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Gaps in COPD guidelines of low- and middle-income countries: a systematic scoping review

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4 **Gaps in COPD guidelines of low- and middle-income countries: a**  
5 **systematic scoping review**

6 **Running head:** Gaps in low- and middle-income COPD guidelines

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**66 Abstract***67 Background*

68 Guidelines are critical for facilitating cost-effective COPD care. Development and  
69 implementation in low-and middle-income countries (LMICs) is challenging. To guide future  
70 strategy, an overview of current global COPD guidelines is required.

*71 Research question*

72 We systematically reviewed national COPD guidelines, focusing on worldwide availability  
73 and identification of potential development, content, context and quality gaps that may  
74 hamper effective implementation.

*75 Study Design & Methods*

76 Scoping review of national COPD management guidelines. We assessed: (1) global guideline  
77 coverage, (2) guideline information (authors, target audience, dissemination plans), (3)  
78 content (prevention, diagnosis, treatments), (4) ethical, legal, socio-economic aspects and (5)  
79 compliance with the eight Institute of Medicine (IOM) guideline standards. LMICs guidelines  
80 were compared to those from high-income countries (HICs).

*81 Main results*

82 Of the 61 national COPD guidelines identified, 30 were from LMICs. Guidelines did not  
83 cover 1.93 billion (30.2%) people living in LMICs, whereas only 0.02 billion (1.9%) in HICs  
84 were without national guidelines. Compared with HICs, LMIC guidelines targeted fewer  
85 healthcare professional groups and less often addressed case finding and co-morbidities. Over  
86 90% of all guidelines included smoking cessation advice. Air pollution reduction strategies  
87 were less frequently mentioned in both LMICs (47%) and HICs (42%). LMIC guidelines  
88 fulfilled on average 3.37 (42%) of IOM standards compared to 5.29 (66%) in HICs ( $p < 0.05$ ).

89 LMICs scored significantly lower compared with HICs regarding conflicts of interest  
90 management, updates, articulation of recommendations and funding transparency (all,  
91  $p<0.05$ ).

92 *Interpretation*

93 Several development, content, context and quality gaps exist in COPD guidelines from  
94 LMICs that may hamper effective implementation. Overall, COPD guidelines in LMICs  
95 should be more widely available and should be transparently developed and updated.  
96 Guidelines may be further enhanced by better inclusion of local risk-factors, case finding and  
97 co-morbidity management, preferably tailored to available financial and staff resources.

98 **Key words:** Pulmonary Disease, Chronic Obstructive, Developing Countries, Consensus,  
99 Reference Standards

100

## 101 **Introduction**

102 According to the Global Burden of Disease study, over 90% of COPD deaths occur in low-  
103 and middle-income countries (LMICs).<sup>1</sup> Notably, these deaths are accompanied by a  
104 significant socioeconomic burden for patients, their families and societies.<sup>2</sup> As such, to  
105 achieve the greatest impact in reducing premature COPD deaths around the world, efforts  
106 should focus on optimizing COPD treatment in LMICs. One of the ways in which treatment  
107 can be optimized is through effective dissemination and implementation of guidelines.

108 Guidelines should provide standardized, evidence-based prevention, diagnosis, and  
109 management recommendations. Some countries have developed their own guidelines, and  
110 from 2001 the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Strategy  
111 Report has been established. Since then, multiple countries have adopted the GOLD updates  
112 that followed.<sup>3</sup>

113 While guidelines are critical to help improving COPD care around the world<sup>4-6</sup>, guidelines are  
114 of no use when poorly implemented. Notably, for proper implementation, several  
115 prerequisites need to be considered. According to the APEASE criteria<sup>7</sup>, interventions can  
116 only be successful when affordable, practicable, (cost-)effective, acceptable, safe, and  
117 equitable. The ability to meet these criteria differs between (and within) countries.

118 Interventions can be feasible in one setting, but not in another depending on factors such as  
119 demographics, infrastructure, healthcare budgets, culture and environment.<sup>8-11</sup>

120 Historically, COPD guideline reviews dating back over a decade, included 15 to 41 guidelines  
121 and focused on assessing the quality of the development, content<sup>12</sup> and specific monitoring of  
122 recommendations<sup>13</sup>, with limited focus on LMICs.<sup>14,15</sup> The two latest reviews of COPD  
123 guidelines assessed diagnosis and treatment criteria<sup>16</sup>, development, authors and audience<sup>17</sup>,  
124 but focused on European guidelines only.

125 We have not identified any previous review that focused on COPD guidelines in LMICs. To  
126 stimulate effective implementation of COPD guidelines in LMICs, a systematic assessment of  
127 which aspects related to development, content, quality should be targeted is critical.

128 We systematically reviewed national COPD guidelines, focusing on global existence as well  
129 as on potential gaps in development, content, context and quality that may hamper their  
130 implementation in LMICs. We therefore undertook a scoping review to identify the  
131 gaps/topics that should be prioritized in future focused systematic reviews.

## 132 **Methods**

### 133 *Study design*

134 This global COPD guideline scoping review was informed by a systematic literature search,  
135 performed and reported (Online supplement, e-Table 1) according to PRISMA scoping review  
136 standards.<sup>18</sup> Given this work did not involve human subject research, no ethical approval was  
137 required. The work is part of the Global Alliance for Chronic Diseases (GACD) COUNCIL  
138 project.

