ESC congress, full-text publication, and number of two-year citations. Among 1002 abstracts from 63 countries, per-capita GDP was positively correlated with all three study endpoints. After adjusting for markers of research quality and infrastructure, per-capita GDP remained a strong predictor for acceptance at the ESC congress (adjusted OR for every 10,000 USD increase in per-capita GDP, 1.44; 95% CI, 1.15 to 1.80), full-text publication within 5 years (adjusted OR, 1.49; 95% CI, 1.17 to 1.90), and high citation frequency (adjusted OR, 2.30; 95% CI, 1.31 to 4.04). These findings were largely consistent in a subgroup of abstracts of high-quality, prospective clinical trials.

Conclusion: Investigators in less wealthy countries face challenges to disseminate their research, even after accounting for potential differences in the quality of their work and research infrastructure.

1. Introduction

Economic indicators have been correlated with scientific productivity with a gap between poor and wealthy nations [1–3]. Although the mechanism for this observation remains unknown, it has been postulated that much of this gap may be a result of less research infrastructure, education, and training to perform high-quality work in poor nations [1,4]. A potential bias in the dissemination of research from investigators in poor nations also has been suggested, but there is little empirical evidence to support it [4–7].

Our objective was to better understand if and how the dissemination of research may be influenced by the wealth of the country in which it

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was produced. Thus, we studied the abstracts submitted to the European Society of Cardiology (ESC) congress in 2006, and followed the fate of a randomly selected sample of 1002 studies over five years. A distinct advantage of this approach over earlier studies [3,16,17] was the opportunity to dissect differences in study design and other putative markers of research quality and infrastructure, thereby isolating the effect of wealth on the dissemination of research. It also allowed us to evaluate the process of research dissemination along a continuum from acceptance at a major scientific meeting to subsequent publication to citations following full-text publication. Finally, this approach leveraged a unique aspect of the ESC congress by allowing us to examine the impact of national wealth across a broad range of countries that included both developing and developed countries.

We anticipate that our findings will increase the awareness and may improve the understanding of potential challenges faced by investigators from less wealthy nations in the dissemination of their research, and may help to determine potential solutions to address these concerns.

2. Methods

2.1. Study design

All abstracts submitted to the ESC congress 2006 (n = 10,020) were retrieved and a representative random sample of 10% (n = 1002, margin of error 0.01) [8] was analyzed according to pre-specified variables including known predictors of scientific impact [9]. A five-year bibliometric follow-up for full-text publication in peer-reviewed journals and the number of two-year citations, together with acceptance at congress-level, served as parameters for the successful dissemination of research [10,11]. Multivariable logistic regression analyses were performed to quantify the predictive value of economic indicators on successful dissemination of research after adjusting for putative markers of research infrastructure, quality or impact.

2.2. Data collection

The reliability of the computer-assisted representative random selection was assessed and confirmed through comparisons of the distribution of the variables common to both the original sample of all 10,020 abstracts and the randomly selected sample of 1002 abstracts. As described, no differences in the distribution of common variables were observed [9].

All abstracts within the representative subsample (n = 1002) were assessed by one out of four independent reviewers (SW, DAR, JHW, MH) according to a set of pre-specified variables including markers of scientific impact as detailed in the web extra material. In an initial pilot study a random sample of 3% of the study sample (n = 30) was assessed independently by each of the four reviewers to address inter-observer variances. Fleiss' kappa values were 0.853 or above (categorical variables) and intra-class correlation coefficients (metric variables) were 0.996 or higher [9].

Socioeconomic indicators including the per-capita gross domestic product (GDP, in current U.S. dollars) of the country of the last author (considered the respective principal investigator), national expenditures on education, research and development, as well as the number of researchers per country were retrieved from the World Bank Data Catalogue (World Development Indicators) [12]. All indicators refer to the year 2006 to appraise the economic conditions under which the research submitted to the ESC congress 2006 was performed. We chose per-capita GDP for the following reason: Referring to the market value of goods and services produced within a country in a given period of time the GDP allocates production based on physical location as opposed to national ownership. Therefore, it serves better to appraise the physically existing wealth of a country in comparison to the gross national product (GNP), which allocates production based on ownership of national accounts.

