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Applicability of European Society of Cardiology guidelines according to gross national income

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Abstract

Aims

To assess the feasibility to comply with the recommended actions of ESC guidelines on general cardiology areas in 102 countries and assess how compliance relates to the country's income level.

Methods and results

All recommendations from seven ESC guidelines on general cardiology areas were extracted and labelled on recommended actions. A survey was sent to all 102 ESC national and affiliated cardiac societies (NCSs). Respondents were asked to score recommended actions on their availability in clinical practice on a four-point Likert scale (fully available, mostly/often available, mostly/often unavailable, fully unavailable), and select the top three barriers perceived as being responsible for limiting their national availability. Applicability was assessed overall, per World Bank gross national income (GNI) level, and per guideline.

A total of 875 guideline recommendations on general cardiology was extracted. Responses were received from 64 of 102 (62.7%) NCSs. On average, 71.6% [95% confidence interval (CI): 68.6–74.6] of the actions were fully available, 9.9% (95% CI: 8.7–11.1) mostly/often available, 6.7% (95% CI: 5.4–8.0) mostly/often unavailable, and 11.8% (95% CI: 9.5–14.1) fully unavailable. In low-income countries (LICs), substantially more actions were fully unavailable [29.4% (95% CI: 22.6–36.3)] compared with high-income countries [HICs, countries 2.4% (95% CI: 1.2–3.7); $P < 0.05$]. Nevertheless, a proportion of actions with the lowest availability scores were often fully or mostly unavailable independent of GNIs. Actions were most often not available due to lack of reimbursement and other financial barriers.

Conclusion

Local implementation of ESC guidelines on general cardiology is high in HICs and low in LICs, being inversely correlated with country gross national incomes.

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Structured Graphical Abstract

Key Question

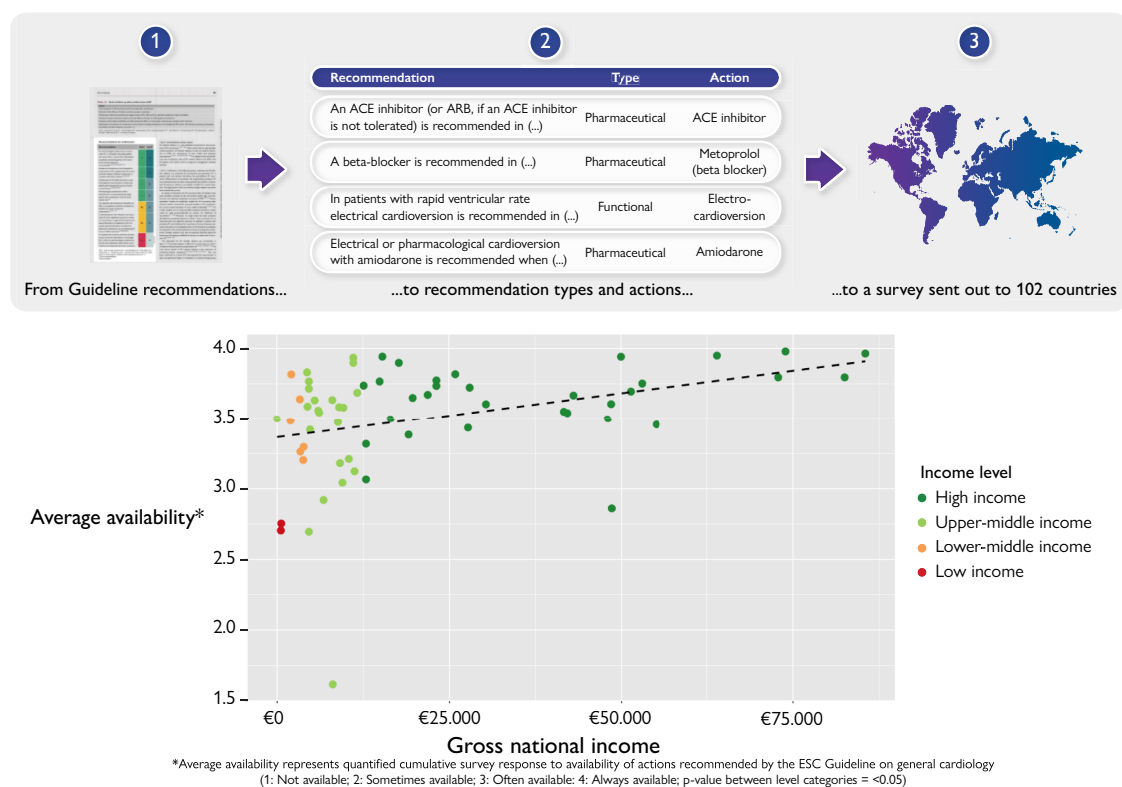
How applicable are European Society of Cardiology (ESC) Guidelines according to country income levels?

Key Finding

Application of ESC Guidelines differed among countries. They were less applicable in countries with lower income levels than in those with higher income levels.

