

## Review Article

# The One Medicine concept: its emergence from history as a systematic approach to re-integrate human and veterinary medicine

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The COVID-19 pandemic has resulted in the global recognition for greater inter-disciplinary and multi-disciplinary working, and the need for systematic approaches which recognise the interconnectedness and interactions between human, animal and environmental health. The notion of such a One Team/One science approach is perhaps best exemplified by the One Health concept, a systematic approach which is rapidly entering into the mainstream. However, the concept of One Health, as we presently know it, originated from One Medicine, a notion which is much older and which emerged to promote collaboration between the human and veterinary medicine professions and the allied health/scientific disciplines. Whilst One Medicine is perhaps better known by the veterinary community, some misconceptions of what One Medicine is have arisen. Therefore, this review introduces this emerging concept and how it can help to address overlapping (communicable and non-communicable disease) health challenges faced by both human and veterinary medicine.

## Introduction

The COVID-19 pandemic has emphasised the interconnection that exists between humans and animals and the need to connect the veterinary, medical and scientific disciplines. In doing so, it has highlighted the effectiveness and need for integrated systematic approaches which deliver benefits to all.

One Health has emerged into the mainstream as one such integrative approach to enable future global responses to infectious diseases, specifically zoonoses. Its advocates encompass medicine, science, international agencies e.g. the tripartite of the Food and Agriculture Organisation of the United Nations (FAO), the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE) [1] and also the European Union [2]. This short review introduces One Medicine (the precursor concept of One Health), and its emergence from history to re-integrate human and veterinary medicine for future health challenges.

## What is the One Medicine concept?

This review considers the central tenet of the One Medicine concept as being to promote collaboration between the medical and veterinary disciplines to benefit both human and animal health via parallel studies of naturally occurring spontaneous disease, comparable to each other due to genetic and physiological similarities. The two-way flow of data and knowledge gained creating a positive feedback loop of reciprocal benefits to both animal and human health.

Although 'One Medicine' has been thought to be self-explanatory [3], or synonymous to 'One Health', the two terms are distinct from each other [4]. Currently, there is no universal standard definition for either 'One Health' [5], or 'One Medicine'. Whilst related due to their common denominator of inter-disciplinary collaboration between human and veterinary medicine, the lack of standardised definitions for both concepts leaves them open to differing interpretations. For example, Gibbs [6]

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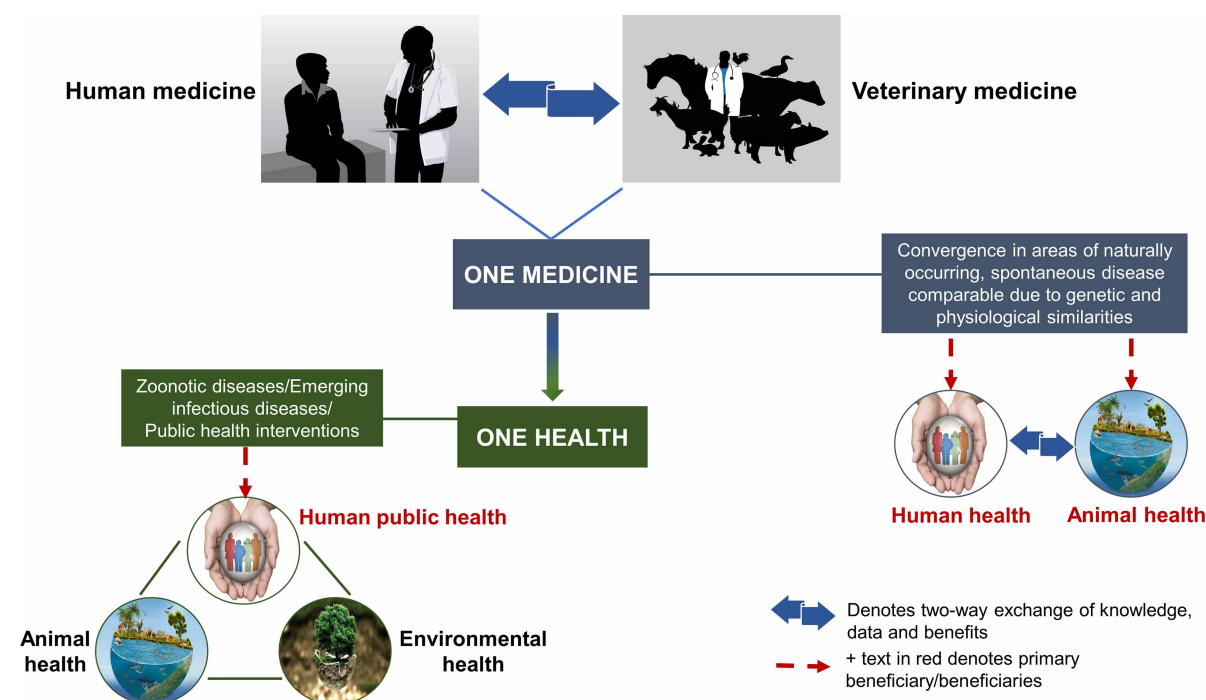
provides examples of six definitions for One Health, whilst Lerner and Berg [5] considered in their analysis that One Health relates to how human health is affected by animal health and thus its focus is on public human health. An interpretation of how the two concepts are related but differ from each other is presented in Figure 1.

