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# 1 Healthcare as a driver and casualty of antimicrobial resistance: 2 Opportunities for interventions

3  
4 Derek Cocker<sup>†1,2</sup>, Gabriel Birgand<sup>†3,4,5</sup>, Nina Zhu<sup>4,6</sup>, Jesus Rodriguez-Manzano<sup>4,6</sup>, Raheelah  
5 Ahmad<sup>4,7,8</sup>, Kondwani Jambo<sup>2,9</sup>, Anna S. Levin<sup>10</sup>, Alison Holmes<sup>1,4,6</sup>

6 <sup>1</sup> David Price Evans Infectious Diseases & Global Health Group, University of Liverpool, Liverpool,  
7 UK

8 <sup>2</sup> Malawi-Liverpool-Wellcome Research Programme, Blantyre, Malawi

9 <sup>3</sup> Centre d'appui pour la Prévention des Infections Associées aux Soins, Nantes, France

10 <sup>4</sup> National Institute for Health and Care Research Health Protection Research Unit in Healthcare  
11 Associated Infections and Antimicrobial Resistance at Imperial College London, London, UK

12 <sup>5</sup> Cibles et médicaments des infections et de l'immunité, IICiMed, Nantes Université, Nantes,  
13 France

14 <sup>6</sup> Department of Infectious Disease, Imperial College London, London, UK

15 <sup>7</sup> Department of Health Services Research & Management, City, University of London, London, UK

16 <sup>8</sup> Dow University of Health Sciences, Karachi, Pakistan

17 <sup>9</sup> Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK

18 <sup>10</sup> Department of Infectious Disease, School of Medicine & Institute of Tropical Medicine,  
19 University of São Paulo, São Paulo, Brazil

20 <sup>†</sup>contributed equally:

21  
22 Corresponding author:

23 Prof Alison Holmes, NIHR Senior Research Investigator

24 Address: David Price Evans Infectious Diseases & Global Health Group, University of Liverpool,  
25 Liverpool, UK.

26 E-mail address: [alison.holmes@liverpool.ac.uk](mailto:alison.holmes@liverpool.ac.uk) (A. Holmes).

27  
28 **Abstract** | Antimicrobial resistance (AMR) is a global health challenge that threatens human,  
29 animal and environmental conditions. Evidence is emerging for the role healthcare infrastructure,  
30 environments and patient pathways play in promoting and maintaining antimicrobial resistance  
31 via direct and indirect mechanisms. Advances in vaccination and monoclonal therapies alongside  
32 integrated surveillance, rapid diagnostics, targeted antimicrobial therapy and infection control  
33 measures offer opportunities to address healthcare-associated AMR risks more effectively.  
34 Additionally, innovations in AI, data linkage and intelligent systems can be employed as  
35 overarching methods to better predict and personalise the fight against AMR. In this review, we  
36 examine the mechanisms by which healthcare acts as a driver, reservoir and amplifier of AMR  
37 contextualised within a One Health framework, and the opportunities and innovative solutions  
38 that can be employed to combat AMR throughout the patient journey. We provide a perspective  
39 on the current evidence base for interventions designed to mitigate healthcare-associated AMR  
40 and promote healthcare resilience within high-income and resource limited settings, in  
41 conjunction with the challenges to their implementation.

42  
43  
44

## 45 Introduction

46

47 Antimicrobial resistance (AMR) constitutes a present and ongoing risk to human life and  
48 healthcare resilience, threatening the safe provision of clinical care with an associated economic  
49 and societal impact <sup>1</sup>. Various human, animal and environmental factors play a role in driving AMR  
50 <sup>2</sup>, although, to date, the relative proportion of the global epidemiology of AMR attributed to each  
51 of these One Health sectors remains largely unknown. Variations in healthcare systems,  
52 structures, environments and processes, and their design and utilisation by staff and patients may  
53 promote the emergence and spread of AMR. The impact of these activities on AMR are seen  
54 beyond the frontiers of the healthcare system. For example, individuals acquiring resistant micro-  
55 organisms during their healthcare pathway serve as reservoirs for human-to-human transmission  
56 in healthcare and community settings <sup>3,4</sup>, and antimicrobials and antibiotic-resistant organisms  
57 (AROs) released from healthcare facility sewage can potentiate the spread of AMR into  
58 environmental and animal compartments <sup>5</sup>. In this regard, healthcare can act as a powerful driver  
59 and amplifier of AMR globally, with setting-specific risks.

60

61 For over two decades, concerted efforts have been made globally to improve infection  
62 prevention, diagnostic, and treatment options to mitigate AMR in healthcare. Although these  
63 efforts have produced some effect, AMR persists and is even progressing amongst patient  
64 populations, hampering our ability to curtail the AMR crisis globally. It is therefore imperative that  
65 the key role healthcare plays in the maintenance and transmission of AMR is better appreciated,  
66 and interventions, innovations and opportunities to address AMR are considered which also  
67 protect the delivery of safe healthcare <sup>6</sup>. Within this review, using the patient pathway as a focus,  
68 we evaluate the mechanisms by which healthcare acts as a driver, reservoir and amplifier of AMR,  
69 and present areas for innovation, illustrating how these can be implemented to prevent AMR,  
70 both within healthcare, and beyond healthcare networks. We describe how advances in  
71 surveillance, diagnostics, preventative-therapies and targeted antimicrobials, combined with  
72 novel approaches to the delivery of care and individualised medicine technologies, can be  
73 integrated across the patient journey to protect individuals and populations from healthcare-  
74 associated AMR. Interventions need to be tailored for the variable contexts globally, and methods  
75 to make assessments of relevance and fit are included along with barriers to actions and future  
76 challenges. Lastly, we highlight how adoption of these systems and approaches would strengthen  
77 our ability to deliver safe healthcare and promote healthcare resilience.

78

### 79 **[H1] The role of healthcare as a driver, reservoir and amplifier of AMR**

80

81 Healthcare is delivered across a range of settings, from informal care/self-care, rural health  
82 centres, community and social care facilities to tertiary hospitals. The design of health systems  
83 and healthcare infrastructure (Bismark, Beveridge, single/multi-payer national insurance, out-of-  
84 pocket or pluralistic) and resulting capacity, differs globally, with variation in financing and care  
85 delivery having implications for public/patient health seeking, healthcare professional

86 motivations and behaviours and governance approaches <sup>7</sup>. Healthcare serves as a continuum of  
87 processes and activities along a patient journey and can drive AMR through several interlinked  
88 mechanisms, influenced by a variety of contributing factors (**Figure 1**).