2.3. Bibliometric follow-up

We followed the cohort of abstracts for five years for full-text publication in peer-reviewed journals and the number of subsequent two-year citations, beginning at the time of publication. Acceptance at congress level, publication – in conjunction with the impact factor of the journal of publication – and the number of two-year citations served as parameters for successful research dissemination [10,11,13]. Identification of published articles was achieved using a step-wise search algorithm as described [9]. Briefly, the full or simplified abstract title, in conjunction with the names of first and last author, or the last author alone, were used as search terms in PubMed®, Google Scholar or Google in this order. Thus, articles published in journals not indexed in PubMed® were also retrieved. All full-text publications identified were published in peer-reviewed journals indexed in PubMed® (Table S2). Validation of identified articles was accomplished through the comparison of the respective endpoints, the number and size of study groups, and the conclusion as described in the web extra material. The number of two-year citations was determined using the citation indexing and search service of the ISI Web of Science (Thomson Reuters).

2.4. Statistical analyses

Uni- and multivariable binary logistic regression analyses were performed for the dependent variables "acceptance at congress level", "full-text publication", "publication in scientific journals with an impact factor above the 75th percentile of journals where these works were submitted (i.e., >5.36)", and a "two-year citation rate above the 75th percentile of this study cohort (i.e., >6 citations)". The following variables were entered into the final model: Type of research (basic vs. clinical), study design of clinical research (randomized controlled trials vs. prospective non-randomized data collections vs. retrospective studies vs. systematic reviews vs. meta-analyses vs. other), number of enrolled patients (≥100 vs. <100), topic of research (rhythmology vs. heart failure vs. coronary artery disease vs. interventional cardiology vs. prevention and epidemiology vs. hypertension, peripheral artery diseases and cardiovascular surgery vs. other), continent of origin of the last author, genders of first and last authors, national expenditures on research and development, on education, number of researchers per million inhabitants, and per-capita GDP. To determine the goodness of fit of the final model, c-statistics were calculated. Collinearity between related explanatory variables (such as the national expenses on research and development and the per-capita GDP) were assessed using progressively segregated groups of variables in four regression analyses for each endpoint (Table S5). In a sensitivity analysis, countries of the lowest per-capita GDP group (<10,000 USD) were excluded to assure that findings were not driven disproportionately by these nations (Table S3). A second sensitivity analysis was conducted to ascertain that the use of first as opposed to last author origin of randomized controlled trials did not significantly impact on the results (Table S4). p values were two-sided and considered statistically significant for $p < 0.05$. Statistical analyses were performed using IBM SPSS Statistics 20.

3. Results

3.1. Geographic distributions of wealth and research dissemination are similar

10,020 abstracts were submitted to the ESC congress 2006 from 63 different countries. National per-capita gross domestic products (GDP) of the submitting countries ranged from less than 1000 USD (e.g., India) to over 70,000 USD (e.g., Norway) (Fig. 1, Table S1). For nations with a medium to high scientific activity (abstract submission rates above one per million inhabitants) markers of successful research dissemination (i.e. abstract acceptance at the ESC congress, subsequent publication in peer-reviewed journals, and later citation) followed a similar distribution compared with economic indicators (i.e. the per-capita GDP and expenditures on Research and Development) (Fig. 1).

3.2. GDP-based stratification of submitting nations associates wealth with research dissemination

When stratifying submitted studies to four per-capita GDP groups (<10,000 USD [*low*], 10,000–20,000 USD [*medium*], >20,000–30,000 USD [*high*], >30,000 [*very high*]) the following observations were made: Most abstracts originated from very wealthy or very poor countries, only few from those in between. Acceptance rates at the ESC congress, publication rates, and subsequent two-year citation rates rose in parallel with per-capita GDP. The highest proportion of published studies in the top 25% journals (according to their impact factor) was reached by studies submitted from countries with the highest per-capita GDP and vice versa (Fig. 2).