One Health's current interpretation has existed since 2003, but the history of its precursor, One Medicine, goes back much further [3], its origins having been covered previously in reviews e.g. Cardiff et al. [7], Zinsstag et al. [8] and Mobasher [9]. A comprehensive review on the history of both concepts was published by Woods et al. [10].

It has been postulated that animal medicine preceded human medicine [11]. Historically, livestock animals were of high importance due to the expense in producing meat, eggs and dairy products [12]. In ancient Egypt, the importance of cattle led to the knowledge of their anatomy and physiology gained through their domestication, care and ritual bull sacrifices. By applying this acquired knowledge to human analogues this led to the origin of human medicine in ancient Egypt [13]. Common knowledge between both animal and human health also occurred during the Greek and Roman eras [14]. However, human and veterinary medicine diverged during the 19th century continuing apace during the 20th century [14]. Contributory factors to such divergence could be veterinary medicine's close association to livestock and horses, before companion animal medicine gained prominence from the 1970s [12].

Numerous calls have been made for closer alignment and greater collaboration between human and veterinary medicine to generate a 'common pool of knowledge' which will benefit both animal and human health [15–17]. Notable historical exponents of the links between human and veterinary medicine have included Xu Dachun [8] and Rudolf Virchow [18]. In the 1960s, its most notable exponent, Calvin Schwabe, attempted to re-integrate the medical and veterinary disciplines and is credited with coining the term 'One Medicine' [14,19]. In the UK, the most notable exponent advocating the integration of human and animal health was Lord Lawson Soulsby, a veterinary surgeon who worked in the areas of microbiology and parasitology and who bridged both the medical and veterinary professions [3].

Despite these calls, and acknowledging that there are cross-disciplinary groups such as the UK's Human Animal Infections and Risk Surveillance (HAIRS) group, overall, such collaborations still do not routinely



**Figure 1. Schematic outline diagram indicating the relationship and differences between the concepts of One Medicine and One Health.**

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occur. In response to the COVID-19 pandemic, some in the veterinary profession have questioned why their considerable expertise and knowledge has not been better utilised in terms of animal coronaviruses, laboratory testing facilities, infectious disease, population medicine, epidemiology and public health strategies such as those developed for livestock e.g. ‘predict and prevent’ [20–22]. Furthermore, veterinarians and animal vaccine developers have considerable expertise with regards lessons that could be learnt from animal coronavirus vaccine development and vaccinating and testing populations en-masse [23,24].

In terms of cross-over publications between the two professions, these are sporadic e.g. joint editorials between the BMJ and Veterinary Record in 2005 and again in 2018 [25]. There have also been discussions on the links between human and animal health by UK Chief Medical Officers and Chief Veterinary Officers in 2005 [26] and 2016 (regarding antibiotic stewardship) [27] and in Australia by the then Chief Medical Officer on public health in 2012 [28].