Take Home Message

More attention needs to be paid to the implementation of ESC Guidelines in lower income countries in order to promote health equity.



Global availability and applicability of ESC guidelines on general cardiology is high in high-income countries and low in low-income countries

Keywords

Clinical practice guidelines • Global Health • Cardiology

Introduction

Morbidity and mortality related to cardiovascular disease (CVD) have decreased substantially in the past half-century.¹ Nonetheless, CVD remains one of the leading causes of death globally.¹ Countries with lower gross national incomes (GNIs) per capita have higher morbidity and mortality rates for CVD with broad differences between countries.^{1,2}

To improve CVD outcomes, clinical practice guidelines encourage clinicians to provide care according to evidence-based standards.^{3,4} In optimizing global cardiovascular care, guidelines of major international cardiovascular societies play an important role.^{5,6} The European

Society of Cardiology (ESC) aspires to support cardiovascular care globally, as reflected with her 102 member and affiliated national cardiac societies (NCSs), representing more than 80% of the world population.⁷ Comprehensive implementation of ESC guidelines would have considerable impact on the burden of CVD worldwide. However, for guidelines to be applicable globally, recommendations in these guidelines need to be available across countries.

To assess applicability of the current ESC guideline recommendations in general cardiology areas, we surveyed the 102 ESC NCSs and investigated whether availability of recommended actions was influenced by country income levels.

Methods

We extracted all guideline recommendations from ESC clinical practice guidelines on general cardiology areas (Diabetes, Pre-Diabetes and CVD [2013]; Non-Cardiac Surgery [2014]; CVD Prevention [2016]; Dyslipidemias [2016]; CVD during pregnancy [2018]; Arterial Hypertension [2018]; Syncope [2018]) and categorized them into actions (e.g. 'prescribe metoprolol'), and associated recommendation types (e.g. pharmaceutical intervention). Guidelines were defined as being on general cardiology according to classifications used previously.^{8,9} Only guidelines on general cardiology were included as these were considered to be most relevant in a global context. If general cardiology guidelines were not applicable, we assumed that subspecialty guidelines would also not be applicable. Subsequently, we disseminated a survey to all 102 ESC NCSs to score recommended action on their availability (Figure 1).

Collecting guideline recommendations

Guideline recommendations, actions and associated type groups were collected in a similar fashion as described previously.^{8,9} In short, current clinical practice guidelines were downloaded from the ESC website (<https://www.escardio.org/Guidelines>). All documents were categorized as comprehensive practice guidelines, focused updates, definition guidelines, position papers and other documents by one author (W.D.). Guidelines were categorized to their cardiovascular subspecialty using the same classification as previously done by these and other authors.^{8,9} Guidelines on general cardiology were included for further analysis. From every guideline, all recommendation texts, classes and levels of evidence (LoE) were retrieved using Tabula (version 1.2.1, <https://tabula.technology>) by one author (W.D.). The results were exported to Microsoft Excel (version 16.21.1.1) and manually checked on having a recommendation text, class, and LoE.

Collecting guideline recommendation actions

To be of use to clinical practice, guideline recommendations need to be actionable [e.g. recommend subscribing a beta blocker or a primary

percutaneous coronary intervention (PCI)], to which each recommendation can be labelled (e.g. 'prescribe metoprolol' or 'perform PCI'). For the current study, we derived actions from recommendation texts, and associated type groups (e.g. pharmaceutical intervention or minimally invasive intervention). For example, when the name of a substance was available, this was taken instead of its substance group (e.g. 'metoprolol' instead of 'beta blocker'; the entire list of actions can be found in [supplementary materials online, Table S1](#) of the [supplementary materials](#)).

After extraction and categorization, a random sample of actions and types was manually cross validated by a second author (E.S.). Interrater reliability was assessed using Cohen's Kappa statistic and was considered sufficient (≥ 0.7).

Survey on availability of recommended ESC guideline actions

A survey comprising a list of all recommended actions was sent out to all 102 ESC NCSs to be completed by local country experts on CVD (the full survey can be found in the [supplementary materials](#)). Survey responses were initially collected between June 2020 and September 2020, but later the end date was extended to June 2021 to increase the response rate. NCSs that did not respond to the survey received monthly reminders and were actively contacted by e-mail and phone by members of the ESC Global Affairs committee.

To assess recommendation applicability, NCSs were asked to score every recommended action on its availability in their country on a four-point Likert scale [fully available (score of 4), mostly/often available (3), mostly/often unavailable (2), fully unavailable (1)]. In addition, NCSs were asked for each recommendation type group (e.g. pharmaceutical intervention or laboratory tests) to indicate the top three reasons for their lack of availability. Reasons for actions being unavailable were derived from consensus discussions within the author group and the ESC Global Affairs office.



Figure 1 Data collection methods.