### 139 *Data sources, search and inclusion*

140 To identify as many guidelines as possible, a sequential approach was taken. First, PubMed  
141 (Feb 15, 2019) and EMBASE (Feb 18, 2019) were searched to identify published COPD  
142 guidelines. Prior to manuscript submission (January 14, 2020) the search was repeated, but no  
143 additional guidelines were identified. References of previous reviews and identified articles  
144 were inspected to identify further guidelines. Additionally, authors and the GACD Research  
145 Network collaborators (all health professionals and/or clinical researchers specialized in lung  
146 disease) were asked to identify guidelines in their own country or guidelines they were aware  
147 of from other countries, not yet identified through the database or online searches. Also, the

148 guideline databases of the International Primary Care Respiratory Group, Guidelines  
149 International Network and the Tripdatabase were checked. Thereafter, authors were asked to  
150 reach out to colleagues and national (guideline) websites from all the remaining countries for  
151 which no guideline had been identified. Similar search strategies have been used by earlier  
152 GACD guideline comparisons.<sup>13</sup>

153 The online search strategy in PubMed and EMBASE was based on the list of key words used  
154 in the previous GACD guidelines reviews<sup>19-21</sup>, but with COPD as disease entity. For both  
155 databases, the search terms included “guideline” OR “consensus” OR “recommendations” OR  
156 “protocols” OR “standards” AND “COPD”. No search filters were applied and all years and  
157 languages were considered. The full search strategy is provided in online supplement e-Table  
158 2.

159 Guidelines were included as long as the following inclusion criteria were met: (1) it should  
160 focus on COPD prevention, diagnosis, and management (i.e. not only focusing on specific  
161 treatments such as alpha-1 antitrypsin deficiency); (2) it should have been developed for  
162 intended use as a national COPD guideline. This could include a stand-alone document or a  
163 translation or adaption of an international document (e.g. GOLD). When multiple guidelines  
164 were identified within the same country, the guideline with the largest coverage and/or most  
165 recent update (i.e. this could be a newly developed or updated guideline version) was selected.

#### 166 *Data extraction and quality assessment*

167 Data extraction was performed using a pre-piloted digital form. A first version, based on  
168 earlier GACD guidelines assessments, was made by JvB and AT and commented on by all  
169 authors, a combination of native English and non-English speakers with good understanding  
170 of COPD. Subsequently, small optimizations were made in an iterative process until a final  
171 version with uniform interpretation was agreed on. The final extraction form was circulated to

172 all authors using REDCap. Data extraction was performed by the individual authors and  
173 double-checked by a second person. For countries and/or languages where authors did not  
174 have expertise, additional local clinical experts from the particular country were invited to  
175 complete and double-check the data extraction.

176 Data items extracted included: (1) general guideline information (name, authors, year, target  
177 audience, dissemination plans), (2) coverage of specific COPD prevention, diagnosis and  
178 management recommendations (local epidemiology, case-finding, smoking cessation, air  
179 pollution, vaccination, exacerbations, comorbidity, diet, physical activity, pharmacologic  
180 recommendations, patient education, alternative medicine, and vulnerable populations, such  
181 as Indigenous people), (3) recommendations which addressed ethical aspects (e.g. regarding  
182 experimental high risk treatments, or non-evidence based treatments), legal aspects (e.g.  
183 related to end-of-life care, such as euthanasia, palliative sedation), social aspects (e.g.  
184 addressing the role of informal care givers, family and patient organizations) and economic  
185 aspects (e.g. costs or cost-effectiveness or reimbursement), and (4) compliance with the eight  
186 Institute of Medicine (IOM) standards for optimal development of clinical practice guidelines,  
187 consisting of several evidence quality indicators (transparency of funding, multidisciplinary  
188 author composition, conflicts of interest policy, use of systematic reviews, grading of  
189 evidence, articulation of recommendations, external review, frequency of updates).<sup>22</sup> The  
190 assessment of IOM criteria is further specified in e-Table 3 and was primarily chosen (rather  
191 than the more commonly used, but content-wise largely overlapping AGREE II tool) in order  
192 to be able to compare our results with previous GACD LMIC guidelines reviews that also  
193 used the IOM criteria.<sup>19-21</sup> Note that the IOM standards were published in 2011. Since 2016,  
194 the IOM is known as the “Health and Medicine Division” of the National Academies of  
195 Sciences, Engineering and Medicine of the United States.

196 *Outcomes by income-status*

197 Outcomes included global guideline coverage, defined as the absolute number and percentage  
198 of people in HICs and LMICs covered by a national COPD guideline as part of the total HICs  
199 and LMICs population. Additionally, the four themes as specified under data items (general  
200 guideline information, guideline content, ethical, legal, socio-economic aspects and  
201 compliance with the IOM guideline standards defined as the mean number of standards  
202 fulfilled) were assessed.