## One Medicine as collaborative medicine

Despite their current disconnect, human and veterinary medicine do share commonalities. The length of training for medical and veterinary students is similar and they share a root common clinical language [29]. Both professions provide high levels of patient care [30] and extend values such as love [31]. They further share a common body of knowledge e.g. anatomy, disease origins, pathology and physiology [32]. Given animals share many of the same chronic diseases as humans [29] there are shared disease interests e.g. cancer, heart disease etc [33–35], with solutions e.g. treatments, often being similar [33]. Doctors and veterinarians also face similar dilemmas and ethical challenges e.g. obtaining consent, patient confidentiality, ethical responsibility, the cost of treatment and impact on quality of life [34,36]. As both human patients and caregivers for animal patients are increasingly well informed, greater expectations are placed on both professions, thus requiring good communication skills [37]. Both professions also share similar stressors e.g. long work hours, levels of responsibility and impacts e.g. depression, compassion fatigue and burnout [38].

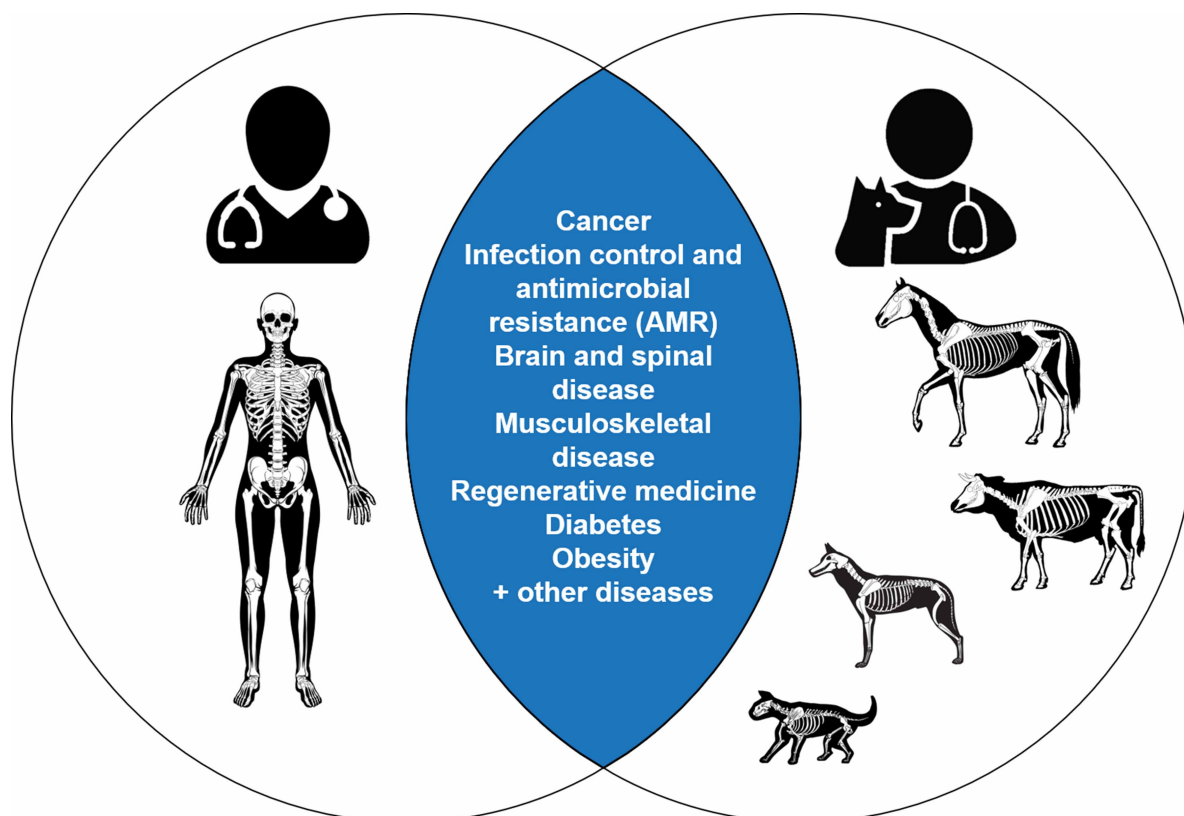
In terms of naturally occurring spontaneous disease, human and veterinary medicine have convergence points and overlap [11,39]. One Medicine (based on the scientific literature) has come to be most associated with companion animals (as comparative and translational models of disease). This is perhaps not surprising given the expectations from animal caregivers to receive high levels of veterinary care [40]. Figure 2 provides an outline of some of the areas of natural synergy and convergence between the two medical disciplines, which are then described then described further, with an emphasis on One Medicine’s central tenet as stated previously.

