

1 **Antimicrobial use in food-producing animals: a Rapid Evidence**

2 **Assessment of stakeholder practices and beliefs**

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14 15 **Abstract**

16 Food-producing animals throughout the world are likely to be exposed to antimicrobial
17 (AM) treatment. The crossover in AM use between human and veterinary medicine
18 raises concerns that antimicrobial resistance (AMR) may spread from food-producing
19 animals to humans, driving the need for further understanding of how AMs are used in
20 livestock practice as well as stakeholder beliefs relating to their use. A Rapid Evidence
21 Assessment (REA) was used to collate research on AM use published in peer-reviewed
22 journals between 2000 and 2016. Forty-eight papers were identified and reviewed. The
23 summary of findings highlights a number of issues regarding current knowledge of the
24 use of AMs in food-producing animals and explores the attitudes of interested parties

25 regarding the reduction of AM use in livestock. Variation between and within countries,
26 production types and individual farms demonstrates the complexity of the challenge
27 involved in monitoring and regulating AM use in animal agriculture. Many factors that
28 could influence the prevalence of AMR in livestock are of concern across all sections of
29 the livestock industry. This REA highlights the potential role not only of farmers and
30 veterinarians but also of other advisors, public pressure and legislation to influence
31 change in the use of AMs in livestock.

32

33 **Introduction**

34 Food-producing animals throughout the world are likely to be exposed to antimicrobial
35 (AM) treatment. Whilst AM use may vary widely between and within countries, species,
36 production systems and individual farms (Sawant and others 2005), over the last 50
37 years AMs have formed a key part of animal agriculture, especially in the developed
38 world (Busani and others 2004). Yet debate is growing over the implications for human
39 health of using AMs in food-producing animals. The crossover in AM use between
40 human and veterinary medicine has also given rise to concerns that resistance to AMs
41 may be spread from food-producing animals to human beings.

42 As a response to these concerns, national and international bodies including the World
43 Health Organisation, the World Organisation for Animal Health (OIE) and the Food and
44 Agriculture Organisation of the United Nations have called for AMs to be used
45 responsibly and appropriately by all those who administer them. On a national level,
46 guidance and legislation surrounding AM use in food-producing animals varies
47 considerably (Scott and others 2015).

48 In order to better understand the role that AMs currently play in human and veterinary
49 medicine, recent calls have highlighted the need for improved monitoring of AM use,
50 particularly in food-producing animals (Gonzalez and others 2010). Monitoring usage
51 alone, however, reveals little about what is driving AM use in practice, such as the
52 beliefs, motivations and activities of stakeholders involved at ground level, particularly
53 farmers and their veterinarians. Such understanding is vital if a true assessment is to be
54 made as to whether AMs are being used as advised (i.e. responsibly and appropriately),
55 as well as to identify potential motivators and barriers to change in practices that may
56 be necessary to meet these requirements.

57 As part of a larger project, a Rapid Evidence Assessment (REA) was conducted to
58 investigate what is currently known about the use of AMs in food-producing animals,
59 encompassing their use at farm level, the practices and perceptions of the stakeholders
60 involved in their administration, and the availability and validity of data on their use in
61 practice. REAs are increasingly promoted as a valid alternative to systematic reviews of
62 the research literature when time constraints do not allow a full systematic review to be
63 undertaken, and are completed in full acknowledgement of the trade-off between a
64 review being exhaustive and it being feasible to complete within a limited period of time
65 (Ganam 2010; Thomas and others 2013). REAs allow for the comprehensive and
66 descriptive assessment of a defined body of literature and, as Varker and others (2015)
67 point out: 'rigorous methods for locating, appraising and synthesizing evidence from
68 previous studies can be upheld and results can be produced in a fraction of the time
69 required for a full systematic review'. Moreover, REAs also 'serve as an informative brief
70 that prepares stakeholders for discussion on a policy issue (Varker and others 2015).

71 While the application of the REA methodology to more qualitative and social material is
72 generally less common than its use in quantitative and technological review (Thomas
73 and others 2013), the increasingly acknowledged explanatory power of qualitative
74 evidence, and its particular relevance here in the case of the ongoing debate over AMR,
75 make a strong case for such evidence- where robustly and convincingly generated- to
76 be appropriately and collectively reviewed.