3.3. Per-capita GDP is an independent predictor of successful research dissemination in cardiology

Using univariate logistic regression analyses, per-capita GDP was found to predict scientific success at all three levels of the process or research dissemination (Table 1). After adjusting for putative markers of research quality and infrastructure, including type of research (clinical vs. basic), study design, number of enrolled patients, study field, institutional affiliation, number of researchers per million inhabitants, and national expenditures on education, as well as on research and development, per-capita GDP remained a strong predictor of research dissemination: for every 10,000 USD increase in per-capita GDP there was a 44% increased chance for acceptance at the ESC congress (OR = 1.44, 95%

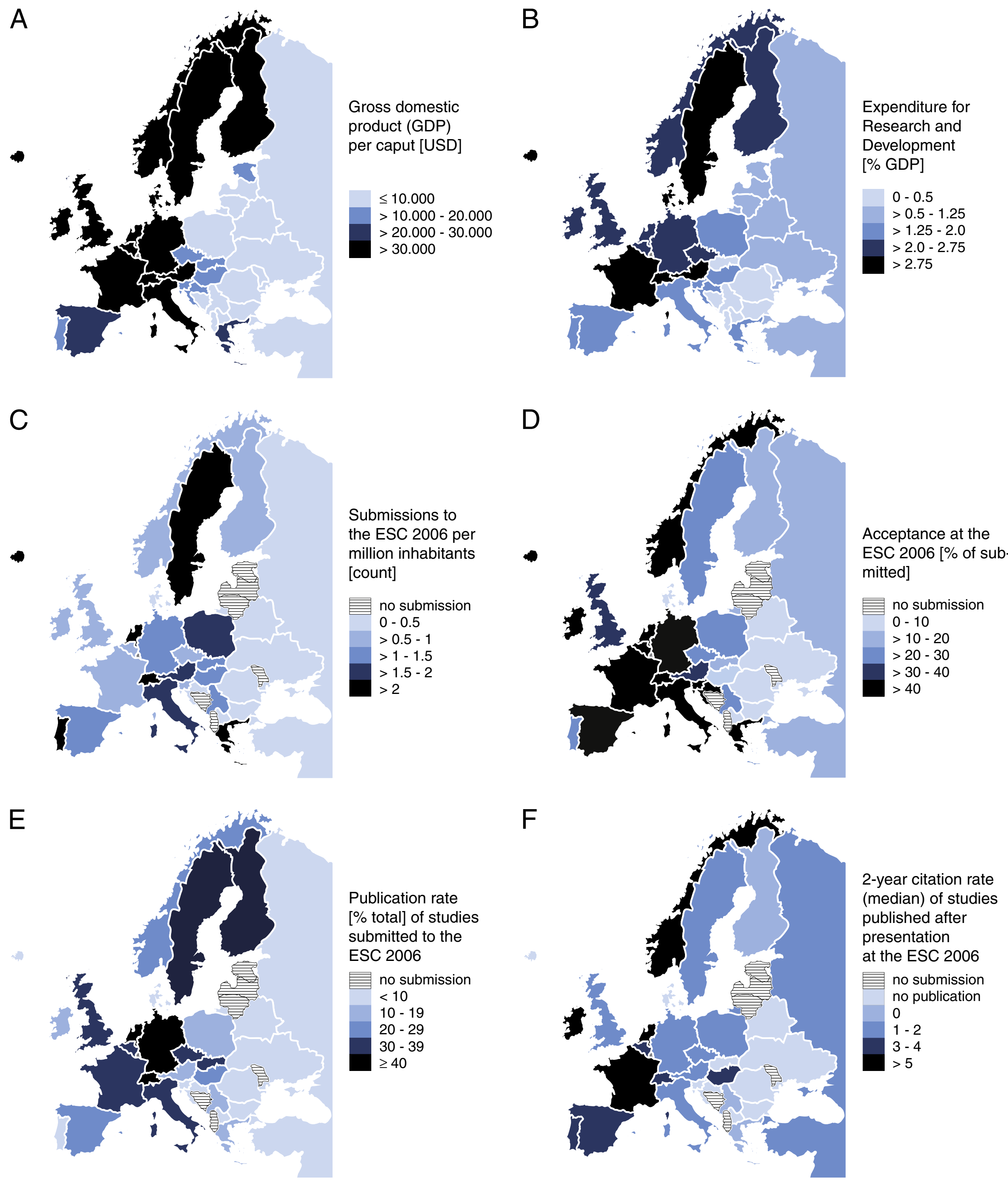

Fig. 1. Qualitative assessment of economic prosperity and scientific performance in Europe. (A) Per-capita gross domestic products 2006. (B) Expenditures on research and development 2006. (C) Number of abstracts submitted to the ESC congress 2006. (D–F) Acceptance, subsequent full-text publication and 2-year citation rates.