## Infection control and antimicrobial resistance

Learned societies, such as The Royal Society [17] have previously considered a One Medicine approach to be of benefit with regards infectious diseases, due to commonality in areas such as immunology, physiology, epidemiology etc. The COVID-19 pandemic has focused considerable attention on zoonoses, for example, bats have been studied with regard to infectious disease spillover events. In contrast, reverse zoonoses had, prior to COVID-19, received comparatively little attention [41–43]. Heightened awareness of this transmission route has prompted calls for animals to be included in SARS-CoV-2 forecasting models, of the detrimental impact to wildlife populations e.g. North American bat populations [44] and in terms of public health, how such spillback events could result in new variants, against which current vaccines could be less effective [42,43].

An estimated 60% of existing human infectious diseases have an animal origin [45], but in terms of One Medicine, it is highly probable we do not know if there is a converse percentage of animal pathogens that have a human origin. Examples of reverse zoonoses include human to swine transmission of influenza [46], probable reverse zoonosis of influenza to Striped skunk [47], elephant TB [48,49] and canine TB [50]. They have also been discussed in terms of their role in impeding parasite eradication efforts [51].

Bacterial pathogens present health challenges to both human and veterinary medicine, e.g. MRSA, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [52,53]. In terms of treatment, some classes of antibiotics such as the high priority critically important antibiotics (HP-CIAs) e.g. 3rd and 4th generation cephalosporins, fluoroquinolones and colistin overlap both veterinary and human medicine [54]. Antibiotic overuse and misuse in both the medical and veterinary professions has been a contributory factor to antimicrobial resistance [55,56]. Bacteria such as *Escherichia coli* can cause severe infections in both humans and animals and can be an important reservoir of resistance genes [57]. MRSA, whilst known in humans, also occurs in animals such as horses, dairy cattle, pigs and companion animals, potentially via reverse zoonoses [58–60]. As such human



**Figure 2. Areas of natural convergence and overlap between human and veterinary medicine considered for One Medicine approaches.**

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to animal transmission of Methicillin resistant *Staphylococcus aureus* (MRSA) has been studied in relation to cats and dogs [61].

In terms of shared benefits, research on bat host defence system and immune tolerance mechanisms, could benefit both bats and humans by increasing understanding on human ageing-related, autoimmune and autoinflammatory diseases [62]. Studies on Feline Infectious Peritonitis (FIP), a fatal disease in cats caused by a cat coronavirus, could inform our knowledge of SARS-CoV-2 [63] and drugs used to treat FIP can potentially inhibit SARS-CoV-2 [64]. With regard to the Ebola virus outbreak in 2013, there was discussion on the shared benefits of inter-species immunity if great apes were to be vaccinated against the Ebola virus [65]. The monitoring of animal sentinel species for zoonotic diseases e.g. the so-called ‘canary in the coal mine’ could be an integral part of bio-surveillance, and potentially be bi-directional, with humans acting as sentinels for animals e.g. Brucellosis [66].

## Neurological and spinal diseases

Companion animals, such as dogs, share many of the same risk factors as humans in relation to diseases such as strokes e.g. age, and its natural occurrence in dogs bear similarities to the human condition. Similarly, epilepsy also naturally occurs in animals e.g. cats, dogs etc., again with noted similarities to the human condition [67,68], thus presenting an opportunity for the two-way exchange of knowledge, data and clinical assessment tools. For example, the National Institute of Health Stroke Scale, a clinical assessment tool used to determine stroke severity in humans has been modified to be used for canine strokes [67].

The healthcare challenges of cognitive disorders is likely to increase, as human and companion animal populations increase and age. Presently, there is no cure for Cognitive Dysfunction Syndrome in cats and dogs, which has similar neuropathy and clinical signs to Alzheimer’s disease in humans [67]. With regards to spinal

conditions, the high prevalence of traumatic spinal cord injury in companion animals, the resultant population and patient data, could help inform human medicine [67].

## Cancer

Cancer is perhaps the area where One Medicine has been most successfully applied and adopted [69]. Naturally occurring spontaneous cancers whilst predominantly in companion animals (notably dogs), also occurs in wild animals e.g. Californian sea lion [70] and Tasmanian devils [71].