203 Countries with guidelines available were grouped and compared by income status (as of June  
204 2018). In particular, all identified countries were classified according to the World Bank Atlas  
205 method, also adopted by the Organization for Economic Cooperation and Development  
206 (OECD).<sup>23</sup> The World Bank assigns a classification for all member countries (189), and all  
207 other economies with populations of more than 30,000. Economies were classified based on  
208 their 2018 gross national income (GNI) per capita in US dollars. World Bank classifications  
209 include low-income countries (\$995 or less), lower-middle income countries (\$996–3,895),  
210 upper-middle income countries (\$3,896–12,055) and high-income countries (\$12,056 or  
211 more). Thus, for our comparison, countries with GNIs per capita up to \$12,055 were  
212 considered LMICs and countries with a GNI per capita of >\$12,056 were considered HICs. In  
213 2018, this classified 218 countries in the world (total population size: 7,594,270,356) in 81  
214 HICs (37%) with a total population size of 1,210,312,147 people and 137 (63%) LMICs with  
215 a total population size of 6,383,958,209 people.

#### 216 *Data synthesis and analyses*

217 All data were summarized per country in Excel 2010 (Microsoft Corp., Seattle, WA, USA)  
218 and presented in tables and figures for visual inspection and review. Categories were  
219 presented as absolute numbers per category and as percentages, continuous variables as mean  
220 and standard deviation (SD). Chi-squared tests and Student t-tests were performed (IBM  
221 SPSS Statistics 23) to assess outcomes by income classification, where guidelines from

222 LMICs were compared to those from HICs (see statistical specifications in e-Table 4). A  $p$ -  
223 value  $<0.05$  was deemed statistically significant.

## 224 **Results**

225 After searching PubMed, 3,030 titles were obtained, but after title screening only 90 were  
226 considered potentially relevant. In EMBASE, the search strategy resulted in 9,376 titles and  
227 after screening, 43 were considered potentially relevant. When removing duplicates and  
228 reading full texts, a total of 27 relevant COPD country guidelines were identified. Of note,  
229 two of these guidelines were written for two countries (Australia/New Zealand and  
230 Germany/Austria); these “two-country” guidelines were only counted once in comparisons.  
231 GACD collaborators suggested 13 additional COPD guidelines not found by the  
232 PubMed/EMBASE search. Finally, the targeted search/outreach by the GACD Research  
233 Network provided 21 more guidelines, resulting in a total of 61 identified COPD guidelines  
234 for 63 countries. The flow diagram of article selection is provided in e-Figure 1.

### 235 *Global population coverage*

236 In total, 63 (28%) of the 218 countries with a World Bank classification had COPD guidelines  
237 (Figure 1). These 63 countries covered a total population size of 5,644,031,801 (74.3% of the  
238 world’s population). Of the 61 guidelines evaluated, 30 (49%) were from LMICs, covering 30  
239 countries and 31 (51%) were from HICs, covering 33 countries. For LMICs, this means that  
240 30 of the world’s 137 LMICs (21.9%) had their own guideline. In terms of total population,  
241 these 30 countries covered 4.46 out of the 6.38 billion people living in LMICs, leaving 1.93  
242 billion people (30.2%) without their own country guideline. In HICs, 33 of the world’s 81  
243 HICs (40.7%) had their own guideline. In terms of total population, these 33 countries  
244 covered 1.19 out of the 1.21 billion people living in HICs, leaving only 0.02 billion people

245 (1.9%) living in HICs without their own country guideline. Country-specific population and  
246 income data are provided in e-Table 5.

## 247 **[FIGURE 1]**

### 248 *General characteristics and target audience*

249 Characteristics and content of all COPD guidelines are provided in Online supplementary e-  
250 Tables 6-18. Guidelines were mostly written by a national (respiratory) association or society  
251 or by the Ministry of Health (e-Tables 6-8). In LMICs, the oldest guideline was from El  
252 Salvador (2005) and the newest was from Bulgaria (2019).

253 An overview of the target audience of COPD guidelines is provided in figure 2 and specified  
254 in e-Table 4 and 9. All guidelines targeted physicians, often both respiratory specialists and  
255 primary care physicians/general practitioners (GP), regardless of income group. LMIC  
256 guidelines tended to explicitly target a smaller group of healthcare professionals compared to  
257 HICs, including significantly less often nurses (37% vs 77%,  $p<0.05$ ), physiotherapists (27%  
258 vs 55%,  $p<0.05$ ) and dieticians (10% vs 32%,  $p<0.05$ ).

## 259 **[FIGURE 2]**

### 260 *Content by income group*

261 An overview of the content of COPD guidelines by country classification is provided in  
262 Figure 3 and specified in e-Tables 10-12. Pharmacological treatment was the only item that  
263 was included in 100% of the COPD guidelines. Compared with HICs, LMICs significantly  
264 less frequently included recommendations regarding case-finding (LMICs: 40%; HICs: 84%,  
265  $p<0.05$ ) and co-morbidity (LMICs: 37%; HICs: 77%,  $p<0.05$ ). In contrast, LMICs guidelines  
266 slightly (but not significantly) more often included alternative medicine recommendations  
267 (LMICs: 10%; HICs: 3%) and paid some more attention to management of vulnerable  
268 populations (although only in two countries, Serbia and Indonesia). Of note, while over 90%

269 of guidelines included smoking cessation advice, management of other airborne exposures  
270 (e.g. indoor and outdoor air pollution) was much less frequently mentioned in both LMICs  
271 (47%) and HICs (42%).

