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1	The 'Antibiotic Apocalypse' – Scaremongering or Scientific Reporting?
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10	KEYWORDS
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12	Antimicrobial resistance, Antibiotic, Apocalypse
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14	ABSTRACT
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16	Antimicrobial resistance is dominating scientific media. We are warned of an
17	impending 'antibiotic apocalypse', where mankind faces its biggest threat, untreatable
18	microbes. However, the world isn't ending. Scientists are responding to the threat;
19	new knowledge and chemotherapeutics are being created to safeguard our future. The
20	future is bright, not gloomy.
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25 In the past few years the emergence of antibiotic resistant infections has increased 26 dramatically. This is largely due to the misuse of antibiotics: misprescribing and 27 overprescribing by clinicians, patient failure to adhere to the treatment course and the 28 extensive use of antibiotics in agriculture and aquaculture [1-3]. There is a public 29 expectation to receive some form of medication when visiting a general practitioner, 30 and although the medical profession is adapting its practices accordingly, antibiotics 31 have often been prescribed as a means to satisfy the patient rather than as a course of treatment [4]. Currently around 700,000 antibiotic resistance-related deaths are 32 33 recorded annually, with a projected rise to 10 million by 2050, overtaking cancer as 34 the leading cause of death worldwide [i]. These projections have led to media hysteria 35 that has been catalysed by the support of the scientific community. This gloomy 36 outlook is considered to be a window into a future where all known antibiotics will be 37 rendered ineffective due to widespread antibiotic resistance. Previously treatable 38 minor bacterial infections may develop into potentially fatal diseases, invariably 39 resulting in a dramatic increase in bacteria-borne mortality [ii]. The slim, but real 40 possibility of a future without antibiotics is recognised by leading academics, 41 government advisors and doctors worldwide, but does this warrant the casual usage of 42 the term 'antibiotic apocalypse'?

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The word apocalypse is defined as "the end of the world or some other event of great destructive violence" [5]. Can we really consider a return to the days pre-advent of streptomycin and penicillin as the end of the world? Mankind survived and thrived for around 200,000 thousand years until the antibacterial properties of penicillin were discovered in 1928 [6]. The cavalier use of this expression in mainstream media and scientific articles will undoubtedly impact the general public's perception of the issue

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50 of antimicrobial resistance (AMR). Recently, this perception was examined and it was 51 found that the majority of people do not believe their actions or decisions can 52 contribute to the development of AMR and that it is not their responsibility to tackle 53 antibiotic resistance [7]. Indeed, 88% of people believe that antibiotic resistance is 54 when a human becomes resistant to antibiotics, rendering the antibiotic ineffective 55 [7]. These misconceptions may in part be down to the dramatisation of the issue as an unstoppable force, a plight of humanity so great that one person's input couldn't 56 57 possibly make a difference. In reality, AMR has developed and escalated as a global 58 healthcare concern as a result of the lack of education and understanding of 59 individuals about antibiotics. However, the battle is far from lost. In 2015, 1618 peer-60 reviewed scientific articles were published containing the phrase 'antimicrobial 61 resistance' and the Medical Research Council awarded £10.7 million for UK research 62 into AMR during the 2015-2016 round [8]. Supporting the hypothesis of an antibiotic 63 apocalypse among the general public at large serves only to mislead rather than 64 inform.

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66 Instead of supporting over-reaction to the subject of AMR, we should encourage 67 thinking of AMR as an example of a natural coevolutionary system. The Red Queen 68 hypothesis of coevolution goes some way to explain AMR whereby predators 69 (bacteria) and prey (humans) sequentially evolve to overcome an evolutionary 70 advantage of their opponent, driving a continuum of evolutionary push and pull [9]. 71 Differing speeds of genetic evolution between humans and bacteria result in humans 72 evolving intellectually rather than physically, with the advent of  $\beta$ -lactam antibiotics 73 [10]. Bacteria then respond accordingly by exploiting  $\beta$ -lactamases, regaining the 74 upper hand. Humans discover new antibiotics, with each discovery, evolving