Many types of cancer are shared between humans and animals [30] e.g. soft tissue and bone (sarcomas), leukaemia, bladder and skin cancer [72]. Various common factors have also been noted e.g. incidence rate, environment and similar diets (companion animals) [73,74], genetic trait similarities [67,75], risk factors e.g. age and obesity [30,76–78] causative factors [73], with patients receiving high levels of care [30]. Naturally occurring spontaneous cancers in animals also have similar clinical signs, biology, pathology, genomic changes and pathophysiology [30,72], thereby potentially more closely mirroring human cancers than experimentally induced cancers in animal models [72,79]. Therefore, the parallel study of cancer in human and veterinary medicine could enhance our understanding of the factors underpinning tumour formation [72]. The selective breeding of purebred dogs, results in restricted genetic variation thus permitting identification of the genetic basis of disease [78], and with their shorter lifespans, companion animals provide a compressed timeframe in which to study the natural progression of disease [30,72], thereby affording better evaluation of novel therapeutics, diagnostics and most importantly, prevention [72].

Naturally occurring mammary cancer, whilst rare in animals such as horses, pigs and ruminants does occur in cats, rodents and dogs, bearing similarities to human breast cancer [74]. Bladder cancer in dogs has been found to closely mimic human invasive bladder cancer [77]. The incidence and age correlation of spontaneous brain tumours is similar in humans and dogs, with secondary spread i.e. metastases, to the central nervous system occurring in both species [67].

Osteosarcoma (a form of bone cancer) occurs in both humans and dogs, its incidence in the latter being much higher (~10 times) [73,80,81]. Osteosarcoma spreads rapidly, usually to the lungs, with treatment options typically limited to chemotherapy and amputation of the affected limb [81], although in dogs limb salvage with endoprostheses surgery is also available [82]. Clinical and molecular evidence suggests that some features and risk factors are shared between humans and dogs [81] whilst noted differences can serve to improve cross-species studies, thus maximising potential for safe and effective strategies which could prevent its occurrence in both species [83].

The cross-species study of cancer defences and translation of such research to clinical practice could lead to improvements for both humans and animals [72,84], given that some animals such as Bowhead whales, elephants, bats and naked mole rats appear to have much lower cancer incidences due to anti-cancer protective mechanisms [72]. Studies on osteosarcoma have provided insights into Peto's Paradox i.e. the lack of correlation between cancer incidence to size and longevity of a species [84] and why this form of cancer is more prevalent in large and giant breed dogs, thought to be a consequence of selective breeding and artificial selection [83].

Human medicine has made significant advances in personalised cancer treatment such as immunotherapies e.g. monoclonal antibodies. In contrast, cancer treatment varies widely in veterinary medicine [80] being mostly reliant on the use of chemotherapy [85]. As noted above, naturally occurring spontaneous cancers in animals e.g. dogs, share many characteristics and similarities with the comparable human cancer [86] and for purebred dogs, facilitate understanding of cancer genomics [84]. Thus the potential for developments in the areas of precision medicine [74], personalised treatment [79], genomic analysis [81] and heritable risks [77]. There is much interest in advancing cancer treatment for animals by both the veterinary profession and animal caregivers [85,86]. Studying comparable cancers in parallel in both humans and animals with regards naturally occurring spontaneous cancers would not only benefit human cancer research and clinical trials [79,87] but offer reciprocal benefits to animal cancer research [86–88], thus affording mutual benefit [72,73,77].

## Musculoskeletal disease: osteoarthritis

Osteoarthritis is common in humans, cats, dogs and horses, its natural occurrence in the latter three species being physiologically and microscopically similar to that in humans, especially so for dogs, with similar risk factors i.e. age and obesity [89]. Dogs and humans also share the same main presenting symptom of pain [90], disease progression [69,89] and treatment approaches e.g. treatment and management of pain and surgery to replace affected joints [69]. Due to their morphological diversity, dogs are not just a model for human



osteoarthritis, but also their own species [91]. Therefore, greater inter-disciplinary collaborations and cross-species long-term studies could generate better understanding of influencing factors e.g. lifestyle, genetics, bio-mechanics and epigenetics, resulting in potential research breakthroughs in osteoarthritis treatment for both species [69].