89

90 By its nature, healthcare brings people together within shared spaces and along pathways that  
91 expose them to risks of AMR transmission, either from patients or staff colonised with AROs <sup>8,9</sup> or  
92 contaminated environments <sup>10</sup>. Particular healthcare settings and pathways provide enhanced  
93 risks, congregating the most vulnerable individuals together, often with increased antibiotic  
94 exposures and high levels of environmental contamination <sup>11</sup>. For example, immunosuppressed  
95 patients, such as those undergoing chemotherapy for cancer or haematological malignancies  
96 frequently require antibiotics for sensitive or resistant infections <sup>12</sup> promoting AMR colonisation  
97 <sup>13</sup>. Antibiotic-induced overgrowth of ARO (e.g., *Enterobacteriales* in the gut microbiota) <sup>14</sup>  
98 associated with faecal incontinence and diarrhoea contribute to the subsequent dissemination of  
99 AMR into the healthcare environment <sup>15</sup>. Even short courses of antibiotics given to hospitalised  
100 patients can select for persistent gut colonisation of ARO over extended periods of time <sup>4,16</sup>. Once  
101 exposed to ARO, individual patient factors, such as those affecting the stability of their  
102 microbiome (e.g. severity of illness or immunosuppression) can trigger acquisition <sup>17,18</sup>.  
103 Modifications of antibiotic therapies (e.g., preferential use of narrower spectrum antibiotics) or  
104 therapies reducing the gastric acidity (e.g., avoidance of proton-pump inhibitors) may preserve  
105 the human microbiome <sup>17</sup>. Selective pressures exerted by antibiotics can drastically alter the  
106 ecological equilibrium of a patient's microbiota. By lowering the bacterial diversity they disrupt  
107 the resistance to colonisation of the microbiome <sup>19</sup>. This "dysbiosis" enables the colonisation by  
108 AMR organisms, with increased load, and dissemination of antimicrobial resistance genes (ARGs)  
109 (i.e., resistome). Antibiotic-resistant opportunistic pathogens and pathobionts can frequently  
110 persist asymptotically within an individual's microbiota, including hard-to-treat pathogens  
111 such as carbapenemase-producing *Enterobacteriales* (CPE) and vancomycin-resistant enterococci  
112 (VRE) <sup>20,21</sup>. This process of continuous pressure from healthcare-associated antibiotic exposures  
113 increases colonisation with ARO and amplifies resistance, leading to local outbreaks of AROs.  
114 Globally, neonatal units suffer a high burden from neonatal sepsis with resistant infections,  
115 particularly in resource-limited settings, and are increasingly recognised as hotspots for outbreaks  
116 of AROs <sup>23</sup>. Similarly, drug-resistant outbreaks are seen in intensive care units <sup>10</sup>, where patients  
117 are regularly prescribed broad spectrum antibiotics and frequently colonised with drug-resistant  
118 organisms <sup>24</sup>. Nosocomial transmission in these locations further amplifies resistance, and can be  
119 associated with factors such as invasive procedures or indwelling devices, mechanical ventilation,  
120 levels of staffing and workforce education <sup>25</sup>. Antimicrobial stewardship programmes represent a  
121 core element for the overall and individual-level reduction of selective pressure in hospitals <sup>22</sup>.

122

123 The proximity of individuals to ARO colonised patients represents a first exposure. In a study of  
124 patients treated in healthcare from across 41 European countries, 16.6% carried multi-drug  
125 resistant organisms (MDROs) varying from 12.1% to 38.1% <sup>26</sup>. Globally, higher rates of extended-  
126 spectrum beta-lactamase (ESBL) *Enterobacteriales* colonisation are generally found in healthcare

127 versus community settings<sup>27</sup>, with some studies in low-income settings showing particularly high  
128 levels within hospital cohorts<sup>28</sup>. Thus, the exposure and risk of acquisition of ARO can increase  
129 once admitted in hospital, and vary according to the local epidemiology, the type of setting (i.e.,  
130 a higher exposure in intensive care unit (ICU)), the type of care required, the severity of illness  
131 and the length of stay. Secondly, contamination of staff hands, gowns, gloves and equipment can  
132 potentially transmit ARO to patients<sup>29</sup>. Colonisation of healthcare workers (HCWs) with ESBL  
133 bacteria have been reported at rates between 4.6%–18.9%, likely to be equivalent to community  
134 exposure<sup>30</sup>. However, colonisation of staff with methicillin-resistant *Staphylococcus aureus*  
135 (MRSA) ranges from 17% to 20% in some settings and is recognised as a risk factor for patient  
136 acquisition. Thirdly, patients acquire bacteria from the environments in which they are situated,  
137 such as the hospital room during the first days of admission, and then transmit their own  
138 microbiota within the room during their stay<sup>31</sup>. Admission to a location which has previously been  
139 occupied by a patient infected or colonised with a specific pathogen therefore becomes a risk  
140 factor for acquisition<sup>32</sup>. Distinct ecological niches of microbes and antibiotic resistance genes co-  
141 exist, characterized by biofilm-forming and human-microbiome-influenced environments<sup>33</sup>. ARO  
142 can persist in hospitals for extended periods (>8 years), and opportunistically colonise and infect  
143 patients<sup>33</sup>. Some pathogens are predicated for the healthcare environment, colonising key  
144 surfaces (e.g., sinks/drains)<sup>34,35</sup> or hospital equipment<sup>10</sup>, and provide an environmental reservoir  
145 for AROs with direct links to patient infections<sup>34</sup>. Colonised individuals and contaminated  
146 healthcare environments can then serve as reservoirs of ARO, and healthcare settings in turn,  
147 become distribution centres<sup>36</sup>, amplifying ARO<sup>37</sup>, that can be recycled within healthcare settings  
148 <sup>3,10,34,36</sup> or dispersed into the community<sup>4,16</sup>.

149

150 Ineffectual or sub-optimal hygiene and infection control measures in healthcare settings provide  
151 human (i.e., hand-hygiene) and environmental (i.e., contaminated surfaces) factors that promote  
152 the exposure, transmission and acquisition of ARO / MDROs<sup>32,34</sup> and HCAs<sup>10,36</sup>. In resource  
153 limited settings, underfunding, inadequate staffing, absent or ineffectual infrastructure and lack  
154 of access to water sanitation and hygiene (WASH) facilities pose significant challenges to  
155 controlling environmental contamination and maintaining IPC practices, increasing the risks of  
156 HCAs<sup>38,39</sup>. HCAs are also an important driver of antibiotic usage. Within European hospitals, 1 in  
157 5 antibiotics are prescribed for infections directly acquired within healthcare premises<sup>40</sup>. HCAs  
158 caused by bacteria or fungi, such as staphylococcal, pseudomonal or *Candida* spp. are often highly  
159 resistant<sup>10,41</sup>, requiring the use of reserve antibiotics, longer hospital admissions<sup>41,42</sup> and are  
160 associated with increased mortality<sup>42</sup>. HCAs from viral aetiologies such as SARS-CoV-2 or  
161 influenza are associated with increased antibiotic exposures<sup>43</sup>, contributing to the generation of  
162 AMR through antibiotic-induced selection pressures<sup>44</sup>.