77

78 **Materials and methods**

79 The validity of the REA method is in large part dependent upon the transparency of the
80 process employed to identify and select papers for consideration. Consequently, a
81 comprehensive description of the overall REA methodology adopted here, time span
82 and search strategies are reported in Figure 1 and in the Supplementary Material.
83 Although the methodology adopted and the restricted number of scientific publications
84 did not allow for an exhaustive appraisal of the study design and validity of every study
85 included, this was not the purpose of the REA.

86

87 **Results**

88 In total, 48 peer-reviewed papers fell within the remit of addressing current practice and
89 attitudes towards AM use in food-producing animals. Highlights of the papers identified
90 and general overviews are presented, by species, in the text. For a comprehensive
91 summary of the papers identified by the REA, please see Supplementary Material.

92

93 ***Comparison of findings by production system***

94 **Pigs**

95 In some countries, the largest proportion of single-species AMs sold for food-producing
96 animals are intended for pigs (VMD, 2014). This may result from the fact that pigs are
97 commonly treated as a group rather than as individuals (Merle and others 2012; Sjolund
98 and others 2015; Sjolund and others 2016; Timmerman and others 2006), although
99 individual treatments were most common in Sweden (Sjolund and others 2016).

100 Furthermore, it has been suggested that a shift over the last decade from in-feed to in-
101 water group treatments has led to an increase in antimicrobial use on pig farms (Fertner
102 and others 2016). Across Belgium, France, Germany and Sweden, weaned pigs tended
103 to have more treatments than suckling or finishing pigs (Sjolund and others 2016).

104

105 **AM use by class**

106 Chauvin and others (2002) noted that French pig veterinarians prescribed numerous
107 AMs to pigs, often prescribing many for similar purposes. Overall, tetracyclines were
108 identified as being prescribed frequently (typically for respiratory conditions), as were
109 peptides (colistin), macrolides (both predominantly for enteric conditions),
110 benzylpenicillins, beta-lactams, doxycycline and amoxicillin (Bashahun and Odoch
111 2015; Chauvin and others 2002; Moreno 2012; Sjolund and others 2016; Timmerman
112 and others 2006; van Rennings and others 2015). Fluoroquinolones and cephalosporins
113 were either not used at all or used in low levels (Chauvin and others 2002; Sjolund and
114 others 2015; Sjolund and others 2016; Timmerman and others 2006), and were often
115 used as injectables administered to individual animals.

116

117 AM dosing

118 Considerable variation in AM use was identified, with treatment durations ranging from
119 1-21 days. The number of daily dosages (NDD) per average pig year ranged from 0-
120 400, indicating that while some farms managed to rear pigs without the use of AMs,
121 others exceeded the defined (registered) animal daily dose for one year (Van der Fels-
122 Klerx HJ 2011). Inappropriate dosing was identified as being a common factor, with
123 reports of 50-75% of oral AM formulations underdosed, and 41->90% of parenteral
124 formulations overdosed (Chauvin and others 2002; Trauffler and others 2014).
125 Vaccination is often touted as an alternative to AM use in production animals, and one
126 paper reported vaccination rates ranging from 11-87% (Stevens, 2007). Group
127 prophylactic or metaphylactic treatments were also common (Timmerman and others
128 2006). Using AMs prophylactically was considered both justifiable and prudent by both
129 veterinarians and farmers (Coyne and others 2014; Stevens 2007), although many
130 farmers felt that the amount of AMs used for this purpose could be reduced (Stevens
131 2007).

132

133 **Cattle**

134 Within the dairy sector, treatments for mastitis along with dry cow therapy administered
135 at the end of lactation made up a large proportion of the AMs administered (Brunton and
136 others 2012; Gonzalez Pereyra and others 2015; Higgins and others 2012; Stevens and
137 others 2016; Swinkels and others 2015). In some countries, routine preventive use of
138 AMs in all cows is forbidden, so AM dry cow therapy can only be used in cows with pre-
139 existing intramammary infections (Swinkels and others 2015). One study comparing

140 organic and conventional systems found the types of antibiotic tubes and injectables
141 used were very similar, although while 85% of conventional farmers used dry cow tubes
142 on all cows at drying off, only 18% of organic farmers did the same (Brunton and others
143 2012).