## Regenerative medicine

Veterinary medicine has been a significant contributor in the field of developing stem cell therapies involving mesenchymal stem cells (MSCs). Its advancement ahead of human medicine being most likely due to the stricter required guidelines and regulatory framework required for the latter [92,93]. The study of veterinary patients, via a One Medicine approach, therefore has potential for both human and veterinary stem cell therapies to evolve [94].

MSCs have predominantly been used in horses and humans, given the horse, like humans, is an outbred species [95] plus factors such as its size, that it ages, exercises and develops naturally occurring injuries, bearing many similarities to the human comparable [92]. Their use has also been studied in cats and dogs [96]. For example, in the reconstruction of bone defects in cats [97], the treatment of degenerative joint disease and osteoarthritis in dogs [98–101] and spinal cord injuries in dogs [102]. Aside from physical injury, MSCs have also been used in the treatment of immune-mediated, musculoskeletal and degenerative diseases [95,103]. Regenerative medicine is also being explored for treatment of diabetes mellitus which occurs spontaneously in dogs, and like type 1 diabetes in humans, is incurable, requiring lifelong insulin therapy [104]. As our understanding of MSCs advances, greater understanding of the ability of equine MSCs to provoke an immune response in horses, will inform the use of heterogeneous MSC therapy in human medicine [95]. One Medicine approaches could enhance sports medicine research. Naturally occurring superficial digital flexor tendon injury in racehorses is a well-accepted and scientifically supported model for the human comparable, exercise-induced Achilles tendon injury. Thus, one may be a model for the other with therapeutics tested in environments similar to those experienced by human athletes [105].

## One Medicine in other areas

Diabetes mellitus naturally occurs in cats and dogs [106–108], birds e.g. Nanday conure parakeet [109], horses and cattle [110]. In dogs, it resembles type 1 diabetes in humans, whilst in cats is similar to type 2 diabetes [106–108]. Clinical signs in both cats and dogs are similar to humans with type 1 diabetes [107] with similar risk factors to type 2 diabetes in humans e.g. obesity, diet, levels of physical activity. Like the human condition, treatment of diabetes in animals is by insulin administration, dietary adjustment and reducing obesity [108]. Most recently, it has been found that dogs with diabetes could act as a potential sentinel given that the owners of such dogs are more likely to develop type 2 diabetes given they share similar behaviours [107].

Experimental animal models of human respiratory disease do not exactly reflect the human condition e.g. mice lack a cough reflex and such models have not always translated into safe and effective treatments for humans [111]. However, chronic respiratory diseases such as progressive fibrosing lung diseases naturally occur in animals such as cats, dogs, horses and donkeys [111]. Such natural occurrences may better resemble the comparable human condition, given they occur spontaneously and that lung pathology in naturally occurring disease has considerable homology to the comparable human condition. Studies of such veterinary patients could help provide important information on respiratory diseases, which represent a major healthcare challenge to both human and veterinary medicine [111].

In addition to cancer treatment, veterinary medicine lags behind human medicine in other areas such as bio-medical informatics (machine learning, big data and artificial intelligence) [112] and pharmacogenomics, of note with regard to personalised medicine i.e. treatment regimes tailored to the individual based on their disease susceptibility, prognosis and response to therapeutics. Information which can be derived from their genome i.e. pharmacogenomics [113]. Just as in humans, variations in drug response occurs in animals, thus pharmacogenomics has the potential to benefit both humans and animals [113]. This current lag may be due to a lack of funding for such research in veterinary medicine [114].

As well as impacting on humans, chronic pain also occurs naturally in livestock e.g. sheep, cattle and swine [115] and therefore could be a candidate for a One Medicine approach, whilst corneal ulcers in sea lions have seen novel treatments developed based on applications from human medicine [116].

## The challenges to achieving greater connection between human and veterinary medicine, One Medicine and how they may be overcome

Traditional boundaries still separate the two medical professions [34], with barriers noted from the scientific literature including opportunities for doctors and veterinarians to come together being more coincidental than routine, and that they rarely speak to each other [29]. They therefore remain isolated from each other, both professionally (throughout their training and beyond) [66] and spatially. Although medical and veterinary schools may be constituent parts of the same academic institution, they may be separated by distance on different campuses [9]. This difference in locales likely has a historical basis e.g. human medical schools located proportionate to population centres, whilst veterinary medicine's historical focus on livestock and horses being why most veterinary schools are located in rural communities [117].