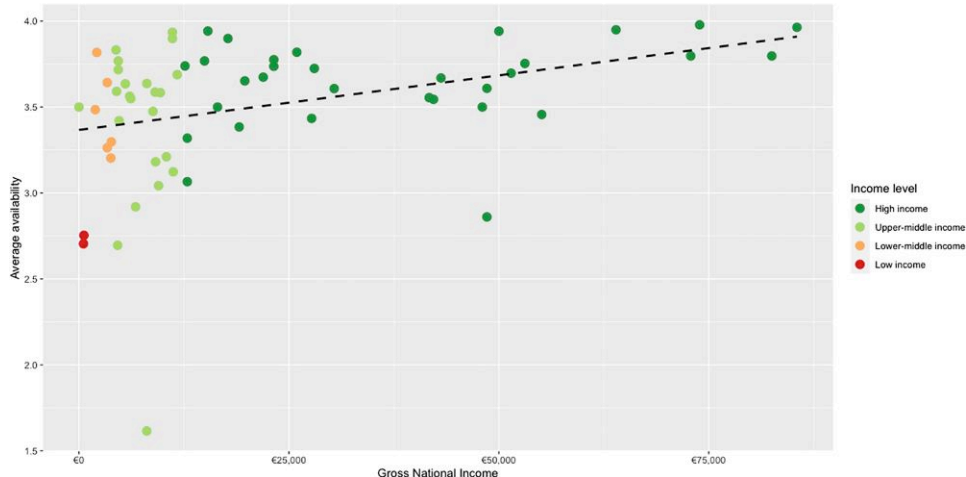


Figure 2 Action availability per country gross national income. Each dot represents a country.

Analyzing guideline applicability

The overall number of action availability scores was calculated and aggregated by response options (i.e. score of 1 to 4). When multiple responses were received from one NCS, averages of these responses were taken. To assess if responder countries differed from non-responder countries, a logistic regression analysis was performed with country GNI as a covariate and response status as the outcome.

Responses were reported by World Bank income level [high-income countries (HICs): >\$12 055 per capita; upper-middle income countries (UMICs): \$3895–12 055 per capita; lower-middle income countries (LMICs): \$996–3895 GNI per capita; low-income countries (LICs): <\$996 GNI per capita; reference year: 2019],¹⁰ country and guideline.

To assess clinical guideline applicability, actions were re-mapped to their original recommendations and aggregated on their corresponding guideline.

A normal approximation was used to calculate 95% confidence intervals (CIs) around the calculated proportions. To test for statistical significance between income levels, regions, and guidelines, one-sided chi-squared tests were performed. *P*-values <0.05 were considered to be statistically significant. Reasons for actions not being available were reported by recommendation type group. All analyses were performed using R software, version 4.0.3.18.

Results

Guideline recommendations and actions

A total of 34 documents were retrieved from the ESC website, on 1 May 2020 latest. Of these, 27 were categorized as comprehensive guidelines, comprising 3351 recommendations. Seven guidelines with 875 (26.1%) recommendations were identified as current guideline on general cardiology areas. These 875 recommendations were used for further analysis.

From the 875 recommendations, 139 different actions were extracted. Most actions were on therapeutic pharmaceutical interventions ($n=38$; 27%), diagnostic non-invasive tests ($n=18$; 13%) and laboratory tests ($n=18$; 13%). For 91 recommendations, it was not possible to retrieve specific actions; these recommendations comprised policy statements ($n=80$), disease definitions ($n=5$), differential diagnosis ($n=5$), and research results ($n=1$).

Action availability

Responses were received from 64 (HIC: 32, UMIC: 22, LMIC: 8, LIC: 2) of 102 countries that were contacted. Logistic regression analysis

showed no association between country income and response status ($P=0.1$).

Overall, 71.6% (95% CI: 68.6–74.6) of the actions were fully available, 9.9% (95% CI: 8.7–11.1) mostly/often available, 6.7% (95% CI: 5.4–8.0) mostly/often unavailable, and 11.8% (95% CI: 9.5–14.1) fully unavailable (Figure 2). Of recommended actions on interventions, 69.1% (95% CI: 65.3–72.9) were fully available, 10.7% (95% CI: 9.2–12.3) mostly/often available, 6.6% (95% CI: 5.0–8.2) mostly/often unavailable, and 13.6% (95% CI: 10.6–16.6) fully unavailable. Of recommended actions on diagnostics, 75.9% (95% CI: 71.1–80.6) were fully available, 8.5% (95% CI: 6.5–10.4) mostly/often available, 6.9% (95% CI: 4.8–9.1) mostly/often unavailable, and 8.7% (95% CI: 5.3–12.2) fully unavailable.

Overall, action availability scores were correlated with country GNIs (Figure 2). Availability of recommended actions decreased substantially with World Bank income levels (Figure 3; for action availability per country see [supplementary materials online, Figure S1](#) of the [supplementary materials](#)), in HICs 2.4% (95% CI: 1.2–3.7) of the actions were scored fully unavailable, in UMICs 4.7% (95% CI: 2.5–6.8), in LMICs 10.6% (95% CI: 7.0–14.2), and in LICs 29.4% (95% CI: 22.6–36.3; $P<0.05$). Notably, actions with lowest availability scores were often fully or mostly unavailable across all country income levels. Per region, Africa comprised most fully unavailable actions [15.4% (95% CI: 11.6–19.1)] (Figures 4 and 5), followed by Asia and the Pacific [6.6% (95% CI: 3.9–9.3); $P<0.05$].