144

145 AM use by class

146 Critically important AMs such as 3rd and 4th generation cephalosporins were used for
147 mastitis extensively in the UK, Belgium and the US (Brunton and others 2012; Stevens
148 and others 2016; Zwald and others 2004), but less so in Italy and Switzerland (Busani
149 and others 2004; Gonzalez and others 2010; Green and others 2010). The use of beta-
150 lactams including penicillins, aminoglycosides, tetracyclines, aminocyclitols, lincomycin
151 and trimethoprim/sulphonamide groups was reported in Argentinian, German, Swiss
152 and American studies (Gonzalez Pereyra and others 2015; Green and others 2010;
153 Merle and others 2012).

154 A small number of dairy herds in two US studies reported using AM products that are
155 either explicitly prohibited for use in dairy cattle (Zwald and others 2004) or not
156 recommended in food-producing animals (Cattaneo and others 2009); this practice was
157 also reported in Nigeria (Ojo and others 2016).

158

159 Calf treatment

160 Calves appear to receive more AM treatments than older animals in dairy production in
161 Sweden and Germany (Merle and others 2012; Ortman and Svensson 2004), although
162 lower use was reported in calves than dairy cows in Argentina (Gonzalez Pereyra and

163 others 2015). Fluoroquinolones were extensively used to treat enteritis in Argentina and
164 Italy (Busani and others 2004; Gonzalez Pereyra and others 2015). A Swedish study
165 (Ortman and Svensson 2004) found that 61% of farmers administered AM treatment
166 without prior consultation with a veterinarian, although veterinarians became
167 increasingly involved in treatment as the animals got older.

168

169 AM dosing

170 Treatment durations were reported to be longer for injectable preparations than for oral
171 preparations (Ortman and Svensson 2004). Inappropriate dosing was reported, with
172 overdosing compromising the stated withdrawal period and underdosing possibly acting
173 as a risk factor for the development and spread of antimicrobial resistance (AMR)
174 (Gonzalez and others 2010). Duration of mastitis treatment was occasionally or
175 frequently extended beyond the duration initially specified (Swinkels and others 2015),
176 and low numbers of farmers said they always completed a course of AMs presented for
177 a given condition (Sawant and others 2005).

178 One of the risk factors for the spread of AMR is the exposure of calves to AMs through
179 the provision of antibiotic waste milk. Although this practice is commonplace (Brunton
180 and others 2012; Zwald and others 2004), waste milk is not the only means by which
181 calves may be exposed to AMs. Commercial milk substitute containing prescription
182 antibiotics was often reported (Brunton and others 2012; Zwald and others 2004).

183 Italian veterinarians reported often or sometimes administering AMs before the onset of
184 clinical signs of diarrhoea (20%) and respiratory disease (28%), while 62% prescribed

185 AMs prophylactically against mastitis at drying off, and often reported failure of AM
186 treatment (Busani and others 2004).

187

188 **Other species**

189 A study into the use of antibiotics in intensive poultry farms in Uganda found that the
190 majority (96.7%) of study participants frequently used antibiotics in their animals and
191 that 33.3% (n=10) used antibiotics for growth promotion, furthermore it was reported
192 that 'most' of the participants admitted to selling their products within the meat
193 withdrawal times (Bashahun and Odoch 2015). Another study assessing the usage and
194 practices of antimicrobial use in production animals in Nigeria surveyed producers
195 farming chicken, turkey, guinea fowl, geese, duck, horse, cattle sheep, goat, dog, rabbit
196 and quail. This study found that AMs were widely used in all production animals, and
197 frequently used for prophylaxis, including the use of critically important AMs for this
198 purpose. The use of antimicrobials banned for use in humans and animals was also
199 reported (Ojo and others 2016).

200

201 ***Attitudes, beliefs and external influences on AM use***

202 **Factors influencing farmers' use of AMs**

203 Type of production system, high production costs and an inability to reinvest in
204 infrastructure were identified as factors that UK veterinarians and pig farmers felt
205 influenced their AM usage, with the implication that AMs were being relied upon in the
206 short term (Coyle and others 2014; Stevens 2007). Farmers who reported that their
207 farm environment could be improved were significantly more likely to use in-feed AMs

208 for their growers and finishers than those who did not (Stevens 2007). In the UK, farm
209 type was found to influence in-feed AM use, and in Austrian pig herds, farm type was
210 found to impact average AM consumption (Stevens 2007; Trauffler and others 2014). In
211 Austria, farm size had no significant impact on AM consumption, although there was an
212 effect of the individual veterinarian on the therapy indication and active substance
213 chosen (Trauffler and others 2014). In Belgian pig herds, a negative association was
214 identified between biosecurity score and treatment incidence (based on used daily
215 dose); fewer prophylactic AM group treatments were given in herds with higher
216 biosecurity (Laanen and others 2013). Farmers in Nigeria also acknowledged that
217 readily available AMs may encourage non-adherence to hygienic principles and
218 management (Ojo and others 2016).