The lack of understanding by doctors and veterinarians that their professional roles complement each other [118] and their ongoing divergence has potentially contributed to perceptions of 'us against them' rather than recognition of shared risks [66]. This may also be affected by professional egos [119] and views of veterinary medicine as a '*second class citizen*' [119] or '*the other branch of medicine*' [11] in comparison with human medicine. The ongoing lack of collaboration and co-operation between the two professions contributing to missed beneficial opportunities [35].

Can human and veterinary medicine be equitable given the difference in size between the two professions? Veterinary medicine is much smaller [117,119]. In 2018, there were 290 492 registered doctors [120] compared with 24 422 practising veterinarians [121] in the UK. However, comparing the UK human and animal (companion and livestock) populations in 2020, there were 67.1 million people [122] compared with 90.7 million animals [123,124]. The increase in numbers of companion and livestock animals has resulted in greater demand for veterinarians, coupled with animals being viewed as moral beings rather than property, contributing to raised expectations from animal caregivers in terms of veterinary care [125].

Certain diseases will have species-specific differences e.g. in genetic pathways, but parallel human and animal studies of naturally occurring spontaneous disease still have the potential to reflect the essence of disease challenges e.g. cancer [86]. A greater understanding of such differences and associated factors e.g. species, body size etc., afforded by integrated approaches can therefore still inform and benefit both humans and animals [84].

A will for closer working between the two professions is required, both medical and political [119] and One Medicine requires an ethical and regulatory framework for such parallel studies e.g. study design, patient confidentiality, informed consent, the collection/use of tissue and control/placebo groups [69,126]. Results gained must be reproducible and reliably predict the outcome in human clinical trials whilst ensuring the health and welfare of veterinary patients [91]. Whilst resolutions have been adopted to address the divergence between the two professions in the US [66], presently UK government policy structures could not support a One Medicine approach [17]. In terms of research dissemination to both human and veterinary medicine, veterinary research has been considered primarily confined to veterinary journals [127,128].

Therefore, to overcome these challenges, greater research funding is required as less human and veterinary medicine graduates are entering research, as noted by Khan [129], along with investment into One Medicine research. If we are to promote greater collaboration between the two professions, there must be a cultural shift both in behaviour and attitudes, the answer most likely lies in the education of the medical students and clinicians of the future [118]. Change is needed in the medical curricula whereby inter-disciplinary groups are taught in both medical and veterinary schools, laying the foundation for teamwork and connection between the two professions, with such a potential model being that of the Zoobiquity Research Institute in the US [35].

## Conclusion

Many of the health challenges faced by both humans and animals have no single answer and require a blended approach if we are to ensure that the benefits are shared equitably and progress made in parallel in both animal and human health. Even where species differences occur, parallel animal and human health studies of naturally occurring spontaneous disease can offer much as a useful foundation to inform on the nature of the challenges faced by both human and veterinary medicine. Such a blended approach will be afforded by the emergence of One Medicine as a holistic two-way exchange, Strengthening the links between the two professions will ultimately benefit both, as '*a problem shared is a problem halved*' [29] and thus human and animal health [130].

As stated by Calvin Schwabe [1984] ‘the attempt to biologically pseudo-oligarchy-ize the human species is one of the most pervasive mistakes of modern science’ [131].

## Summary

- One Medicine is the concept that human and veterinary medicine are interlinked and inter-dependent upon each other. By routinely collaborating with each other, this would afford equitable progress for both animal and human health.
- Whilst One Medicine primarily examines the genetic and physiological overlaps that exist between humans and animals, the study of natural and spontaneous disease in animals may inform the essence of similar problems in diagnosis, treatment and management of comparable human conditions.
- No single approach will be the answer to dealing with the future healthcare challenges faced by humans and animals, and thus One Medicine is emerging as a systematic approach to address such challenges.

## Competing Interests

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## Abbreviations

FIP, Feline Infectious Peritonitis; MRSA, Methicillin resistant *Staphylococcus aureus*; MSCs, mesenchymal stem cells; WHO, World Health Organisation.

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