When recommended actions were mapped back to corresponding guidelines, guideline applicability decreased with World Bank income levels (Figure 6). On average, guidelines comprised 1.6% (95% CI: 0.8–2.4) actions fully unavailable in HICs, 3.1% (95% CI: 1.7–4.4) actions fully unavailable in UMICs, 7.3% (95% CI: 4.9–9.7) actions fully unavailable in LMICs, and 22.8% (95% CI: 18.0–27.7) actions fully unavailable in LICs ($P<0.05$).

Reasons for action type group inapplicability

A total of 664 reasons for actions being unavailable were reported, matching ten responses per country in total and one per recommendation type (Figure 7).

Recommended actions were most often unavailable due to financial reasons, either being not covered or reimbursed by the healthcare

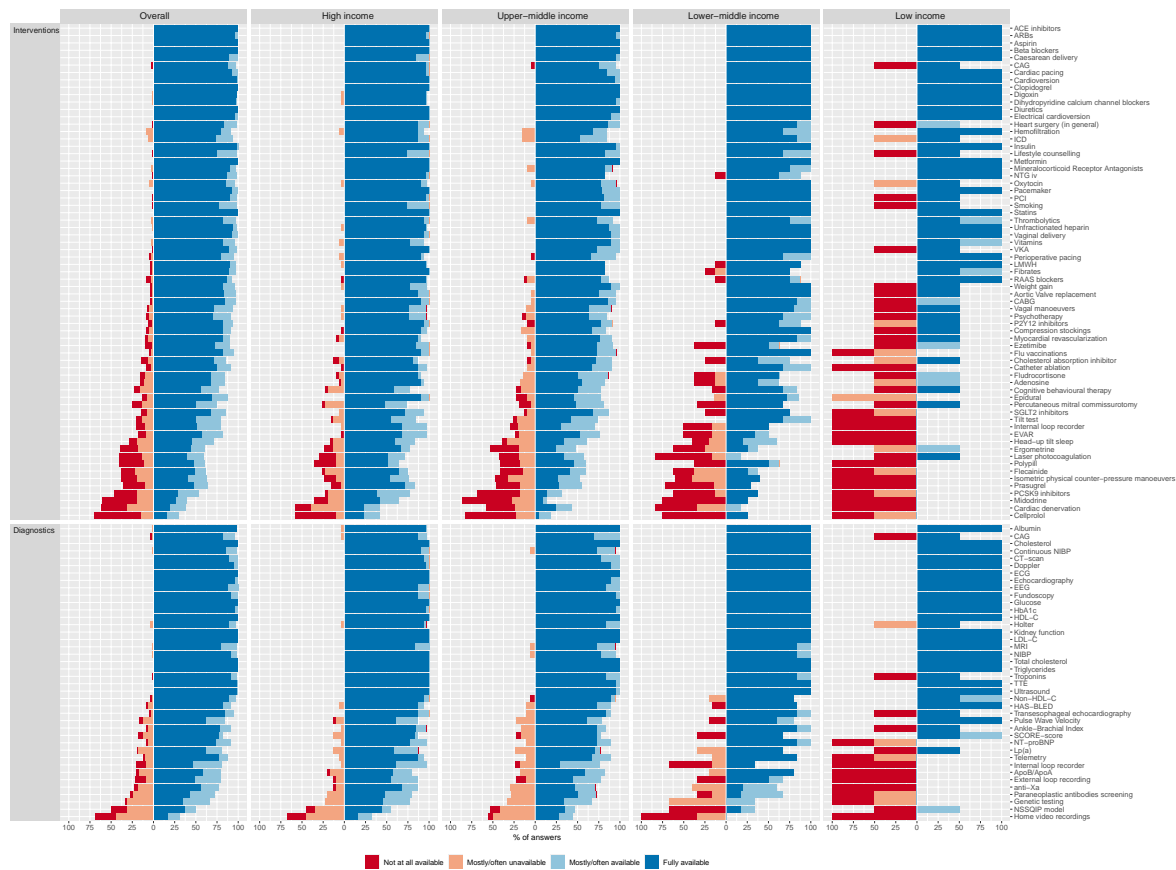


Figure 3 Action availability per type and country income level. Countries per World Bank Income Group; overall: 64, high-income: 32, upper-middle income: 22, lower-middle income: 8, low-income: 2.

system, being too expensive for institutions, or patients. Most responses were received for pharmaceutical interventions ($n = 150$). Most often named reason for pharmaceutical interventions being unavailable was the action not being covered or reimbursed by the health-care system ($n = 32$), followed by too expensive for patients ($n = 27$), and too expensive for institutions ($n = 25$).