219 In beef cattle, herd size and farm type (cow-calf only or multiple operation type) had an
220 influence on AM use (Green and others 2010).

221 A survey of dairy farmers in England and Wales found that only 17% of farmers would
222 ask for veterinary advice before administering antibiotics to their animals (Jones and
223 others 2015). In Ohio, over three-quarters (77%) of dairy veterinarians surveyed
224 believed their clients followed protocols for AM use, while only 23% stated that they
225 supplied protocols for AM use every time they prescribed them (Cattaneo and others
226 2009). Veterinarians in an Ohio-based survey also believed that their clients frequently
227 used AMs without veterinary consultation (Cattaneo and others 2009). Similar findings
228 were reported for Pennsylvania dairy farmers (Sawant and others 2005) as well as
229 Nigerian farmers (Ojo and others 2016). Farmer AM treatment threshold was, however

230 found to have no correlation with the use of protocols or frequency of veterinary visits in
231 US farmers from Michigan and Ohio (Habing and others 2016).
232 Owners and managers of US feedlots perceived the expectations of many other
233 members of the feedlot network (packers, retailers, consumers) to be important
234 considerations in their own decision-making regarding AM use and also reported having
235 a moral obligation to the cattle to treat with AMs, but degree of this perceived obligation
236 varied by circumstance (McIntosh and Dean 2015). Concern for the public health impact
237 due to AM use in livestock seemed to affect AM use of farmers from Ohio and Michigan,
238 US, as those with more concern about this had a significantly higher treatment threshold
239 in their animals (Habing and others 2016).

240 Extending treatment duration for clinical mastitis was found to be a social norm among
241 farmers in the Netherlands and Germany (Swinkels and others 2015). In addition, some
242 farmers reported extending treatment because it made them feel like 'good farmers'
243 (Swinkels and others 2015). Danish organic dairy farmers also tended to perceive AMs
244 as the treatment method with the best prognosis as well as the most responsible
245 method to aid animal welfare and end animal suffering (Vaarst and others 2003).

246

247 **Farmers' knowledge of correct AM use**

248 Just over half (53%) of 71 English and Welsh dairy farmers responding to a survey,
249 reported knowledge of the Responsible Use of Medicines in Agriculture Alliance's
250 (RUMA) guidelines for use of AMs in cattle production in the UK, and 30% were not
251 aware of concerns over the use of 3rd and 4th generation cephalosporins (Jones and
252 others 2015). Furthermore, 20% of these farmers admitted that they do not always

253 complete a full course of AMs as prescribed (Jones and others 2015). Spanish farmers
254 are also “not very knowledgeable” about the proper use of AMs, and some may not be
255 clear about the differences between curative and preventive uses (Moreno 2014).

256 Approximately half (14/30) of Ugandan farmers were not aware of withdrawal periods
257 for antibiotics (Bashahun and Odoch 2015). Farmers from various European countries
258 tended to think they used AMs more judiciously and less frequently than their peers
259 (Coyne and others 2014; Visschers and others 2015).

260 One study identified ‘learning processes’ that farmers used to implement new health
261 practices, along with the role of the veterinarian and other technical advisors who
262 facilitated farmers to implement change by aiding these learning processes (Fortane
263 and others 2015).