### 272 **[FIGURE 3]**

#### 273 *Context, dissemination and quality*

274 Besides specific prevention, diagnosis and treatment recommendations, guidelines had non-  
275 significant differences regarding the extent to which ethical, legal and socio-economic context  
276 was considered. LMICs guidelines scored similarly on incorporation of ethical aspects (30%  
277 vs 29%,  $p=0.93$ ), and non-significantly lower on the legal (20% vs 35%,  $p=0.18$ ), social (27%  
278 vs 35%,  $p=0.46$ ), and economic aspects (27% vs 42%,  $p=0.21$ ). In LMICs, 23% of the  
279 guidelines had dissemination plans in place, while this was the case in 32% of HICs (e-Tables  
280 13-15).

281 In Figure 4 and e-Tables 16-18, fulfilment of IOM quality standards for good guideline  
282 development are shown for all COPD guidelines. Statistical comparisons are provided in e-  
283 Table 4. On average, LMICs guidelines fulfilled 42% (mean: 3.37; SD: 2.09), while HICs  
284 guidelines fulfilled 66% of the eight IOM criteria (mean: 5.29; SD: 2.02) ( $p<0.05$ ). For both  
285 LMICs and HICs, updating of guidelines was the worst scored criterion, with fewer than 50%  
286 of guidelines fulfilling this item but with better fulfilment in HICs ( $p<0.05$ ). Additionally,  
287 guidelines from LMICs scored significantly lower compared with HICs guidelines regarding  
288 conflicts of interests ( $p<0.05$ ), articulation of recommendations ( $p<0.05$ ) and transparency of  
289 funding ( $p<0.05$ ). If the five LMIC guidelines that were published before the IOM guidance  
290 launch (2011) were excluded, IOM criteria fulfilment was similar (mean: 3.24; SD: 2.09).

### 291 **[FIGURE 4]**

## 292 Discussion

293 We assessed the availability of COPD guidelines in LMICs and identified gaps in  
294 development, quality, content and context that may hamper their effective implementation.  
295 Regarding availability, we found a national guideline in only 30 out of 137 LMICs (21.9%),  
296 while in HICs this was the case for 33 of the 81 HICs (40.7%). In absolute numbers, this  
297 means that 1.93 billion (30.2%) people living in LMICs were without national COPD  
298 guidelines whereas of the 1.2 billion people living in HICs only 0.02 billion (1.9%) were  
299 without a national guideline. Regarding quality, LMIC guidelines fulfilled significantly fewer  
300 IOM standards for good clinical practice guideline development. LMIC guidelines scored  
301 significantly lower compared with HIC guidelines regarding conflicts of interests, updates,  
302 articulation of recommendations and funding transparency. Regarding content, risk factor  
303 management was mostly restricted to smoking cessation, while air pollution received far less  
304 coverage despite the importance of this in causing COPD in many LMIC settings.  
305 Pharmacological treatment was covered in all guidelines yet LMIC guidelines generally  
306 targeted a smaller group of healthcare professionals, mostly physicians and significantly less  
307 often nurses, physiotherapists and dieticians compared with HIC guidelines. Case-finding and  
308 comorbidities received relatively little attention in LMIC guidelines. Regarding context,  
309 incorporation of ethical, legal and socio-economic aspects in LMIC guidelines seemed  
310 numerically, but not statistically, lower than in HIC guidelines. Regarding dissemination, less  
311 than one quarter of LMIC guidelines had dissemination plans in place, compared to one third  
312 in HICs.

313 The difference between guideline availability in HICs versus LMICs highlights an  
314 unequivocal health disparity. Almost 2 billion people and their healthcare advisors (over a  
315 quarter of the World's population) are not directly advised on how to manage COPD  
316 according to their country context. In particular, countries in sub-Saharan Africa have no

317 COPD guidelines, despite the existence of the GOLD Strategy Report which can be used as a  
318 tool to frame local guidelines. The absence of national guidelines may be partly due to  
319 insufficient resources and international aid, but also due to local health, academic and political  
320 priorities that may have historically focused more on communicable diseases such as  
321 tuberculosis, malaria and HIV. However, given increased infection control and rising life  
322 expectancy, non-communicable diseases such as COPD may become a new epidemic.  
323 Therefore, timely development of COPD guidelines seems key.

324 In some countries, regional or direct GOLD translations were used (e.g. Romania). While  
325 these translations are available, local physicians' understanding may fall short and more  
326 efforts on implementation of these recommendations is required.<sup>24</sup> This may not only hold  
327 true for LMICs but also for smaller HICs including Andorra, Belgium and Luxemburg that  
328 simply use translated GOLD or neighboring countries' guidelines. Similarly, countries such as  
329 Uruguay and Panama mostly follow regional Latin American Thoracic Association (ALAT)  
330 guidelines.<sup>25</sup> For LMICs this may also be the case, for example in Middle Eastern countries  
331 that use the guideline of the Gulf Cooperation Council countries and Middle East-North  
332 Africa region.<sup>26</sup>