Discussion

In this study, we assessed global availability of actions recommended by current ESC guidelines on general cardiology. Moreover, we used this availability to derive global applicability of current ESC guidelines on several general cardiology areas.

We found that recommended actions, availability and applicability of ESC guidelines on general cardiology decreases with country income levels. Notably, some actions proved to be poorly available independent of country income level. Reasons for recommended actions not being available were primarily financial. In particular, for pharmaceutical interventions financial barriers were often indicated to limit availability. Collectively, these findings show that the clinical practice guidelines of the ESC on general cardiology are not globally applicable and cannot be expected to be implementable by default. Furthermore, some actions recommended by guidelines are unavailable regardless of income level (Figures 3–7).

The unequal global distribution of medical resources is well documented in literature.¹¹ In 2013, a systematic review on the distribution of trials globally found that 0.15% of trials were conducted in LICs.¹² In like manner, a joint working group of multiple large international public health organizations recently concluded that published research on cardiovascular risks was often inapplicable in LICs.¹³ Literature on cardiovascular guidelines shows similar patterns.⁶ A systematic review in low and lower-middle income countries (LLMICs) from 2016 found just a single guideline published on hypertension in LICs and just a few in MICs, most of these not peer-reviewed.¹⁴ Alike, guidelines on stroke, dyslipidemia and risk scores often do not exist or are deemed inapplicable in LLMICs.^{15–18}

The present study shows that despite the aspiration to develop guidelines that are globally applicable, overall, cardiovascular guidelines do not meet this standard. With an estimated 90% of global CVD burden placed in LMICs representing <10% of global resources, it is important to support these countries with suitable strategies to reduce and manage CVD risks.¹ And if strategies were indeed available, bidirectional communication would be important for optimising the uptake of guidelines. Many authors and several large organizations, including the World Health Organization (WHO), regularly call for internationally applicable guidelines. However, although this call is often acknowledged, it remains mainly expressed in words rather than actions.¹⁹ Positive exemptions, putting words into practice, are the World Heart Federation (WHF) and World Gastroenterology Organization,