264

265 **Farmers’ motivation for AM use and reduction**

266 Just over 70% of surveyed dairy farmers from England and Wales agreed that reducing
267 AM use in their herd over the next year would be a good thing, with 59% stating that
268 they had the skills and knowledge to do so (Jones and others 2015). Restricting AM use
269 was also considered important by 87% of Dutch dairy farmers (Scherpenzeel and others
270 2016) . Both the UK and Dutch farmers as well as farmers from Belgium, France,
271 Germany, Sweden and Switzerland cited a reduced cost of production as the primary
272 reason driving them to reduce AM use (Brunton and others 2012; Jones and others
273 2015; Scherpenzeel and others 2016; Visschers and others 2015). Dutch farmers also
274 cited ‘improving public health’ as one of the most positive outcomes of restricting AM
275 use (Scherpenzeel and others 2016). French pig farmers cited various reasons for

276 choosing to reduce AM use, including health events, new economic and health
277 strategies and ethical considerations (Fortane and others 2015).

278

279 **Farmer concerns regarding AM reduction**

280 Over half (53%) of British pig farmers believed that AM use resulted in the production of
281 increased amounts and cheaper food, and 21% indicated the use of AMs for growth
282 promotion was justified (Stevens 2007). A minority (18%) of English and Welsh dairy
283 farmers, however, thought that milk production would decline if they reduced AM use in
284 their herds (Jones and others 2015). Spanish farmers also agreed that AMs play a role
285 in enhancing performance parameters (Moreno 2014). Dutch dairy farmers cited
286 uncertainty over recovery of sick cows and the number of sick cows as concerns
287 regarding reduced AM use as well as additional labour requirements and feeling that
288 they were being pushed to follow rules they do not agree with (Scherpenzeel and others
289 2016). In this same study, Dutch farmers implementing selective dry cow therapy
290 considered 'financial consequences' a negative impact of reduced AM use less often
291 than those using blanket dry cow therapy (Scherpenzeel and others 2016).

292

293 **Farmer attitudes towards AMR**

294 The threat of AMR was typically underplayed by food-producing animal stakeholders
295 (Moreno 2014), with it being felt that there was insufficient evidence to decisively prove
296 the link between using AMs in food-producing animals and the development of AMR in
297 pathogens infecting humans (Coyne and others 2014). Most farmers from South
298 Carolina that participated in one study seemed unconcerned that AM use in animals

299 could lead to resistance among farm workers (Friedman and others 2007), while 58% of
300 conventional farmers from Ohio and Michigan, US, disagreed that antibiotic use in
301 agriculture led to resistant bacterial infections in people. In the UK, 7% of organic
302 farmers felt similarly (Habing and others 2016). UK farmers were uncertain as to
303 whether reduced AM use on their farms would affect animal health and welfare or
304 whether such a decrease would reduce AMR (Jones and others 2015).

305

306 **Veterinarian attitudes towards AMR**

307 In the UK, veterinarians were cited as farmers' most trusted information source (Jones
308 and others 2015). The majority of Dutch and Flemish veterinarians responding to a
309 survey reported to have become more aware of the need to restrict the use of AMs and
310 were aiming to reduce AM use in their practice as far as possible (Postma and others
311 2016). In the US, however, a negative correlation between the number of years a US
312 veterinarian had been in practice and their knowledge of AMR was identified (Cattaneo
313 and others 2009). Furthermore, years qualified was associated with veterinarians being
314 less concerned about AMR (Speksnijder and others 2015a) and more confident in their
315 independent prescribing practice (Dean 2011). Ohio dairy veterinarians were more likely
316 to agree that AMR will negatively affect animal health (86%) than human health (63%;
317 Cattaneo and others 2009). Key information sources for prescribing AMs were reported
318 by veterinarians to be other veterinarians, their own personal experience, the label or
319 leaflet accompanying the product, training or literature with which they were familiar,
320 previous experience or the results of culture and sensitivity testing (De Briyne and
321 others 2013; Dean 2011; Gibbons and others 2013; Postma and others 2016).