75 intellectually, driven by the eventual resistance of bacteria to each new chemical 76 class. Bacteria have recently gained the upper hand due to a reduced rate of antibiotic 77 discovery [10]. However, new advances such as combination antibiotic therapy and 78 the discovery of new drugs, novel targets and innovative technologies will help 79 humans regain and retain the evolutionary advantage. Furthermore, our improved 80 understanding of how resistance occurs, spreads and how to prevent it will ensure our 81 advantage is not short lived. As Sun Tzu put it in The Art of War, "If you know the 82 enemy and know yourself, you need not fear the result of a hundred battles. If you 83 know yourself but not the enemy, for every victory gained you will also suffer a 84 defeat" [11]. It is rather fortunate we have been studying bacterial resistance almost as 85 long as we have been discovering antibiotics.

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87 Evidence for the complexity of this push and pull dynamic between bacteria and 88 humans can be exemplified by recent epidemiological data. In our possibly 89 overzealous attempts to tackle AMR by reducing the quantities of antibiotics 90 prescribed for non-bacterial or immune-susceptible infections such as tonsillitis, we 91 may have neglected to consider those rare occasions where antibiotics are absolutely 92 necessary. In the UK, the incidence of Scarlet fever (a complication of untreated or 93 inappropriately treated tonsillitis due to Streptococcus pyogenes, the group A 94 streptococcus) has increased since 2013, an inverse correlation to the number of 95 antibiotic prescriptions per head in the UK (Figure 1). Clearly, improved diagnostics 96 at the point of care are essential to making the decision for or against antibiotic 97 administration. Sudden and dramatic changes to our antibiotic prescribing behavior 98 will invariably result in an epidemiological backlash. A more considered clinical 99 response to AMR maybe required wherein prevention is pursued instead of panic-

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induced kneejerk reactions in response to media hysteria. Our transition into a society
where clinicians are fearful of prescribing antibiotics, and the general public are
equally fearful of taking them needs to be halted. Public perception is key; the
antibiotic apocalypse is not upon us.

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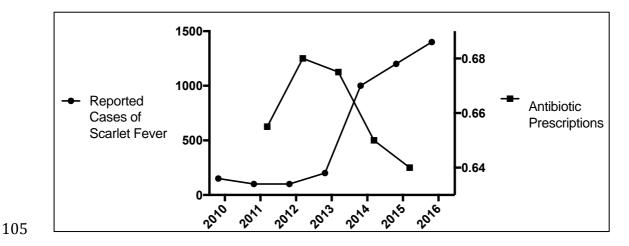


Figure 1. The number of reported cases of Scarlet Fever (UK) versus the yearly antibiotic prescriptions per head (UK). Responding to antimicrobial resistance requires improved, rapid clinical diagnostics at the point of care to ensure antibiotics are provided when necessary. Data shown in this figure are from [iii-iv].

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111 Government and private funding is integral to sustaining scientific research and a 112 wider public understanding of the important issues of the day drives this funding, but 113 I believe there are considerable ethical boundaries that scientists must operate within. 114 Feeding and supporting inaccurate sensationalist journalism because it fits our 115 funding aspirations serves only to mislead the public. As scientists we strive for truth, 116 we therefore should not discredit scientific fact with sensationalism. When discussing 117 AMR publically we must provide clear and objective summaries based on hard data, 118 not assumptions that will fuel public misconception. Referring to the highly unlikely 119 possibility of a future without antimicrobial treatment as the post-antibiotic era, or

- 120 AMR as a global antibiotic crisis, resonates true without unnecessary scaremongering,
- as in this authors view, the truth is scary enough! (Figure 2).

## 122



- 124 Figure 2. The Antibiotic Apocalypse. Is this the end of the world as we know it?
- 125 Unlikely. Scientists should promote education over sensationalism using facts, not
- 126 fear.
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## 128 ONLINE RESOURCES

- 129 i.https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-
- 130 <u>%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20</u>
   131 nations\_1.pdf
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