163

164 The movement of people through healthcare settings and across international borders can  
165 promote the transmission of AMR<sup>45</sup>. Transferring patients between beds and wards within  
166 healthcare can drive nosocomial outbreaks<sup>46</sup>. Nursing home residents, who themselves have high  
167 rates of antibiotic usage<sup>47</sup> and colonisation with MDRO, including increasing important fungi such

168 as *Candida auris*<sup>48,49</sup> are frequently transferred between hospitals and community settings, and  
169 this process can potentiate or sustain epidemics across the healthcare network<sup>3,48</sup>. International  
170 human movement, whether related to short-term travel, migration or through forcible  
171 displacement can be associated with high rates of AMR and HCAs<sup>50</sup>. Additionally, the operational  
172 aspects of healthcare systems can influence the spread of AMR within the healthcare network,  
173 especially when services designed to control AMR break down. This is impacted by a broad range  
174 of external drivers such as economic and human resource investment, conflict scenarios or the  
175 effects of climate change<sup>45,51,52</sup>.

176

177 The physical architecture and utilisation of the healthcare environment also impacts the spread  
178 of resistance<sup>53</sup>. Single rooms can reduce cross-transmission, and temperature, humidity, and  
179 hospital water sources effect contamination levels with ARO<sup>31</sup>. Animals, such as flies,  
180 cockroaches, rodents or geckos that interact with hospital environments may act as reservoirs or  
181 vectors of AMR transmission<sup>54</sup>. Lastly, the dispersal of hospital waste may impact downstream  
182 AMR risks. Hospital wastewater provides an outflow of resistance-driving chemicals such as  
183 antibiotics, biocides, and ARGs and AROs into the broader environment<sup>55</sup>. The precise role that  
184 hospital effluent plays in the maintenance and promotion of human AMR is unclear. Nevertheless,  
185 the failure of hospital sewage treatment to eradicate resistance-driving chemicals, ARGs and ARO  
186 in high-income settings, and limited sewerage treatment in resource-limited settings enable AMR  
187 entry into the food chain and contamination of drinking water<sup>55</sup> which may pose risks for onward  
188 transmission<sup>56</sup>.

189

190 **[H1] Use of vaccines and immunotherapy to prevent healthcare-associated**  
191 **infections and minimise AMR.**

192

193 **[H2] Vaccines**

194

195 Vaccines impact AMR through the prevention of infections associated with antimicrobial usage or  
196 the reduction in the incidence of disease by sensitive or resistant pathogens, via direct or indirect  
197 protection, without major side effects<sup>57,58</sup>. The most common cause for inappropriate  
198 antimicrobial prescribing comes from vaccine preventable respiratory diseases, such as influenza,  
199 COVID-19 or respiratory syncytial virus (RSV)<sup>59</sup>. In the recent pandemic, up to three-quarters of  
200 patients with COVID-19 received an antibiotic, despite the absence of data supporting a coexisting  
201 bacterial or fungal coinfection<sup>43,60</sup>. Pre-COVID-19 pandemic, RSV accounted for ~10% of antibiotic  
202 prescribing in primary care in the UK, amounting to >400,000 antibiotic prescriptions annually<sup>61</sup>.  
203 Optimisation of vaccination coverage can provide a simple method for preventing attributable  
204 deaths, and reducing unnecessary antibiotic use within patients situated in community and  
205 healthcare settings, with the largest impact felt in low-resource settings<sup>62</sup>.

206

207 In low- and middle-income countries (LMICs), inappropriate healthcare-associated antimicrobial  
208 prescriptions are also commonly seen in the treatment of malaria, typhoid, and arboviral  
209 infections <sup>63,64</sup>. Large-scale campaigns for safe and efficacious typhoid conjugate vaccines,  
210 intelligent use of malaria and dengue vaccines are being considered to reduce AMR through  
211 inappropriate prescribing <sup>65,66</sup>. Gastrointestinal infections, which account for 29.3% of diarrhoea-  
212 related deaths in young children in resource-limited settings are of key importance <sup>67</sup>. Here, the  
213 implementation of rotavirus vaccination protects against severe disease <sup>68</sup> and its rollout is  
214 currently estimated to prevent 13.6 million episodes of antibiotic-treated illness annually among  
215 children <5 years old <sup>69</sup>. The rotavirus vaccine also provides an excellent example of how vaccines  
216 can prevent healthcare attendance and admissions, including indirect protection of non-  
217 vaccinated individuals within the community <sup>70</sup>. Vaccine-induced reduction in healthcare  
218 attendance has been seen for a range of vaccines and can limit exposure risks to HCAI and  
219 antibiotic usage, reduce AMR transmission in hospital and community settings, and improve  
220 healthcare functionality <sup>59,71</sup> (**Figure 2**).

221

222 Vaccines that target bacterial pathogens harbouring drug-resistant strains of global importance,  
223 such as *Streptococcus pneumoniae* and *S. aureus*, are also available. Pneumococcal conjugate  
224 vaccines (PCVs) rollout has been well evidenced to reduce antibiotic usage <sup>72</sup>, lower rates of  
225 antibiotic-resistant invasive pneumococcal infections in children, and reduce non-susceptible  
226 invasive infections in populations in both high- and low-income countries <sup>73</sup>. However, the effect  
227 of PCVs on AMR has been complicated by the emergence of non-susceptible serotypes, and high  
228 residual carriage rates in low-resource settings <sup>74</sup>. Novel *Klebsiella pneumoniae* and *Neisseria*  
229 *gonorrhoeae* vaccines are in clinical trials <sup>75</sup>, alongside vaccines in the development pipeline  
230 against gram-negative bacteria <sup>75,76</sup> or *Mycobacterium tuberculosis* <sup>76</sup>. For *Clostridium difficile*, the  
231 goal of obtaining a preventive vaccine seems to be near <sup>77</sup>, and the results of large advanced phase  
232 trials will provide information on their effectiveness, cost and tolerance.

233

234 Vaccines offer an effective method to decrease the overall burden of HCAs and associated use of  
235 antimicrobials, whether this is from viral (e.g., influenza and COVID-19), or bacterial (e.g., *C.*  
236 *difficile*, *S. aureus* and gram-negative pathogens) aetiologies <sup>78</sup>. Vaccination can take place pre-  
237 admission, throughout attendance or during periods of follow-up. Hospitalisation provides a  
238 unique opportunity to track unvaccinated cases <sup>79</sup>, especially in vulnerable groups. Targeted  
239 vaccination could be incorporated with intelligently-designed surveillance systems, integrated  
240 with advances in diagnostic technologies to prevent AMR (**Figure 2**). Vaccines can also be used in  
241 surgical populations to reduce post-operative infections with sensitive or resistant *S. aureus* and  
242 associated antimicrobial usage. Whilst historical trial data on *S. aureus* vaccines has not yet shown  
243 efficacy in reducing *S. aureus* infections amongst surgical cohorts, the use of novel vaccine  
244 candidates (e.g., SA4Ag) in elective populations is still attractive, and ongoing trials of these  
245 candidates is warranted <sup>80</sup>. The pre-operative phase is critical, and intelligently designed pre-  
246 operative pathways that integrate screening and targeted-vaccination is needed. This period also

247 provides an opportunity to recover missed opportunities for SARS-CoV-2 <sup>81</sup>, influenza virus and  
248 pneumococcal vaccinations in vulnerable populations, with pre-operative influenza vaccination  
249 shown to reduced episodes of pneumonia and in-hospital mortality <sup>82</sup>. Ultimately, improved  
250 vaccine uptake will assist with elective surgical system strengthening and surgical preparedness  
251 <sup>83</sup>.