322

323 **Veterinarian motivation for prescribing**

324 Veterinarians in the UK, Ireland, the Netherlands and Belgium reported that demands
325 from farmers, advisors or other veterinarians did influence their prescribing; they also
326 felt under more pressure from legislation and public perception than farmers reported
327 (Coyne and others 2014; Gibbons and others 2013; Postma and others 2016;
328 Speksnijder and others 2015b). Dutch and Flemish veterinarians reported to have little
329 concern over the farmers' preference for AM product when prescribing (Postma and
330 others 2016). Social pressure from other feedlot veterinarians and nutritionists,
331 however, was found to have more of an influence on beef feedlot cattle veterinarian
332 attitudes towards AMs; these veterinarians cited their highest perceived expectation for
333 AM prescription was from pharmaceutical companies (Jan 2010). Their levels of trust in
334 other relevant actors (government agencies, other veterinarians, etc.) also influenced
335 their decision making (Dean 2011). A sense of moral obligation to the public was found
336 to be associated with a negative attitude to prescribing AMs (McIntosh and others
337 2009). The influence of these factors varied in different clinical situations, and social
338 pressure (particularly that of colleagues and co-workers compared to, for example,
339 nutritionists or clients) had more of an influence (Jan 2010). No evidence was found that
340 veterinarians prescribing habits were driven by revenue or profit margin (De Briyne and
341 others 2013; Gibbons and others 2013; Postma and others 2016), and preserving the
342 veterinary pharmacy for future years was found to be a strong motivator for Dutch and
343 Flemish veterinarians to reduce AM use (Postma and others 2016).

344 In the Netherlands, benchmarking that made the prescription patterns of veterinarians
345 transparent was introduced in the hope of shifting social norms and encouraging
346 veterinarians to self-regulate AM use (Bos and others 2015).

347

348 **Sensitivity testing**

349 The use of sensitivity testing varied widely between the European countries surveyed,
350 with veterinarians reporting their decision whether to test depended on the animal's
351 response to initial therapy as well as the veterinarian's knowledge of that animal or farm
352 (De Briyne and others 2013). More rapid results and cheaper sensitivity testing were
353 described to be key factors that would encourage veterinarians to make more use of
354 sensitivity testing (De Briyne and others 2013).

355

356 **Quality of data on AM use**

357 It is challenging to measure on-farm AM usage due to the difficulty in obtaining an
358 accurate account of the dosage and duration of treatment, with farmers often relying on
359 their memory alone for recalling past treatments (Zwald and others 2004) and often
360 under-reporting medicine use (Redding and others 2014). Veterinary records have been
361 found to be more accurate than those of farmers, although both were reported to be
362 incomplete or implausible (Gonzalez and others 2010; Merle and others 2012; Trauffer
363 and others 2014). Data from the VETSTAT system in Denmark indicated that most of
364 the entries from pharmacies were correct, while there were a high percent of errors in
365 data originating from veterinarians and feed mills (Stege and others 2003).

366

367 **Discussion**

368 The 48 papers identified by the REA and summarised above highlight a number of
369 issues regarding current drivers for the future use of AMs in food-producing animals.
370 Table 1 summarises the key drivers of current antimicrobial use and the identified
371 barriers for change, as taken from the REA. In terms of barriers to change, these
372 summary findings reveal what can be interpreted as a sense of inflexibility particularly in
373 the organisation of production systems and, as a consequence, in the potential ‘spaces’
374 for change, but also, though arguably to a lesser extent, in producer sensibilities around
375 the nature of good husbandry. There is also, however, a clear indication that amongst
376 respondents to the various surveys reviewed, there is both an awareness of the issue
377 and a willingness to explore the potentials for change in antimicrobial use.
378 The huge variation between and within countries, production types and individual farms
379 demonstrates the complexity of the challenge involved in monitoring and regulating AM
380 use in animal agriculture.

381 **Table 1.** Identified key drivers and barriers to change of antimicrobial use in food-
382 producing animals

Identified drivers in reducing antimicrobial use
Higher levels of on-farm biosecurity lead to lower prophylactic use
New methods of knowledge exchange and learning improve farmer awareness of and response to more sensible antimicrobial use
Reducing costs of production would encourage reduced antimicrobial use
Farmers recognise and acknowledge the need to reduce antimicrobials
Veterinarians in general support antimicrobial use reduction
No evidence exists that medicine sales by veterinarians are a factor driving overuse of antimicrobials
Better diagnostics or wider use of diagnostics would improve the ability to use medicines more effectively
Wider use of vaccines to prevent disease would reduce antimicrobial use

Identified barriers to more sustainable use

Production system inflexibility hinders reduction in antimicrobial use

High production costs reduce capacity for antimicrobial use reduction

Low capacity for reinvestment in farm buildings reduces capacity for reduction in antimicrobial use

Farmer concern over being a 'good' farmer hinders reduces antimicrobial use

Farmer concern for welfare and health of animals leads to a reluctance to reduce antimicrobial use

Farmer failure to follow treatment guidelines leads to over- or under-dosing of antimicrobials