CI = 1.150–1.802), a 49% increased chance for publishing in a peer-reviewed journal (OR = 1.49, 95% CI = 1.171–1.903), a 269% increased chance for publishing in one of the top 25% of journals per impact factor (OR = 3.69, 95% CI = 1.660–8.239), and a 130% increased chance to reach the top 25% two-year citation rate (OR = 2.30, 95% CI = 1.312–4.037) (Table 1).

To assess the association between national wealth and research dissemination specifically in high-quality clinical research, a subgroup analysis was performed involving only prospective clinical trials (n = 357, Table 2). In this subgroup, per-capita GDP was an even stronger predictor for research dissemination at the levels of full-text publication in a peer-reviewed journal, and publication in one of the top 25% journals according to their impact factor. Due to the low number of published studies that reached the top 25% two-year citation rates (n = 69) significance was not reached at the citation level, though results trended in the same direction. When adjusting for markers of study quality including known predictors of scientific impact in cardiovascular research, for every 10,000 USD increase in the per-capita GDP there was a 64% increased chance for publishing in a peer-reviewed journal (OR = 1.64, 95% CI = 1.101–2.445), and a 351% increased chance for publishing in a journal among the top 25% (OR = 4.51, 95% CI = 1.168–17.417) (Table 2C). These findings suggest an even stronger independent correlation of the per-capita GDP with research dissemination in the subgroup of prospective clinical trials.