252

253 The recent COVID-19 pandemic highlighted how vaccines can limit stresses on a healthcare-  
254 resources and improve health system resilience. COVID-19 disruptions to antimicrobial  
255 stewardship and IPC services impacted the ability to control AMR and provide good clinical care  
256 <sup>84</sup>. Occupational exposures to infections lead to negative effects on the health and wellbeing of  
257 HCWs <sup>85</sup>, and opportunities to optimise vaccination in this group could avoid preventable disease,  
258 avert transmission of HCAIs <sup>86</sup>, and improve health-system resilience via reduced staff absence  
259 <sup>85,87</sup>. Overall, innovations that prioritise and improve vaccination availability and uptake in HCWs,  
260 given the hesitancy amongst HCWs, will enhance patient care, reduce HCAIs and associated  
261 antimicrobial usage, whilst simultaneously improving healthcare resilience via staff protection  
262 and economic efficiencies.

263

## 264 [H2] Immunotherapy

265

266 Preclinical pipelines for antimicrobials highlight a growing number of monoclonal antibody (mAb)  
267 programmes for infectious disease <sup>88</sup>. Reverse vaccinology technology is being used to discover  
268 therapeutic mAbs against AMR-bacteria <sup>89</sup>, and more than 20 mAbs against bacterial pathogens  
269 are reaching efficacy evaluation <sup>89</sup>, suggesting that mAb may provide a creative alternative in the  
270 future. Monoclonal antibodies currently in clinical development include those targeted against *S.*  
271 *aureus* and *Pseudomonas aeruginosa* for prevention or adjunctive treatment of pneumonia or  
272 adjunctive treatment of bloodstream infections <sup>90</sup>. Other antibodies have been approved for  
273 clinical use include those active against *Clostridium botulinum*, *C. difficile* <sup>91</sup> and *Bacillus anthracis*  
274 <sup>90</sup>.

275

276 Like vaccination, mAbs have the potential to impact AMR via a reduction in HCAIs and the  
277 incidence and length of infectivity for diseases associated with antibiotic usage <sup>92</sup> alongside a  
278 reduction of ARO colonisation and disease <sup>89,93</sup> (**Figure. 2**). Monoclonal antibodies have the added  
279 benefit of being able to generate immediate immune responses, unlike vaccines which require  
280 time and competent immune systems; factors which are often lacking in hospitalised patients <sup>94</sup>.  
281 The targeted nature of their design also enables them to be less toxic to patients or disruptive to  
282 the microbiome than small molecules <sup>93</sup>. Therefore, their use as prophylactic or therapeutic  
283 treatment for bacterial infection, particularly in key vulnerable groups, provides an exciting  
284 avenue for reducing healthcare-associated AMR <sup>31</sup>.

285

286 **[H1] Combined advances in rapid diagnostics, screening and surveillance, and**  
287 **intelligently-targeted antimicrobial prophylaxis and therapy.**

288

289 Point-of-care testing (POCT) and novel molecular diagnostics play a pivotal role in transforming  
290 how infections are diagnosed and treated. These technologies enable rapid identification of  
291 pathogens<sup>95,96</sup> and their antimicrobial resistance profiles<sup>97</sup>, and offer the promise for healthcare  
292 providers to make timely, informed decisions at the bedside. By facilitating quick and accurate  
293 diagnoses, these tests contribute to reducing unnecessary antimicrobial usage and enhancing  
294 antimicrobial optimisation, thereby mitigating the selective pressure driving AMR<sup>98,99</sup>. POCTs  
295 which differentiate between viral and bacterial infections are an example of a proposed solution  
296 in combatting AMR, and the use of rapid-diagnostic tests (RDTs) is recommended by a number of  
297 authorities<sup>100,101</sup>. The introduction of rapid POCT for respiratory microbes has been shown to  
298 reduce prescriptions in viral respiratory illness<sup>102</sup>. Additionally, molecular tests targeting specific  
299 pathogens, like MRSA or *Streptococcus pyogenes*, enable precise identification and tailored  
300 treatment, avoiding unnecessary broad-spectrum antibiotics<sup>103,104</sup>. Antimicrobial stewardship is  
301 enhanced through the use of rapid POCTs for malaria<sup>63</sup> or arboviruses<sup>105</sup> in travellers and  
302 endemic settings. AI-guided analysis of radiological imaging can also be implemented to optimise  
303 infection diagnosis in low-resource settings<sup>106</sup>, improving antimicrobial stewardship and  
304 surveillance. Lastly, the use of POCTs can reduce AMR through indirect mechanisms, and their  
305 uptake has been associated with prevention of hospital admissions, helping to control outbreaks  
306 and reducing healthcare costs<sup>105,107–109</sup>.

307

308 Within laboratory settings, rapid AMR diagnostics can be used to augment traditional  
309 antimicrobial susceptibility testing, and ongoing research in this field is focused on novel  
310 techniques, such as microfluidics, spectroscopy, mass-spectrometry and WGS<sup>97,110,111</sup>. POCT and  
311 AMR diagnostics can also be fed back to clinical decision-makers through easy-to-interpret  
312 innovations, such as smartphone applications or data platforms, further optimising antimicrobial  
313 stewardship<sup>112</sup>.

314

315 Advancements in precision medicine offer opportunities to optimise antimicrobial usage through  
316 tailored therapies and prophylaxis<sup>113</sup>. Tailored antimicrobial prescribing involves the selection of  
317 specific agents based on the patient's individual characteristics, including their microbiome,  
318 genetic makeup, and susceptibility patterns, and can be targeted at key AMR pathogens in  
319 hospital settings<sup>114</sup>. This approach ensures that the chosen antimicrobial is effective against the  
320 identified pathogen and minimises collateral damage to the patient's commensal flora. This  
321 process can also be dovetailed with diagnostic information to guide antimicrobial selection,  
322 dosing, and duration using intelligent data linkage systems.