333 That less than one quarter of LMIC guidelines had dissemination plans in place underlines an  
334 important, but modifiable gap. We argue that efficient, wide-scale implementation can only be  
335 successful when effective guidelines and dissemination plans are in place, with proper  
336 understanding of local infrastructure, culture and environment, additionally tailored to local  
337 COPD prevalence, risk factors and resources available. Of note, most LMICs guidelines did  
338 not include local data and lacked economic considerations. Guidelines in LMICs tend to use  
339 some "copy paste" from HICs in relation to risk factors and did not always take into account  
340 regional differences. Notably, COPD risk factors other than smoking, such as early life  
341 disadvantages, household and ambient air pollution are now increasingly recognized<sup>27-29</sup> yet

342 are covered in less than half of current LMIC guidelines. Also, regional risk differences  
343 require attention. For example, in Latin America, tobacco smoking is primarily an urban  
344 problem, and not very prevalent in rural areas. These urban-rural disparities have also been  
345 observed in Uganda.<sup>30</sup> Early life disadvantages such as undernutrition may also be more  
346 prevalent in particular vulnerable populations such as Indigenous and nomadic populations in  
347 both HICs (e.g. Australia or Greenland) and LMICs, as well as the lack of early detection of  
348 COPD, limited access to treatment and lack of appropriate health education and poor  
349 engagement with health resources, that is often evident in Indigenous populations. Generally,  
350 research in these populations is scarce and recommendations tailored to these sub-populations  
351 are therefore lacking.

352 Regarding pharmacological treatment, covered by 100% of LMICs guidelines, it is important  
353 to note that most clinical evidence to support such medicines came from trials conducted in  
354 HICs. These often included current and former heavy-cigarette smokers, that do not always  
355 represent “real-world “ COPD heterogeneity<sup>31</sup> and do not necessarily have the same  
356 phenotype as non-smokers with other COPD risk factors as frequently seen in LMICs.  
357 Therefore, more trials should include LMIC populations. Furthermore, availability and  
358 affordability of recommendations should be considered, especially related to more expensive  
359 pharmacological treatment.<sup>32</sup> This question was considered too detailed for this broad scoping  
360 review and a more targeted systematic review focusing on specific pharmacologic  
361 recommendations in LMIC, considering availability and relationship with outcomes, would be  
362 highly valuable.

363 Regarding content, the low inclusion of case-finding and comorbidity management may have  
364 to do with the relatively slower uptake of novel findings. Indeed, the GOLD report has only  
365 put more emphasis on comorbidity since 2011 and even in the current version<sup>3</sup>, proper

366 guidance on multi-morbidity is lacking. Case-finding is only recommended from the 2019  
367 update following a large HIC trial.<sup>33</sup>

368 An important finding is related to transparency of guideline development. While proper  
369 reporting of funding and conflicts of interest are important these are significantly less often  
370 addressed in LMICs. These issues are not restricted to guidelines and also include  
371 consideration on who funds the COPD training for clinicians. Of note, a future focused  
372 systematic review could examine the reduced attention to conflict of interest in LMIC  
373 guidelines and whether this may have influenced the selection of medication  
374 recommendations.

375 Beyond COPD, similar guideline reviews comparing LMICs with HICs have been published  
376 including those for diabetes, hypertension and stroke.<sup>19-21</sup> While the content cannot be  
377 compared, adherence to IOM standards showed similar gaps, with a mean fulfillment of just  
378 under 2.5 IOM items for LMIC diabetes guidelines versus a mean of 5.2 in HICs. Similarly,  
379 “updating” was the lowest scored item and the largest gaps between LMICs and HICs were  
380 related to transparency, evidence quality and articulation of recommendations.

381 Given that in the vast majority of LMICs no specific COPD guideline was in place, policy  
382 makers should stress the need for a COPD guideline to be developed. In doing so, there is a  
383 strong need to harmonize the methodology of guideline production and implementation. We  
384 do however consider that stand-alone development of guidelines with standardized  
385 methodology is challenging, expensive and time consuming. This would for example include  
386 assessment of the strength of evidence with the Grading of Recommendations Assessment,  
387 Development and Evaluation (GRADE ) approach.<sup>34</sup> As such, as a minimum viable option,  
388 international guidelines (e.g. ERS, ALAT) are encouraged with local context-specific  
389 adaptations beyond simple translation.<sup>35</sup> Developers of future COPD guidelines should pay  
390 attention to IOM (or other recognized) standards for good clinical practice guideline

391 development. In particular, transparency, updating and conflict of interest management are  
392 important issues to be improved. Guideline development and targeting should include  
393 multidisciplinary experts and contain views from patients' organizations and a public  
394 consultation process. Guidance should be provided on dissemination and implementation,  
395 including what are the minimal standards of care for each level of the healthcare system.

396 Regarding implementation, guidelines should include what evidence the suggestions are based  
397 on. Suggestions based on studies from a country with very different context may not be  
398 implementable at all. Therefore, guidelines should include guidance on approaches to  
399 facilitate cultural adaptation and effective collaboration with vulnerable populations such as  
400 Indigenous people, particularly within colonized countries.