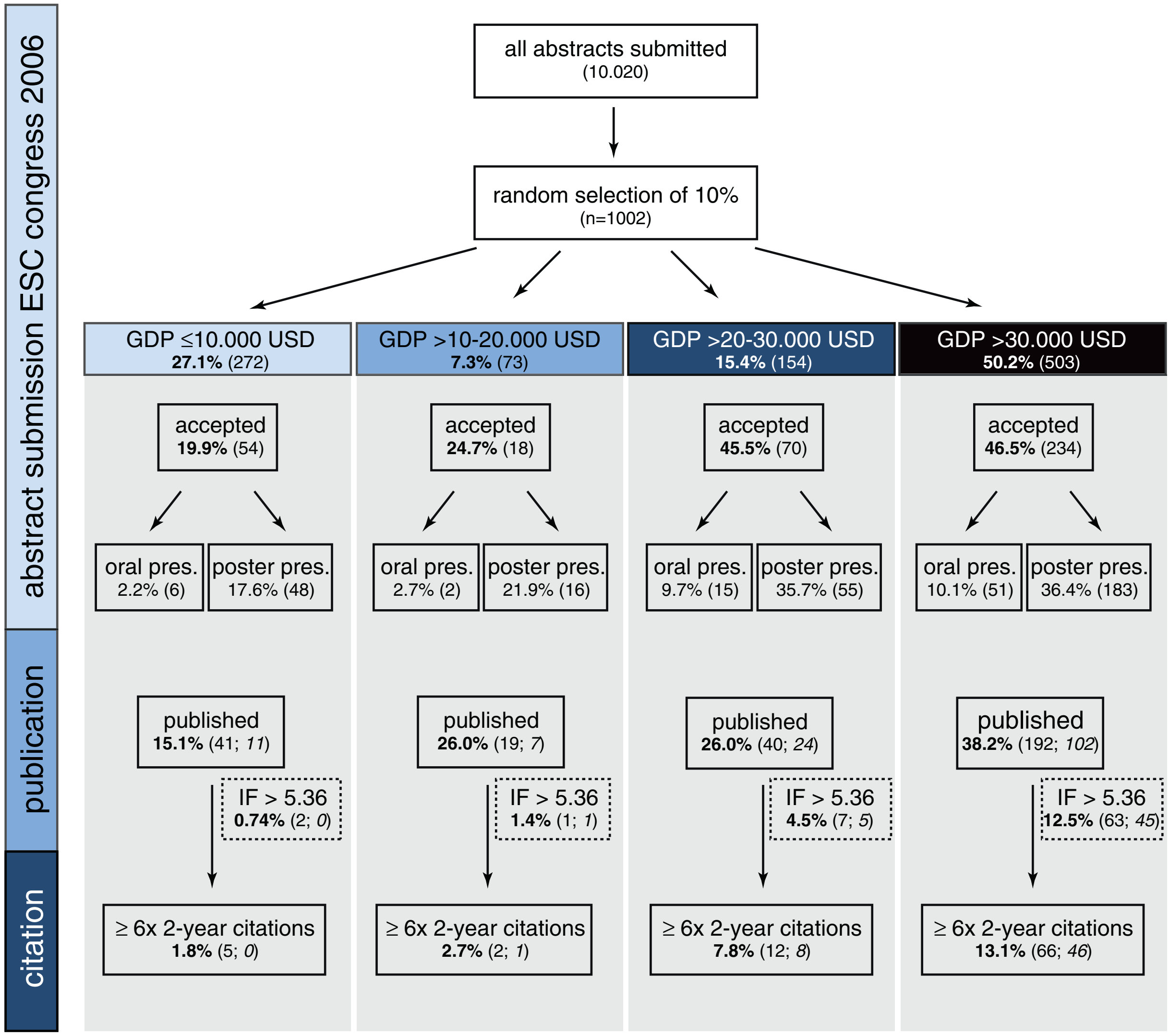

Fig. 2. Stratifying research dissemination according to national wealth within the ESC congress 2006. Submission, acceptance, full-text publication, and 2-year citation rates were stratified into four groups based on per-capita gross domestic products (GDP). Percentages (gray) refer to the respective GDP category, (n) to the number of abstracts, italic numbers represent those studies initially accepted at the ESC congress.

4. Discussion

4.1. Principal findings

Our study reveals that economic strength predicts scientific performance on all key steps of the generation and dissemination of scientific knowledge, independent of known predictors of scientific impact or research infrastructure [9]. After adjusting for origin and type of research, study design, number of enrolled patients, study field, institutional affiliation, author gender, and markers of research infrastructure, per-capita GDP remained a strong predictor for research dissemination from abstract acceptance to full-text publication, and subsequent citation. An increase of the per-capita GDP in 10,000 USD increased overall chances for publication in one of the top 25% peer-reviewed journals by 269%.

As a concrete example of what these latter findings indicate, an RCT lead by a principle investigator in The Netherlands was over 350% more likely to be published in one of the top 25% journals compared with an RCT including the same number of patients, in the same research field, by an investigator at a similar institution, located in Spain; chances rose to over 700% when compared with an RCT lead by an investigator e.g. in the Czech Republic or Portugal.

4.2. Strengths of this study and important differences to previous studies

To our knowledge this is the first study in which associations between economic indicators and scientific performance have been adjusted for widely accepted markers of research quality, such as study design or the number of enrolled patients in clinical trials [14,15]. The conception that the interdependence of economic strength and scientific performance may be due alone to the fact that large trials with an elaborate and costly design cannot be performed in economically less powerful countries is challenged. Our results are based on a five-year bibliometric follow-up of a cohort of cardiovascular studies representative for over 10,000 abstracts from 63 different countries.

Most previous studies are based on only one level of research dissemination such as the number of published documents and/or the impact factor of the journals in which the research was published [2,3,16,17]. In this study, three different levels of dissemination of scientific knowledge, i.e. acceptance at the ESC congress 2006, publication in peer-reviewed journals (including the respective impact factor), and the subsequent study-specific citation rates have been assessed separately. Therefore, our results are based on a more detailed assessment of scientific performance.