323

324 Precision antimicrobial prescribing relies on the accurate identification of pathogens and their  
325 susceptibility patterns. However, challenges exist in rapidly determining antibiotic concentrations  
326 to enable dose optimisation, especially in critically ill or overweight patients <sup>115</sup>. Technological  
327 solutions, such as continuous monitoring of antibiotic levels in real-time, are needed to overcome  
328 these challenges <sup>116</sup>. Studies have shown that precision prescribing, involving selection, dosing  
329 and duration of antibiotic, may help prevent CPEs and associated hospital-acquired infections,  
330 and play a role in infection prevention and control strategies <sup>114</sup>. Additionally, innovations in  
331 wearable devices, sensors and smart technologies could provide a means to achieve this, ensuring  
332 that antibiotic doses are tailored to the patient's specific needs, thereby minimising the risk of  
333 under- or over-dosing <sup>117</sup>. Improved targeting of prophylaxis, particularly in pre-surgical settings,  
334 can contribute to AMR mitigation. Rather than administering broad-spectrum prophylactic  
335 antibiotics routinely, tailored prophylaxis considers the patient's individual risk factors and the  
336 anticipated pathogens associated with a specific surgical procedure. This strategy reduces  
337 unnecessary exposure to antibiotics and the subsequent risk of resistance development <sup>118</sup>.

338

339 To maximize the impact of rapid diagnostics and screening, it is essential to integrate these  
340 technologies seamlessly along the patient pathway <sup>11,119</sup>. This integration spans pre-hospital  
341 attendance, inpatient treatment algorithms, and community-based screening and surveillance  
342 pathways. For instance, pre-hospital diagnostic tools can aid emergency medical personnel in  
343 identifying infectious agents promptly, influencing initial treatment decisions even before hospital  
344 admission <sup>120</sup>. In hospitals, the incorporation of rapid diagnostics into treatment algorithms  
345 ensures timely and targeted interventions <sup>121</sup>. Community-based screening and surveillance  
346 programs, supported by advanced molecular tests, enhance the early detection of infectious  
347 diseases, enabling proactive measures to contain their spread <sup>122</sup>. In LMICs, patient pathways  
348 informed by health and/or treatment seeking behaviours contribute to a repetitive cycle of  
349 antibiotic consumption, exacerbating AMR <sup>123</sup>. Within these settings, improved access to  
350 diagnostics and refinement of healthcare pathways are likely to be paramount to address the  
351 overuse of antibiotics <sup>123</sup>. Lastly, we should be mindful of the vulnerabilities in patient pathways,  
352 with regards to fragmented care structures and inefficient resource allocation, and future  
353 pathways should be developed that take a whole health economy approach that spans across  
354 health sector boundaries <sup>11,124</sup>.

355

356 **[H1] Opportunities to minimise reservoirs, improve IPC and limit environmental**  
357 **contamination.**

358

359 The prevention and minimisation of AMR reservoirs among hospitalised patients is paramount.  
360 Antimicrobial stewardship which avoids unnecessary antimicrobial therapy, shortens  
361 antimicrobial duration as much as possible, and favours antibiotics with low anti-anaerobe activity  
362 can prevent dysbiosis, acquisition and overgrowth of ARO <sup>125</sup>. More personalised approaches can  
363 be used to emphasise these efforts, such as applying targeted drug delivery approaches to the

364 infected sites<sup>126</sup>, pathogen or species-specific drugs<sup>127</sup>, or drug combinations to antagonise the  
365 activity against commensal species. These evolutions are dependent on advances in rapid  
366 pathogen detection technologies and big data analytics. Antibiotic adsorbents or administration  
367 of enzymes (e.g.,  $\beta$ -lactamase) represent interesting strategies to mitigate the collateral damages  
368 of antimicrobial therapy on the gut microbiota<sup>128,129</sup>, and the targeted administration of live  
369 bacteria can preserve colonisation resistance, favour microbiota resilience or decolonise patients.  
370 Faecal microbiota transplantation (FMT)<sup>130</sup> or probiotics have been trialled, to variable effect  
371<sup>131,132</sup>. These modalities have been evidenced to increase gut microbial diversity and improve  
372 sustained CPE eradication, although their effectiveness for intestinal decolonisation, applicability,  
373 and safety are still to be confirmed. Selective decontamination of the digestive (SDD) tract has  
374 shown benefits in lowering rates of ARO infections in low-prevalence settings<sup>133</sup>. The lack of  
375 evidence on SDD effectiveness and long-term side effects has led to its use not being  
376 recommended in gram-negative *Enterobacteriales* carriers to control the AMR reservoir amongst  
377 hospitalised patients<sup>134</sup>. Early evidence exists for bacteriophage therapy providing sustained  
378 decolonisation with AROs, such as Carbapenemase-producing *Klebsiella pneumoniae*<sup>135</sup>.  
379 However, further research is needed to examine the role of bacteriophages in decolonisation,  
380 alongside the technical capacities and costs to develop these customised therapies. Safer and  
381 simpler, the patient diet with high-fibre nutrition seems promising in microbiome resilience, ARO  
382 implantation and expansion<sup>136</sup>.

383

384 The hospital microbiome harbours a significant, uncharacterised diversity of ARG combinations  
385 and represents a fertile ground for the evolution of AMR. The microbiota community composition  
386 and ARO abundance on hospital surfaces is site-specific<sup>137</sup>, dynamic according to patient  
387 occupancy, and subject to modifications of the built environment (e.g., renovations)<sup>138</sup>. Sink  
388 drains, for example, are a major reservoir for ARO with direct links to patient infections<sup>139</sup>. The  
389 rapid development of *P. aeruginosa* colonisation and its association with patient infections  
390 emphasises the need for future work to decrease the spread of AROs in hospital built-  
391 environments, complemented by efforts towards decolonising and eliminating sink drain AMR  
392 reservoirs<sup>139</sup>. Plasmid-mediated transmission accounts for 50% of CPE acquisition in hospitalised  
393 patients<sup>140</sup>, and clonal and plasmid-mediated transmission may be differentially affected by  
394 existing infection prevention and control measures. Plasmid CPE transmission and persistent  
395 carbapenemase gene reservoirs in the hospital will need to be considered in future research.  
396 Developing and using anti-plasmid agents could be a complementary strategy to curb the spread  
397 of ARGs through hospital environments<sup>141</sup>.

398

399 Compliance with environmental cleaning and disinfection processes and reprocessing measures  
400 of medical goods (e.g., bed pans) influences the level of environmental contamination<sup>142</sup>.  
401 Traditional cleaning methods are notoriously inefficient for decontamination<sup>143</sup>, and innovative  
402 technologies such as disinfectants, steam, automated dispersal systems, and antimicrobial  
403 surfaces offer an alternative strategy for environmental hygiene purposes<sup>144</sup>. Hydrogen peroxide  
404 vapour or ultraviolet devices demonstrate effectiveness in reducing the incidence of *C. difficile*,

405 VRE and hospital-onset gram-negative bloodstream infections <sup>145,146</sup>. Aside from the costs of  
406 equipment, the wide variability of impact among hospitals highlights the need for clear  
407 implementation strategies that consider the training, management, personnel, and logistical  
408 complexities to maximise effectiveness <sup>147</sup>. The utility of antimicrobial surfaces needs urgent and  
409 considered attention including evaluation of the resources and economic investment required for  
410 installation, durability, possible toxicity, resistance, and allergenic properties, alongside which  
411 sites and surfaces to coat, and the relative contribution of self-disinfecting surfaces toward hand  
412 contamination. Systematic metagenomic surveys of the hospital microbiome providing detailed  
413 measures with reference maps and visualisation of variations in human influence scores may offer  
414 an opportunity to target resources and fine-tune cleaning practices.