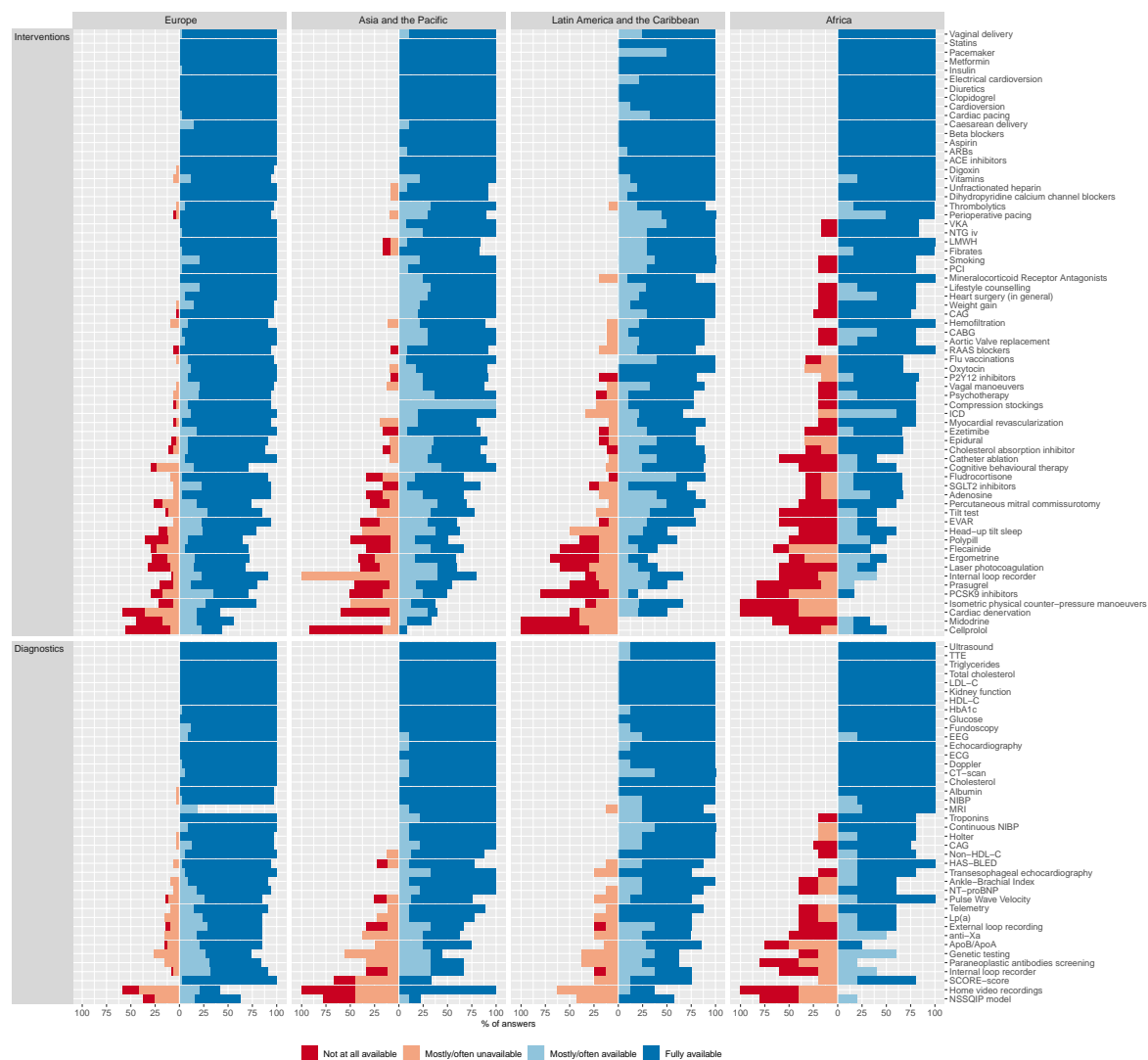


Figure 4 Action availability per type and region. Countries per region; Europe: 34, West Asia: 14, Latin America and the Caribbean: 10, Africa: 6.

both actively publishing and applying new methods to improve worldwide applicability of their guidelines.^{5,20}

Current cardiovascular guidelines often offer best evidence recommendations only.²¹ In LICs, however, applying best evidence is often not possible, as applying best evidence often also bears more costs.²² Globally applicable guidelines would therefore benefit from providing second and third best recommendations, for example based on income levels, all becoming first best when higher level bests are not available.²³ In addition, including cost-benefit trade-offs in guideline development processes to assess whether costs are in proportion to health benefits gained might help guidelines to become more globally applicable. Furthermore, providing guidance in clinical practice guidelines on how to implement their recommendations or recommended actions might help to improve the applicability of guidelines.

Ethically, the question is whether the guidance developed in HICs is also the best standard for the standard of care in LLMICs. A globally applicable standard does not mean that everyone should be treated in the same way, but that morally relevant differences are allowed.²⁴ If the standard of a HIC

will never be feasible nor sustainable in an LMIC due to infrastructure or local health care norms, the standard of care of the HIC may not be the best standard for the LMIC. At the same time, in order to determine what is the best standard in a particular setting populations and communities should be engaged. The best standard of care cannot be determined only by members of HICs present in the ESC. A challenge in this regard is the absence of professional medical associations in many LLMICs.²⁵ For example, the ESC only counts three NCSs from LICs (of whom two responded to the survey for this article) among the 28 LICs worldwide.^{7,10} The number of NCS members from LICs remains low, despite extensive recruiting efforts of the ESC Global Affairs Committee in recent years.²⁶

Solid cardiovascular guidelines delineate clinical practice in HICs today, leading to better patient outcomes.³ By contrast, the absence of applicable guidelines in LLMICs hinder these countries to lower their CVD burden at the same rate as higher income countries. Efforts to transfer the large impact that cardiovascular guidelines have in HICs to LLMICs need more attention to lower the global burden of CVD.