401 From a research perspective, more work on barriers and facilitators to effective  
402 implementation of guidelines in LMICs is required. This would include local data collection  
403 and strategies to facilitate local adaptation and implementation of evidence taking into  
404 account environmental, demographic, social, cultural, legal, and economic dimensions. In  
405 addition, guidelines should address the cultural needs of Indigenous populations in HICs  
406 where colonization has resulted in health inequities. Lastly, when guidelines are in place,  
407 frequent updating and monitoring of adherence to specific recommendation is essential.

408 Periodical auditing may facilitate improvement of adherence to guidelines and ultimately  
409 more cost-effective COPD care. Ultimately whether, after adjusting for income and other  
410 factors, countries with a national country-tailored guideline have better COPD health  
411 outcomes should be explored.

#### 412 *Strengths and limitations*

413 To our knowledge, this is the first global COPD guideline scoping review and informs future  
414 guideline development around the world as well as more targeted systematic reviews. Authors

415 and guideline reviewers represented all continents and made use of local understanding of  
416 clinical practice. Although extensive searches were performed, for some countries, general  
417 (non-communicable disease) treatment guidelines are in place that may include treatment of  
418 various chronic diseases, including COPD.<sup>21</sup> Also, guidelines that were published in English  
419 and traceable using online data sources had a higher likelihood of being included. For some  
420 guidelines, we could only find main documents and we may have therefore missed some  
421 specific recommendations only provided in appendices of the main document. GACD  
422 network members actively reached out to colleagues in countries for which no guidelines had  
423 been identified through online searches. Still, in some LMICs, we had no direct contacts,  
424 therefore the establishment of a wider network of contacts is required. Having this network in  
425 place would also allow for further qualitative, in-depth data collection on physicians'  
426 expectations and actual implementation barriers on a local practice level, and allows more  
427 targeted approaches to wide scale guideline implementation. It should however be mentioned  
428 that given many guidelines were only identified through the GACD network, it is not possible  
429 for independent researchers to obtain the set of guidelines used for our analysis simply by  
430 repeating the database searches with the exact search criteria. Also, we acknowledge that the  
431 AGREE-II tool is currently more commonly used to assess guideline quality. However, data  
432 items covered to largely overlap with the IOM standards.<sup>36</sup> As such, we do not expect that this  
433 part of the scoping review would have resulted in much different messages when the AGREE  
434 II tool would have been used instead. Regarding the content of COPD care covered by the  
435 country guidelines, we should acknowledge the review focus on broad COPD management  
436 guidelines but that in fact, for some aspects of COPD care, separate guidelines may be in  
437 place in some countries (e.g. exacerbation management). Finally, we note that a wide range of  
438 guideline publication dates were found (2005-2019). While we aimed to minimize potential

439 time-related differences by performing a sub-analysis for the IOM quality criteria in LMIC,  
440 this still warrants careful interpretation of the content of care comparisons.

#### 441 *Interpretation*

442 Several development, content and quality gaps exist in COPD guidelines from LMICs that  
443 may hamper large-scale effective implementation. Of note, COPD guidelines in LMICs  
444 should be more widely available and should be transparently developed and updated.

445 Furthermore, they may be enhanced by more focus on the inclusion of local risk-factors, case  
446 finding and comorbidity management, preferably tailored to financial and staff resources  
447 available.

448

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463 comments on the draft and approved submission. JvB is the guarantor of the study.

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- 562
- 563

564 **Figure legends**

565

566 **Figure 1:** World map showing countries with and without COPD guidelines

567 *Light blue: high- income country without country guideline; dark blue: high- income country with guideline; light red: low-*  
568 *and middle- income country without guideline; red: low- and middle- income country with guideline*

569

570 **Figure 2:** Overview of target audience of COPD guidelines around the world

571 *\*significant difference,  $p < 0.05$ ; GPs: general practitioners; HICs: high-income countries; LMICs: low- and middle-income*  
572 *countries*

573

574 **Figure 3:** Overview of coverage of COPD management recommendations met by COPD  
575 guidelines in high income countries and low-and middle-income countries

576 *\*significant difference,  $p < 0.05$ , HICs: high-income countries; inf: influenza; LMICs: low-and middle-income countries;*  
577 *pneu: pneumococcal*

578

579 **Figure 4:** IOM guideline quality standards met by COPD guidelines in high income countries  
580 and low-and middle-income countries

581 *HIC: high-income countries; IOM: Institute of Medicine; LMIC: low-and middle-income countries*