415

416 Compliance of staff with standard precautions (mainly hand hygiene and excreta management)  
417 and personal hygiene by patients are universally applied to reduce a broad range of risks, including  
418 the hidden ARO reservoir <sup>142</sup>. The use of alcohol-based hand rub has been shown to improve HCW  
419 compliance, reducing HCAI rates and ARO transmission <sup>148</sup>. Despite significant improvements,  
420 innovative methods addressing both the quantitative and the qualitative aspects of hand hygiene  
421 are required <sup>149</sup>. Reduction in the burden of ARO present on patients' skin may reduce  
422 transmission by decreasing the contamination on health care workers' hands. Multiple large trials  
423 have shown that universal body surface decolonisation of patients with chlorhexidine bathing and  
424 nasal mupirocin can significantly reduce ARO prevalence in high-risk settings and long-term acute  
425 care facilities <sup>150</sup>. However, its widespread use over many decades, has raised questions about  
426 chlorhexidine resistance, coincident biocide resistance and clinically relevant antibiotic resistance  
427 <sup>151</sup>. Importantly, the implementation of standard precautions requires an adequate built  
428 environment with IPC and WASH factors providing complementary opportunities for  
429 interventions at health facilities, both during outbreaks and in non-outbreak situations<sup>39</sup>.

430

431 Surveillance of ARO in healthcare facilities is complicated by the diffuse nature of AMR  
432 epidemiology, pathogen heterogeneity and predilection for particular subtypes transmitting and  
433 persisting within hospitals <sup>152</sup>. The real-time use of whole genome sequencing (WGS) in healthcare  
434 may allow IPC teams to identify transmission, target interventions, and provide surveillance and  
435 infection control benchmarking <sup>153</sup>. The use of patient-level microbiome or metabolome data to  
436 predict and assess an AMR reservoir in hospitals is of utmost importance. Functional  
437 metagenomics and long-read sequencing offer perspectives to better characterise the  
438 proliferation of mobile gene elements within (human) and across (human and environment)  
439 microbiomes, and presents new opportunities and challenges for pathogenome and resistome  
440 monitoring <sup>154</sup>. They are an invaluable resource as we move toward a future of microbiome-  
441 directed methods of identifying and preventing the spread of AMR and infection (e.g., routine  
442 assessment of patient's microbiome before antimicrobial therapies, abundance, and clearance of  
443 ARO carriage). Targeted screening, for example, in travellers and patients repatriated from  
444 endemic regions can be a beneficial strategy <sup>155</sup>. The prompt identification of these patients and  
445 rapid assessment of the risk of ARO carriage may prevent in-hospital transmission and

446 amplification of the AMR. Additionally, patients who acquire ARO during hospitalisation can  
447 contribute to onward spread in the community <sup>156</sup>, with a high frequency of acquisition and  
448 transmission events occurring early after discharge. Educating ARO colonised patients and carers  
449 about key hygiene measures may prevent transmission in community settings. Equally, admission  
450 screening for patients known to have ARO colonised household or nursing home contacts should  
451 be considered, given intra-household community transmission <sup>157</sup>. The current gap in predicting  
452 ARO carriage at hospital admission may be solved by the availability of artificial intelligence (AI)  
453 and health data hubs <sup>158</sup>.

454

455 New methods based on the microbiologic analysis of wastewater appear a promising option to  
456 accurately identify, quantify and describe the epidemiology of the AMR in healthcare settings <sup>159</sup>.  
457 Sewage monitoring represents a valuable modality for early warning of emerging ARO in low  
458 prevalence settings <sup>160</sup>, and might be able to estimate the prevalence of ARO at a population level,  
459 simultaneously sampling healthcare, nursing homes and community-associated populations <sup>161</sup>;  
460 avoiding biases in current surveillance methods. Additionally, large amounts of antimicrobials and  
461 ARO are dispersed in wastewater and the broader environment. Whilst their contribution to the  
462 global ARO epidemiology still needs to be ascertained, innovative and cheap wastewater  
463 treatment processes should be developed to eliminate ARO from hospital effluents.

464

465 Finally, measures that assist in coordination of IPC measures alongside oversight and  
466 management of antibiotic use, healthcare facility connectivity and patient transfers at a regional  
467 scale are important avenues for innovation <sup>162</sup>. Coordinated responses in the prevention of ARO  
468 spread across interconnected healthcare facilities has been shown to reduce ARO acquisitions  
469 over time <sup>163</sup>. Mathematical models of healthcare networks may also serve to identify facilities  
470 which serve as reservoirs for the spread of ARO at a large scale <sup>162</sup>, and inform decision-makers  
471 on priorities for the surveillance and IPC efforts.

472

## 473 **[H1] Innovations in data linkage, intelligent systems and AI**

474

475 Intelligent systems provide many avenues to benefiting AMR in healthcare (**Figure 3**). Access to  
476 healthcare data has dramatically increased with the use of electronic health record (EHR) systems  
477 and interconnected devices, giving rise to the age of “big data” <sup>164</sup>. The complex nature of AMR in  
478 healthcare requires linking data of drug-resistant pathogens, characteristics of patients, social  
479 demographic environments, and health systems and services contexts. At the patient level,  
480 routine EHRs can be linked with antimicrobial usage and AMR data for hospitalised inpatients.  
481 Population-level linkage of administrative data and EHRs have started to emerge <sup>165</sup>, and more  
482 recently, whole genome sequencing data has been linked with laboratory and clinical data to form  
483 national-level integrated genomic surveillance of AMR <sup>166</sup>. These linked datasets not only allow  
484 genotypic and phenotypic characterisation of AMR, but also enable the assessment of emergence  
485 and transmission pathways, care quality and outcomes for drug-resistant infections, and social

486 and health-system determinants of AMR burden. Although data protection must be addressed,  
487 risk/benefit evaluations should be performed to ensure that data access and availability is  
488 preserved.

489

490 Ideally, AMR data would be integrated across settings of human health systems (i.e., primary,  
491 secondary, and social care), across One Health domains (i.e., human, animal, agricultural, and  
492 aquaculture), and across data types (i.e., isolate-based genomic and pathogen data, patient-based  
493 demographic and clinical data). Examples of data integration are seen in recent research  
494 methodologies<sup>167</sup> including the World Health Organisation-funded Tricycle project, which  
495 provides a holistic, multisectoral approach to monitor ESBL-producing *Escherichia coli* derived  
496 from human, food, and environmental sources using whole genome sequencing<sup>168</sup>. Research  
497 must be done to understand and develop the minimum dataset prior to implementation, and  
498 novel methods, such as simulation and systems dynamics modelling, allow the development and  
499 piloting of the minimum dataset in an iterative manner by engaging policy makers, data  
500 generators and users<sup>169</sup>. To overcome ethical issue regarding AMR data sharing, online platforms  
501 such as Trusted Research Environments (TREs) provide real-time feeds from local laboratories,  
502 patient and hospital operational data enabling the rapid reporting of AMR and HCAI trends to  
503 local IPC personnel<sup>170</sup>. TREs can access and analyse de-identified data, and benefit from AI-driven  
504 automated pseudonymisation processes, minimising time delays, and enabling cloud-based  
505 solutions for data storage and accessibility in low-resourced settings<sup>171</sup>.