Farmer belief that antimicrobial use will improve profitability hinders reduction in antimicrobial use

Veterinarians are under pressure from farmers, feed suppliers and others to use antimicrobials

Changes in antimicrobial use in feed regimes (e.g. from feed to water) represents potential for increased antimicrobial use

Farmers initiating treatment without seeking veterinary advice leads to inappropriate use of antimicrobials

Some farmers and veterinarians believe that antimicrobial prophylaxis is justifiable and prudent

383

384 The sample sizes and associated response rates in these studies illustrates the
385 difficulties in recruiting participants for AM research, and should be taken into account
386 when interpreting results. Other challenges include concerns about the ease of
387 comparing the findings of studies across methodologies, countries and production
388 systems. While some papers report AM product names, others use classes or active
389 substances to categorise AMs. Complexity increases when the amount of AMs used is
390 considered. A document published by the European Medicines Agency in 2015 set out
391 principles for the calculation of defined daily dose for animals (DDDvet) and defined
392 course dose for animals (DCDvet) as a veterinary equivalent to the defined daily dose
393 developed for human medicine, taking medicine potency into account (EMA 2015).
394 These methods are not globally recognised, however, and there remains a variety of
395 different usage measures or dosage calculations included in the literature (Gonzalez
396 and others 2010; Moreno 2012; Taverne 2015; Timmerman and others 2006).

397 Over half of the papers included in this REA reported research conducted within the EU.
398 This may reflect the greater regulation of AM use in this region compared to other parts
399 of the world (Scott and others 2015). The research question addressed by this REA
400 focused particularly on pigs, poultry and cattle, yet only two papers on AM use in poultry
401 could be identified for inclusion, suggesting a deficit of published peer-reviewed
402 research in the poultry sector. The majority of papers identified in this REA instead
403 covered AM use in pigs and cattle. Only one study performed within the EU made
404 reference to AM use by a food-producing animal other than pigs and cattle, highlighting
405 the impact of a few prescriptions for quinolones used in aquaculture on kilograms of
406 AMs distributed per month by Danish pharmacies, due to the quantities prescribed
407 (Stege and others 2003). Given the expanding global aquaculture industry, research
408 into current AM use and beliefs in this sector should also be a priority.

409 There are a number of limitations of conducting an REA rather than an exhaustive
410 systematic review, including biases relating to publication, language and accessibility,
411 although these are not unique to REAs (Thomas and others 2013). Nonetheless, this
412 work demonstrates the valuable contribution of the REA methodology to research when
413 rapid insight into the current status of research in a given area is needed.

414

415 **Conclusions**

416 Multiple factors which could influence the prevalence of AMR in livestock species -
417 including the improper use of AMs in both the pig and cattle sectors, across all global
418 regions - remain a concern. Prophylactic and metaphylactic use of AMs appears to be
419 common practice across all sectors for which relevant literature was found, largely pig

420 and cattle production within EU countries, but also other sectors worldwide. Literature
421 regarding the use of AMs in poultry production in the EU in particular was lacking from
422 the searches. It is likely that data regarding AM consumption in poultry production are
423 collected by poultry producers in some countries but these data are not available in the
424 published literature. Work should therefore be done to amalgamate and publish any
425 existing data or investigate this area of AM use further. Levels of farmer knowledge with
426 regard to proper and prudent use of AMs varies between groups, although veterinary
427 input regarding the treatment of animals was, on the whole, low across all geographical
428 locations.

429 Economic concerns and restraints relating to farm infrastructure or production type may
430 limit farmers' ability or motivation to alter AM use in their animals. Veterinary advice,
431 public pressures, input from other advisors and moral obligation influence farmers'
432 attitudes to AM use. Similarly, veterinary prescribing habits have been shown to be
433 influenced by similar factors to differing degrees, and veterinarians' confidence in their
434 own knowledge of the AMs they are prescribing also influence prescribing behaviour. It
435 would stand to reason, therefore, that increasing knowledge of the proper use of AMs
436 as well as awareness of AMR and encouraging a reduction in AM use in all of these
437 sectors is necessary, and this could have synergistic effects when compared to
438 strategies targeting only one group of actors.

439

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610 **Figure 1.** PRIMSA flow diagram illustrating the selection process for the final 48 articles
611 (Moher and others 2009)