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1 The 'Antibiotic Apocalypse' – Scaremongering or Scientific Reporting? 2 3 Jonathan A. G. Cox* & Tony Worthington 4 5 *Correspondence: j.a.g.cox@aston.ac.uk 6 Twitter: @originaljoncox 7 School of Life and Health Sciences, Aston University, Aston Triangle, Birmingham 8 **B47ET** 9 10 **KEYWORDS** 11 12 Antimicrobial resistance, Antibiotic, Apocalypse 13 14 **ABSTRACT** 15 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. 21 22 23 24

In the past few years the emergence of antibiotic resistant infections has increased dramatically. This is largely due to the misuse of antibiotics: misprescribing and overprescribing by clinicians, patient failure to adhere to the treatment course and the extensive use of antibiotics in agriculture and aquaculture [1-3]. There is a public expectation to receive some form of medication when visiting a general practitioner, and although the medical profession is adapting its practices accordingly, antibiotics 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 recorded annually, with a projected rise to 10 million by 2050, overtaking cancer as the leading cause of death worldwide [i]. These projections have led to media hysteria that has been catalysed by the support of the scientific community. This gloomy outlook is considered to be a window into a future where all known antibiotics will be rendered ineffective due to widespread antibiotic resistance. Previously treatable minor bacterial infections may develop into potentially fatal diseases, invariably resulting in a dramatic increase in bacteria-borne mortality [ii]. The slim, but real possibility of a future without antibiotics is recognised by leading academics, government advisors and doctors worldwide, but does this warrant the casual usage of 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

of antimicrobial resistance (AMR). Recently, this perception was examined and it was found that the majority of people do not believe their actions or decisions can contribute to the development of AMR and that it is not their responsibility to tackle antibiotic resistance [7]. Indeed, 88% of people believe that antibiotic resistance is when a human becomes resistant to antibiotics, rendering the antibiotic ineffective [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 possibly make a difference. In reality, AMR has developed and escalated as a global healthcare concern as a result of the lack of education and understanding of individuals about antibiotics. However, the battle is far from lost. In 2015, 1618 peer-reviewed scientific articles were published containing the phrase 'antimicrobial resistance' and the Medical Research Council awarded £10.7 million for UK research into AMR during the 2015-2016 round [8]. Supporting the hypothesis of an antibiotic apocalypse among the general public at large serves only to mislead rather than inform.

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

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

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

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.



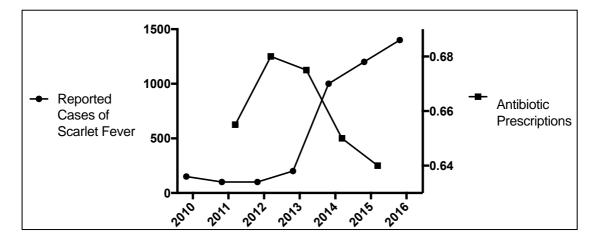


Figure 1. The number of reported cases of Scarlet Fever (UK) versus the yearly antibiotic prescriptions per head (UK). Responding to antimicrobial resistance requires improved, rapid clinical diagnostics at the point of care to ensure antibiotics are provided when necessary. Data shown in this figure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

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

AMR as a global antibiotic crisis, resonates true without unnecessary scaremongering,

as in this authors view, the truth is scary enough! (Figure 2).

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Figure 2. The Antibiotic Apocalypse. Is this the end of the world as we know it?

Unlikely. Scientists should promote education over sensationalism using facts, not

fear.

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ONLINE RESOURCES

i.https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-

130 %20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20

131 <u>nations_1.pdf</u>

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ii.http://www.bbc.co.uk/news/health-21702647

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iii.http://www.antibioticresearch.org.uk/wp-content/uploads/2015/11/EXASOL-Analyses_Antibiotic-Research-UK-Final-121115.pdf

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iv.https://www.gov.uk/government/collections/group-a-streptococcal-infections-

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