506

507 Optimal analysis and interpretation of complex health datasets can be enhanced by supervised or  
508 unsupervised machine learning (ML) tools<sup>172</sup> providing patient-specific assessments to better  
509 predict and prevent HCAI or to optimise antimicrobial treatment with personalised approaches  
510 for better individual outcomes and lesser impact from AMR<sup>173</sup>. Precision infection-prevention is  
511 the next frontier in infection prevention<sup>174</sup>. ML algorithms that incorporate EHRs and surveillance  
512 data can efficiently identify demographic data, select laboratory values, diagnoses, medications  
513 and vital signs, and help prioritise IPC interventions for patients at greatest risk of HCAI<sup>175</sup>. AI  
514 hand-hygiene applications can deliver behaviour change, though it requires further evaluation in  
515 different clinical settings<sup>176</sup>. ML tools using dynamic contact networks are able to identify patients  
516 who are most at risk of developing COVID-19 or *C. difficile* infections while in hospital<sup>177</sup>. In clinical  
517 practice, a ML-based tool could support prophylactic measures, earlier diagnosis, and timelier  
518 implementation of IPC measures<sup>178</sup>. In addition to improving effectiveness, the implementation  
519 of AI may significantly reduce the time spent by IPC team reviewing clinical records manually for  
520 HCAI surveillance<sup>179</sup>.

521

522 Innovations in pathogen and genomic surveillance can be enhanced by ML systems<sup>180</sup>, and their  
523 application in AMR surveillance is of vital importance<sup>181</sup>. ML systems have shown promise in  
524 analysing metagenomic data to predict antibiotic-resistant genes from humans and  
525 environmental sources, such as hospital wastewater<sup>182</sup>, which could provide improved  
526 surveillance of ARG dissemination and transmission pathways. AI can provide source identification  
527 and early warning of AMR outbreaks in healthcare networks<sup>183</sup>. AI-assisted automated data  
528 mining of EHRs is able to detect hidden transmissions and outbreaks of AMR pathogens early and

529 cost-effectively<sup>184</sup>. These methods have even shown the resolution to identify a specific source,  
530 for example, a contaminated gastroscope in the case of an *Pseudomonas aeruginosa* outbreak<sup>185</sup>.  
531 These measures could be further explored to improve efficiencies and targeting of IPC services in  
532 healthcare.

533

534 The use of ML to improve pathogen identification and phenotypic or genotypic AMR profiles is  
535 attractive<sup>186</sup>. To date, a number of ML systems have been shown to predict antibiotic resistance  
536 from genomic and metagenomic data for a number of key bacterial species, such as *E. coli* and  
537 MRSA<sup>182</sup>. Additionally, ML technology has been linked with matrix-assisted laser  
538 desorption/ionization–time of flight (MALDI-TOF) mass spectra data in the laboratory to rapidly  
539 identify AMR in clinically important pathogens, accelerating timing of antimicrobial optimisation  
540<sup>187</sup>. Low-resource options for AI integration into the laboratory also exist. This is exemplified by  
541 the use of AI-based mobile phone technology which enables automatic reading of disk diffusion  
542 antibiotic susceptibility testing, highlighting that AI technologies already have a global reach<sup>188</sup>.  
543 These systems can be integrated into cloud-based technologies, automatically forwarding to  
544 international systems of pathogen surveillance, enhancing the tracking of global AMR in  
545 healthcare.

546

547 ML-Clinical Decision Support Systems (ML-CDSS) have been trialled to improve choices of  
548 antimicrobials in sepsis<sup>189</sup> primary care prescriptions<sup>190</sup>, and hospital AMS programs<sup>191</sup>. These  
549 systems are still in their infancy with limitations in their utility relating to the quality of information  
550 inputted (e.g, absence of clinical or therapeutic history, isolate antimicrobial susceptibility or local  
551 resistance epidemiology) and the outputs generated (e.g, need for dose, duration and allergy  
552 status). Nevertheless, their ability to identify inappropriate prescriptions compared to expert  
553 systems have been shown<sup>191</sup>, and further trialing of newer ML-CDSS in real-world clinical settings  
554 should be explored, with reporting of clinical and/or microbiological outcomes and their impact  
555 on AMR in healthcare.

556

557 Recognizing that much of healthcare is delivered in environments without experts in infectious  
558 diseases, antimicrobial stewardship, microbiology and infection prevention, virtual platforms  
559 based on ML and AI may be leveraged to assist rural environments and low-resource settings  
560 through real-time, expert consultation<sup>192</sup>.

561

## 562 **[H1] Feasibility, tailoring to context, and prioritising**

563 Health and wider systems present variable barriers and opportunities which decision-makers  
564 must assess through engagement with relevant stakeholders across One Health sectors,  
565 depending on the scale of implementation and innovation type<sup>193</sup> Most innovations require  
566 behavioural change or are behavioural in nature, and require trial and tailoring<sup>194</sup>.

567

568 Defining and measuring impact must also be tested for feasibility and appropriate structures  
569 strengthened. Prioritisation of AMR outcomes of interest (e.g., AMR transmission, AMO,

570 morbidity, mortality, economic and ecological) is necessary to inform policy. Many AMR domains,  
571 such as antimicrobial optimisation require an interdisciplinary consensus to achieve equitable,  
572 scalable, economically viable and contextually appropriate interventions, that can utilise data  
573 across a range of healthcare settings <sup>195</sup>. Additionally, sub-optimal healthcare infrastructure,  
574 resources, staffing-levels, laboratory capabilities and data management systems preclude the  
575 generation of key AMR data needed to initiate, optimise or measure these outcomes of  
576 interventions. Such economic constraints can lead to further global inequalities, and international  
577 bodies have called for urgent improvements in access and infrastructure in LMIC settings,  
578 alongside advancements in data networks to improve the functionality and real-time evaluation  
579 of healthcare systems<sup>194</sup>. Opportunities for creative solutions in diagnostics, immunotherapy,  
580 intelligent-pathway development, laboratory surveillance and genomic sequencing may provide  
581 leapfrog technologies that can overcome key barriers in resource-limited settings <sup>196</sup>. Ethical and  
582 legal issues surrounding the regulation of AI and data privacy provide additional challenges to  
583 AMR interventions <sup>197</sup>. Improved international collaborations and the use of secure online  
584 platforms with user accountability may enhance regulation standards and dissuade negative  
585 public opinions <sup>171</sup>.