Table 1
The gross domestic product (GDP) as predictor of scientific performance in cardiovascular science.

	p value	OR (95% CI)	c-stat
A. Acceptance at congress-level			
Crude	<0.001	1.386 (1.263–1.520)	0.515
Adjusted	0.001	1.440 (1.150–1.802)	0.598
B. Publication in a peer-reviewed journal			
Crude	<0.001	1.387 (1.256–1.532)	0.498
Adjusted	0.001	1.493 (1.171–1.903)	0.541
C. Impact factor ≥5.36			
Crude	<0.001	1.707 (1.319–2.210)	0.507
Adjusted	0.001	3.689 (1.660–8.239)	0.623
D. Two-year citations ≥6			
Crude	0.001	1.473 (1.177–1.844)	0.506
Adjusted	0.004	2.301 (1.312–4.037)	0.655

Binary logistic regression analyses; accepted and rejected studies were followed for five years for publication and two-year citation rates. The per-capita gross domestic product (GDP) of each of the 63 submitting countries at the time of abstract submission (2006) served as surrogate for economic strength. Analyses were adjusted for the following parameters: the type of research (clinical vs. basic), the number of enrolled patients (≤100 or more), the study design, the study field, the continent of origin, academic affiliation of the originating institution, first and last author gender, national expenditures on education, on research and development, and the number of researchers per million inhabitants. Dependent variables were (A) acceptance at the ESC congress 2006, (B) full-text publication in a peer-reviewed journal, (C) publication in one of the top 25% journals according to impact factor (i.e. >5.36), and (D) reaching the top 25% two-year citation frequency (i.e. >6 two-year citations). All analyses are based on a representative 10% selection (n = 1002) of all abstracts submitted to the ESC congress 2006. OR = odds ratio, CI = confidence interval, and c-stat = c-statistic.

Notably, our analyses include the level of abstract submission to a scientific congress, i.e. a level before full-text publication. Considering that 55% of biomedical research abstracts submitted to a scientific meeting remain unpublished after six years [18,19] (in case of the ESC congress 2006 71% remained unpublished after five years) [9] most previous studies focusing on published documents failed to assess a large proportion of the research that has in reality been performed. Follow-up of this share is of particular interest when comparing regions of different scientific activity and performance.

Table 2
The GDP as predictor of scientific success for prospective clinical studies in cardiology — a subgroup analysis.

	p value	OR (95% CI)	c-stat
A. Acceptance at congress-level			
Crude	<0.001	1.415 (1.206–1.660)	0.552
Adjusted	0.074	1.379 (0.970–1.961)	0.653
B. Publication in a peer-reviewed journal			
Crude	<0.001	1.573 (1.309–1.980)	0.510
Adjusted	0.015	1.641 (1.101–2.445)	0.607
C. Impact factor ≥5.36			
Crude	0.005	1.825 (1.201–2.776)	0.516
Adjusted	0.029	4.509 (1.168–17.417)	0.708
D. Two-year citations ≥6			
Crude	0.148	1.267 (0.919–1.745)	0.508
Adjusted	0.107	2.186 (0.846–5.654)	0.686

Binary logistic regression analyses; subgroup analyses including prospective clinical trials only (n = 357). Accepted and rejected studies were followed for five years for publication and two-year citation rates. The per-capita gross domestic product (GDP) of each of the 63 submitting countries at the time of abstract submission (2006) served as surrogate for economic strength. Analyses were adjusted for the following parameters: the type of research (clinical vs. basic), the number of enrolled patients (≤100 or more), the study design, the study field, the continent of origin, academic affiliation of the originating institution, first and last author gender, national expenditures on education, on research and development, and the number of researchers per million inhabitants. Dependent variables were (A) acceptance at the ESC congress 2006, (B) full-text publication in a peer-reviewed journal, (C) publication in one of the top 25% journals according to impact factor (i.e. >5.36), and (D) reaching the top 25% two-year citation frequency (i.e. >6 two-year citations). All analyses are based on a representative 10% selection (n = 1002) of all abstracts submitted to the ESC congress 2006. OR = odds ratio, CI = confidence interval, and c-stat = c-statistic.

Taken together, the size and global distribution of this well-characterized study cohort, along with the multi-leveled assessment of research dissemination provide a novel perspective on the role of the wealth of nations in the dissemination of research.