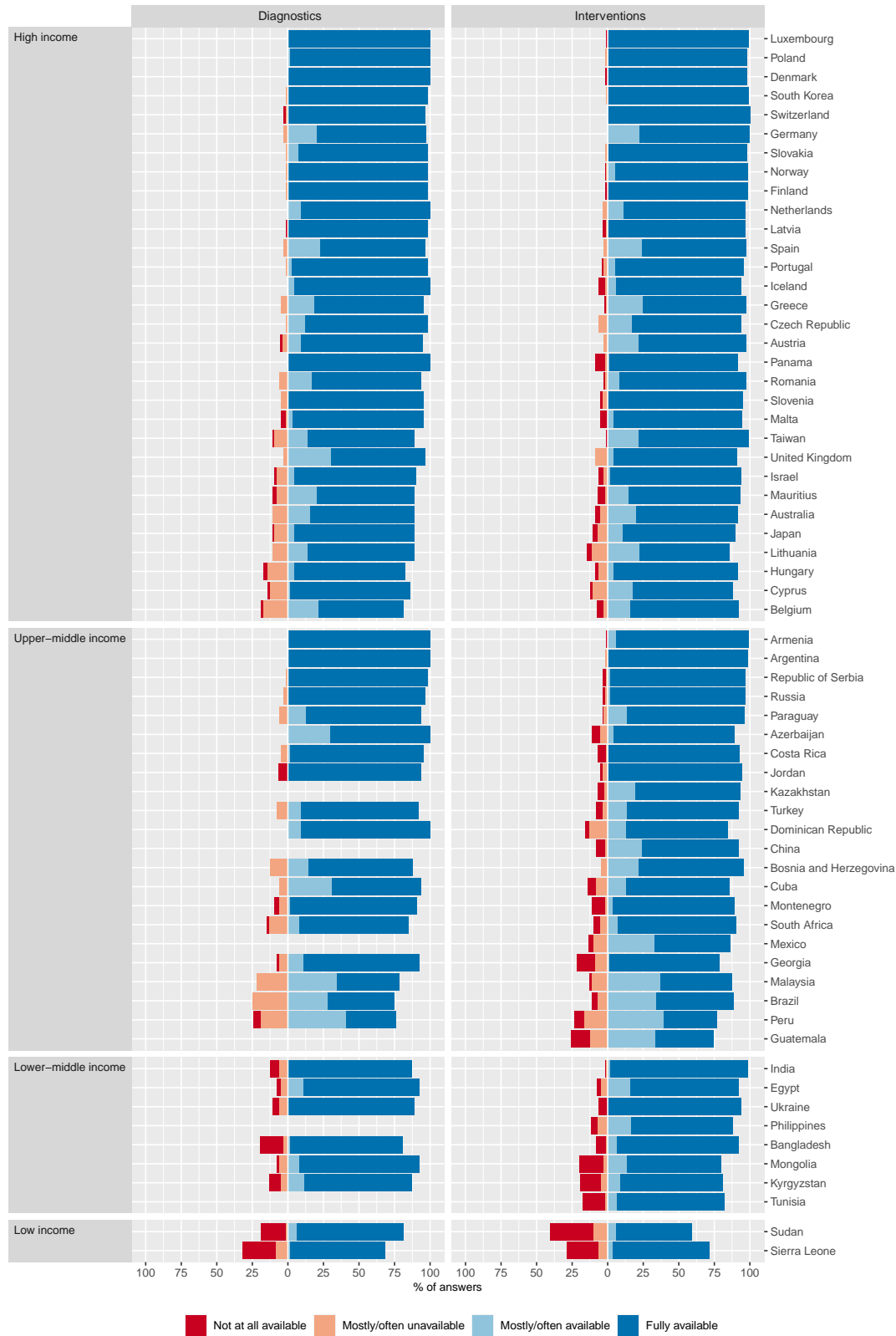


Figure 5 Action availability per type and region.

We recommend that the ESC and other HIC-based developers of guidelines intended to be used globally should consider developing context-stratified recommendations, based on predictable contextual

barriers of implementation such as human and financial resources for health.²² Stratification of guidelines should also consider the level of care in which services are being provided. As indicated by the absence

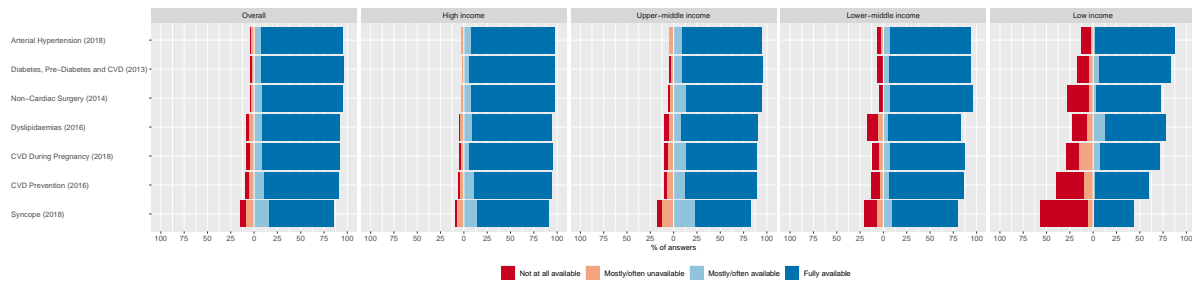


Figure 6 Guideline applicability per country income level. Countries per World Bank Income Level; overall: 64, high-income: 32, upper-middle income: 22, lower-middle income: 8, low-income: 2.