586

587 At the national level, understanding the political context is important, but recent assessments  
588 have perhaps overlooked wider technological and economic factors needed to make informed  
589 decisions <sup>198</sup> However, there are number of frameworks that can help to prioritise and stagger  
590 innovations at the national level according to the maturity of AMR National Action Plans; notably  
591 the AMR Policy Accelerator *SMART CHOICE* process, a tool to help prioritise national level  
592 interventions through facilitated engagement with local stakeholders to identify 'Quick-wins,  
593 Best-buys, Game-changers, and Equity-drivers' <sup>199</sup>. From the health systems perspective the level  
594 of integration of infection prevention and control and antimicrobial stewardship across the  
595 system can be used as marker for readiness to adopt as well as informing roll out plans <sup>124</sup>.  
596 Specifically, the level of integration of IPC and AMS programmes within the wider health system  
597 along the dimensions of stewardship and governance, financing, planning, service delivery,  
598 monitoring and evaluation, demand generation <sup>124</sup>. The approach to governance needs to be  
599 politically and culturally acceptable and feasible and heterogeneity of approaches is found even  
600 within high income countries <sup>200</sup>.

601

602 Lastly, future challenges to the resilience of healthcare may arise from global threats from  
603 pandemics or climate factors <sup>52</sup>, and innovations should be designed and optimised to account for  
604 evolving threats.

605

606

607

608

609 **[H1] Conclusion**

610

611 In high-income and resource-limited settings, healthcare infrastructure, pathways, processes, and  
612 systems play a key role in maintaining and driving AMR transmission beyond the frontiers of  
613 healthcare via a range of modalities. In a vicious circle, the global acceleration of AMR is  
614 threatening the safe functioning of healthcare systems. To address this crisis, it is imperative we  
615 consider innovative solutions to combat the direct and indirect drivers of AMR in healthcare that  
616 span across the patient journey that can also promote healthcare resilience. Innovations should  
617 be tailored within a global context and able to adapt and respond to future challenges.

618

619 Uncertainty and knowledge gaps surround many AMR interventions. The feasibility and success  
620 of implementing putative interventions is further hampered by structural, economic,  
621 technological and behavioural barriers, compounded by challenges relating to local and national  
622 leadership, external policy environments and international barriers to action. International,  
623 transdisciplinary consensus on the desired impact of AMR interventions might enable cross-  
624 evaluation, prioritisation and resource allocation. Collaborations are required at all scales  
625 between experts and non-experts, in high- and low-income settings, to share knowledge and  
626 expertise and develop reciprocal, long-term partnerships built on principles of systems  
627 approaches and capacity strengthening.

628

629 Despite the challenges that exist, opportunities to develop integrated healthcare pathways that  
630 embed novel approaches to preventative therapies (e.g., vaccination), improved diagnostics,  
631 antimicrobial optimisation, IPC and surveillance methodologies should be implemented to  
632 minimise AMR risks to patients. Innovations in these areas should be urgently considered as  
633 research priorities to address the burden of AMR and enhance the protection of healthcare.

634

635 **[H1] References**

636

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### 1164 **[H1] Author contributions**

1165

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1169

### 1170 **Competing interests statement**

1171

1172 The authors declare no competing interests.

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### 1175 **[H1] Display Items**

1176

1177 Figure 1| **Healthcare as a driver, reservoir and amplifier of antimicrobial resistance.**

1178

1179 Healthcare settings congregate people within shared spaces and along pathways exposing them  
1180 to antibiotic-resistant organisms (AROs), selection pressures (i.e., antibiotic exposure) and  
1181 healthcare-associated factors that promote AMR transmission. Colonised or infected individuals  
1182 and contaminated healthcare environments serve as reservoirs of AMR organisms, and healthcare  
1183 settings become distribution centres, amplifying AROs and antibiotic-resistant genes that are  
1184 recycled within healthcare settings or dispersed into the community via people and wastewater;  
1185 leading to onward cycles of AMR transmission before readmission into healthcare (Figure 1A).

1186 A broad range of factors contribute to driving AMR in healthcare settings including patient and  
1187 staff level characteristics such as co-morbidities, vaccination status, attitudes and behaviours and  
1188 colonisation status (Figure 1B). AMR colonisation is influenced by antimicrobial usage, which is in  
1189 turn influenced by antibiotic stewardship and antimicrobial optimisation measures. Here,  
1190 suboptimal access to improved diagnostics, irregular supply chains, or the absence of clear  
1191 antimicrobial prescribing policy can lead to inappropriate antimicrobial prescriptions, increasing  
1192 AMR. Additionally, healthcare infrastructure, patient pathways and IPC practices play a key role

1193 in AMR transmission events and environmental contaminated with AROs, illustrating their role in  
1194 facilitating AMR in healthcare.

1195

1196 Healthcare-associated reservoirs of AMR include (i) the microbiota of medical staff and patients  
1197 and animals present on healthcare grounds, and (ii) surface biofilms on key environments (e.g.,  
1198 sinks), especially in settings with high levels of ARO colonised patients (e.g., ITUs), medical  
1199 equipment and hospital waste and wastewater.

1200

1201 Healthcare can amplify AMR via (i) patient pathways that congregate vulnerable patients with  
1202 high levels of antimicrobials (ii) outbreaks of AROs within hospitals and care homes, (iii) the  
1203 movement of colonised patients between locations and within healthcare networks and (iv) the  
1204 dispersal of contaminated hospital wastewater into the environment.

1205

1206

1207 **Figure 2 | The use of vaccines and immunotherapy to reduce AMR and protect healthcare.**

1208

1209 Vaccines (or monoclonal antibodies) targeted at viral or bacterial aetiologies can limit disease  
1210 and/or colonisation at an individual and population level, preventing healthcare exposure,  
1211 reducing unnecessary antibiotic usage, and limiting transmission outside of healthcare settings  
1212 and reducing transmission events, HCAs and outbreaks within healthcare settings. In turn,  
1213 improved antimicrobial optimisation and a reduction in transmission events from vaccination and  
1214 immunotherapies will limit the burden of AMR and improve healthcare resilience. These  
1215 measures can be integrated with vaccination records, surveillance and diagnostic data through  
1216 improved AI and data linkage systems to personalise and target therapies pre-admission and  
1217 during healthcare attendance.

1218

1219

1220 **Figure 3 | Schematic illustrating the power of AI and data-linkage technology to reduce AMR and**  
1221 **improve healthcare resilience.**

1222

1223 Different types of healthcare and non-healthcare data are available via a spectrum of data  
1224 collection systems (A). Current advances in data technologies permits the integration of complex  
1225 datasets and allows for AI-driven analysis (B). These methodologies can be utilised to provide a  
1226 number of AMR specific applications (C), which can deliver data driven outputs to healthcare staff  
1227 and regulators that protect individuals, populations and health systems (D).

1228