4.3. Potential limitations

Our study needs to be interpreted in the context of the following limitations: Though widely accepted as neutral and quantitative indicator of scientific performance [10,11,20–22], citation analyses may be subject to bias. Having also assessed acceptance at congress level, publication per se, as well as the impact factor of the journal of publication, we consider citation analysis as an adequate tool to complement the other endpoints. Not all citation peaks may be covered in the applied two-year citation window. However, in the rapidly moving field of biomedical research, most citations peak within the first two years after publication [13,23].

There may be other determinants of research quality, such as scientific originality, that were not assessed in this study. Their role cannot be determined by our analyses but may have impacted on dissemination. Moreover, the low numbers of abstract submissions from certain countries limit conclusions about the scientific performance of these countries. Yet this limitation itself provides unique insights. For example, despite its comprehensive nature, this study remains unable to comment on research from the Arabian Peninsula. Though per-capita GDP is largely similar compared with western developed countries, no abstract from this region in the world was among the cohort investigated in this study. Importantly, the potential reasons for the observed results and accordingly their implications discussed in this manuscript have not been scientifically assessed at this stage, and therefore remained speculative. Finally, data reported in this study refer specifically to cardiovascular research. Extrapolation to other fields beyond cardiovascular science may be inaccurate.

4.4. Possible explanations

Investigators in less wealthy countries still face challenges to publish and disseminate their research, even after accounting for potential differences in the quality of their work or research infrastructure. Interestingly, these findings appear to apply beyond developing countries: They also seem to hold true in western nations in Europe or North America, where per-capita GDP ranged from below 10,000 USD as in Poland or Mexico to over 50,000 USD as in Switzerland or Norway.

Thus, we propose the following possible explanations for our findings:

1) *The wealth of nations may be a determinant of other markers affecting scientific success.* These may include investigators' experience and track record, the density and quality of education facilities, English language proficiency, the possibility of postgraduate training abroad, the degree of international collaborations, or the accessibility to published literature. If diminished, all these factors may negatively affect educational advancement of researchers and manuscript quality. Difficult-to-read manuscripts may in turn trouble reviewers and conceal scientific content, and thus lead to premature rejection of potentially relevant studies.
2) *Research from less wealthy nations may appear less relevant, thus interfering with its dissemination.* Most high-ranking journals including the majority of their reviewers are based in western, economically privileged countries. Studies performed in very different surroundings on subjects of a different ethnic background may appear less relevant to reviewers or editors. Judgments alike may not always be seen in the light of an international readership in an increasingly

global scientific community and western populations of increasing ethnic diversity.

3) *Established research networks comprising familiar peers and institutions may affect the ratings of scientific work.* Since our findings imply that also among western nations the per-capita GDP is a strong predictor of the dissemination of research, other reasons associated with the origin of the respective studies may affect manuscript selection during peer review and editorial decision-making. Such a reason may simply be a natural skepticism towards studies performed by unknown researchers or institutions. In this context a double-blinded peer review process, where authors and their affiliations are masked, may decrease a systematic manuscript selection bias.

Taken together, the challenges faced by investigators in less wealthy nations in disseminating their research do not appear to arise only from educational disadvantages. The limited relevance of studies performed under different environmental conditions in an ethnically different population also only insufficiently explains the results of this study. A natural manuscript selection bias, providing an advantage to scientists and institutions familiar to reviewers and editors, may exist.

At this stage, however, it can only be speculated about the exact reasons for the strong predictive value of the wealth of nations for the dissemination of research.

4.5. Potential implications

Researchers, publishers, editors, and organizing committees of scientific meetings should join forces to overcome putative structural disadvantages of less wealthy nations, increase the availability and dissemination of existing scientific information, and diminish manuscript selection bias. Possible means to achieve these goals comprise to foster international collaborations, encouraged through targeted funding by global funding institutions, to consider double-blinded peer review processes, and to continue encouraging open-source publishing.

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Author contribution and acknowledgments

All authors contributed to study concept and design, data interpretation, and critical revision of the manuscript for important intellectual content. All authors contributed to and approved the final version. SW, TS, DAR, JHW, and MH collected and analyzed data. SW, CMM, BKN, TS, TFL, and FR drafted the manuscript and figures. The corresponding author (SW), TS, and CMM had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. We are grateful to Florence Biazeix and Eirini Liova for administrative assistance.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2013.08.101.

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