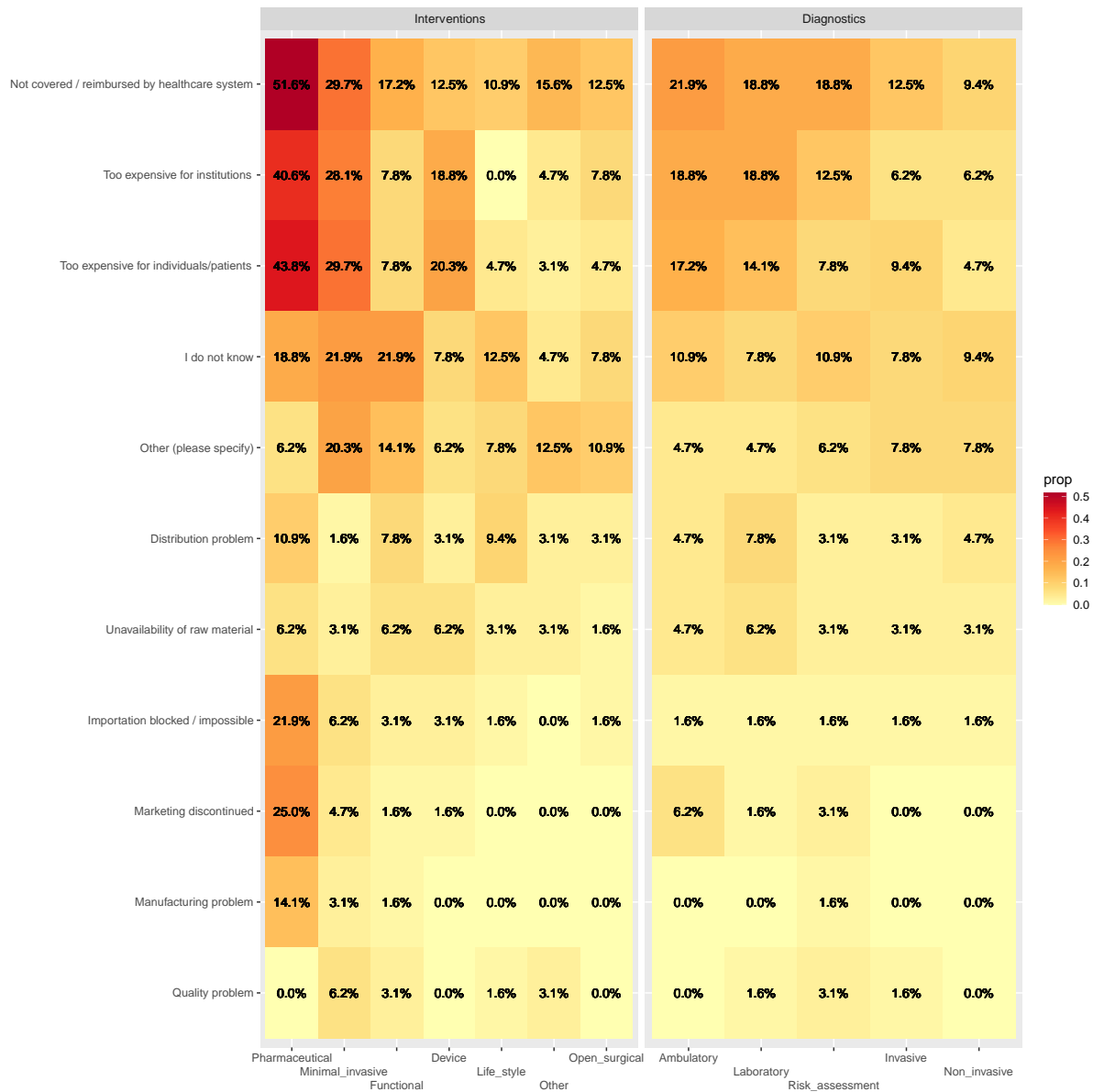


Figure 7 Reasons for action type groups unavailability (percentage of respondents, n = 64).

of NCSs in most LICs, many services provided by cardiologists in HICs are provided in LICs by non-specialists or non-physicians, often in primary health care facilities.^{27,28}

Limitations

To appreciate the findings of the current study, some limitations need to be considered. First, only guidelines on general cardiology areas were included, limiting the conclusions of the current work to general cardiology recommendations issued by the ESC. For more specialistic guidelines such as the guideline on coronary revascularization the applicability might well be (substantially) lower than found in the current study, both overall and across country income levels. Second, the disseminated survey for this study regarded recommended actions and not recommendations. Therefore, correlations between recommended action availability, recommendation classes, and LoEs could not be assessed. Third, the disseminated survey was often completed only by one national ESC NCS representative. Unclear was to what extent the individual completing the survey was representative of the NCSs view as a whole on the availability on one or more of the recommended actions. As a result, individual country scores might have been too positive or negative in estimating the applicability of recommended actions. Fourth, LICs were substantially underrepresented in the number of survey responses for this study. The low number of responses was attributable to underrepresentation of LICs in ESC member associations due to absence of professional medical associations in many developing countries. Fifth and final, NCS representatives often provided less than three reasons for actions being unavailable. Moreover, unavailability reasons were not ranked based on relevance (i.e. most relevant reason listed first). The data on reasons for action unavailability should therefore be interpreted with caution.

Conclusions

Availability and applicability of ESC cardiovascular guidelines on general cardiology differs across country income level, guidelines, and recommended actions, being high in countries with high-income levels and low in countries with lower income levels. Moreover, ESC guidelines comprise multiple recommendations that are limited in their applicability independent of country income levels. Context-stratifying guideline recommendations to resource levels might help make guidelines more applicable globally.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Conflicts of interest: D.E.G. is a member of the board of the ESC and chair of the Global Affairs Committee of the ESC. D.E.G. and M.R. are

members of the practice guidelines committee of the ESC. Barbara Casadei is immediate past president of the ESC (2020–22). R.v.d.G. is a member of an independent ethical advisory committee to Sanofi. All other authors did not report any conflicts of interest.

Data availability

The data on extracted ESC guideline recommendations and actions underlying this article are available in the article and in its online [supplementary material](#) of Dijk et al. (2019) as published previously.

The survey data on ESC guideline availability and applicability underlying this article are available in the article and in its online [supplementary material](#).

The analysis scripts underlying this article will be shared on reasonable request to the corresponding author.

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