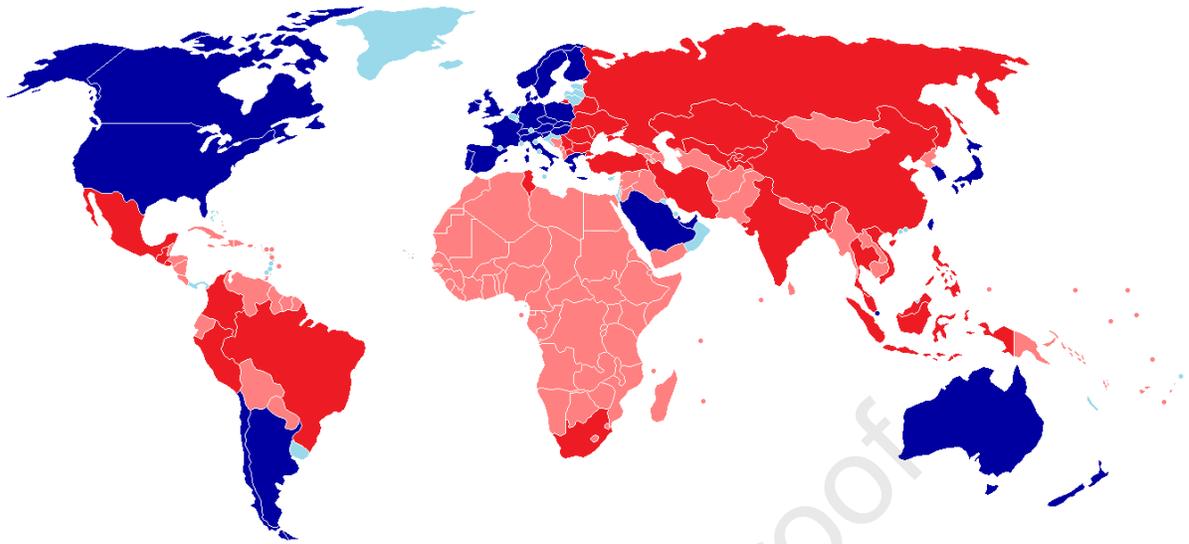
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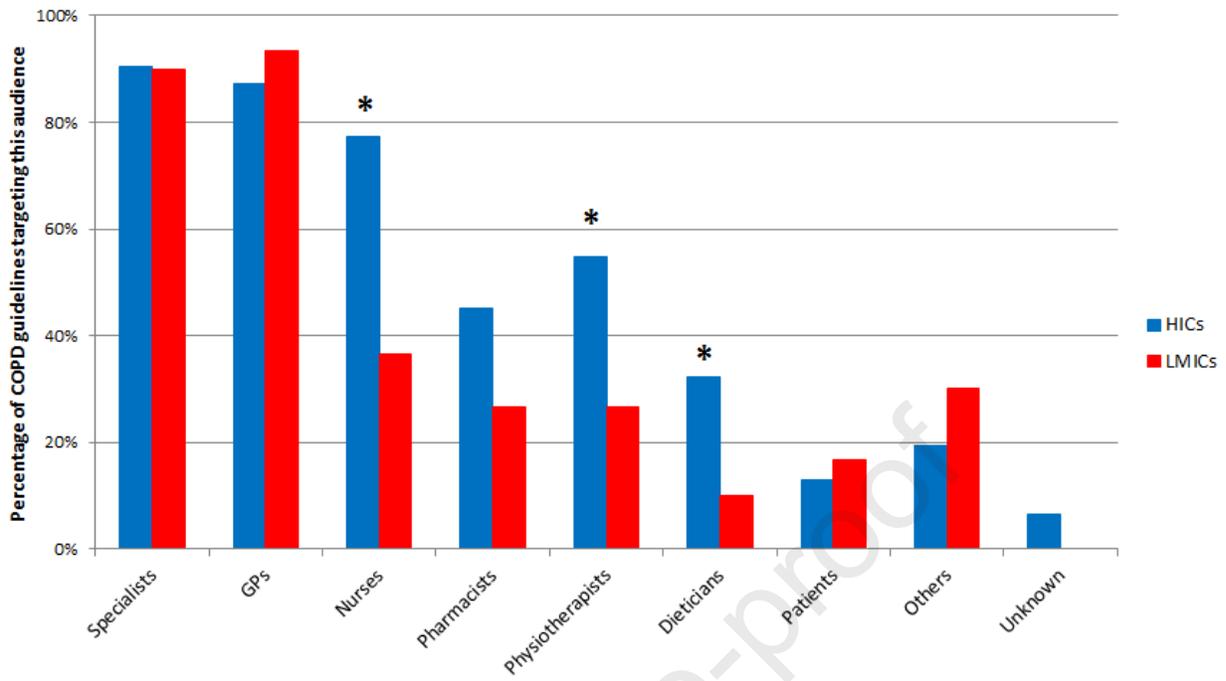
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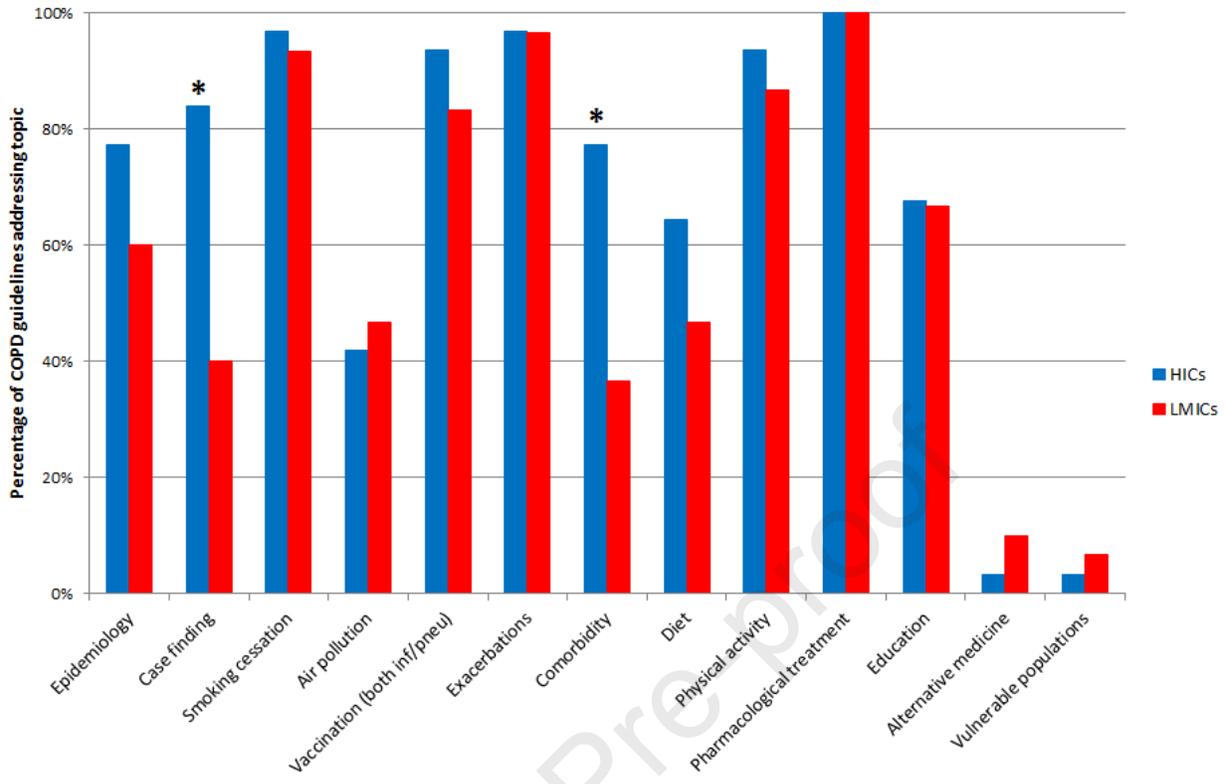
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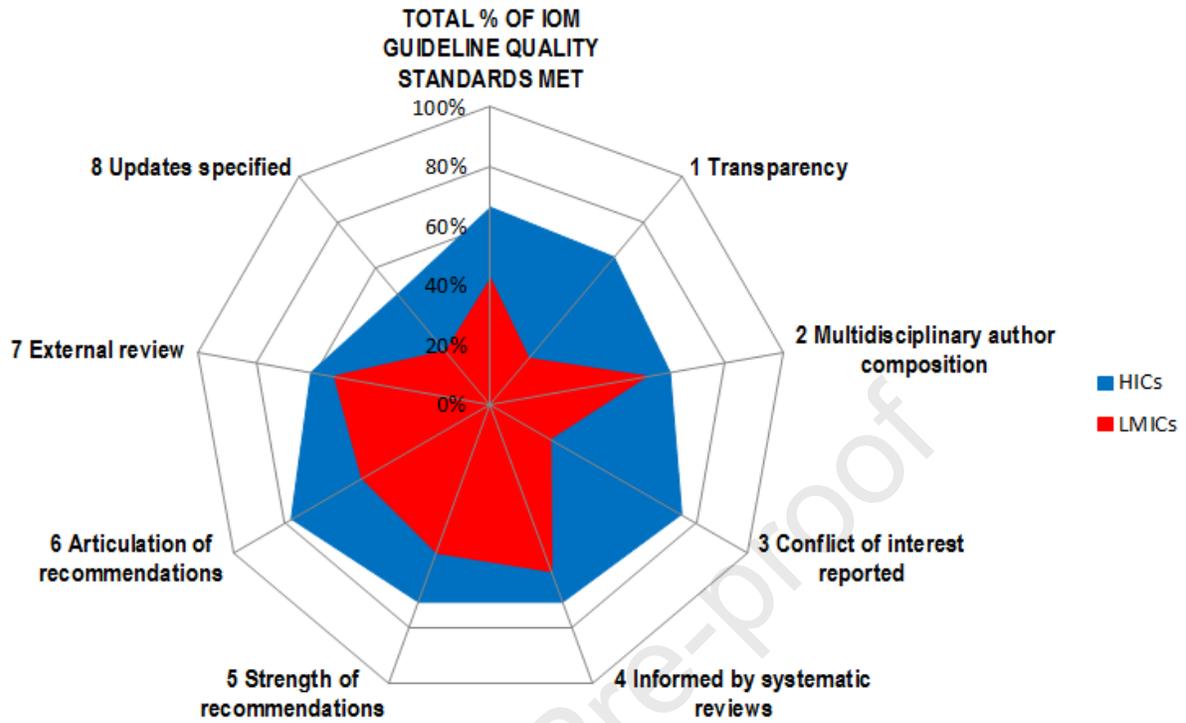
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586









## **Abbreviations list**

AHP: Allied health professionals

ALAT: Latin American Thoracic Association

COPD: Chronic obstructive pulmonary disease

GACD: Global Alliance for Chronic Diseases

GNI: Gross national income

GOLD: Global Initiative for Chronic Obstructive Lung Disease

GP: General practitioners

HIC: High-income countries

IOM: Institute of Medicine

LMIC: Low- and middle-income countries

OECD: Organization for Economic Cooperation and Development