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2	COVID-19 through the One Health lens: adding a missing perspective
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4	Christian Selbach ^{1*} , Maarten P. M. Vanhove ² , Kim N. Mouritsen ¹
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6	¹ Department of Biology, Aquatic Biology, Aarhus University, Aarhus, Denmark
7	² Research Group Zoology: Biodiversity and Toxicology, Centre for Environmental Sciences,
8	Hasselt University, Diepenbeek, Belgium
9	
10	* Corresponding author: christian.selbach@bios.au.dk
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12	Abstract
13	The One Health concept offers an integrative approach to disease and health at the human-
14	animal-environment interface. It has often been suggested to view the COVID-19 outbreak
15	within this framework to better understand and mitigate this global crisis. Here, we discuss how
16	the evolutionary ecology of host-pathogen systems can add a valuable additional perspective to
17	the debate around SARS-CoV-2 and its implications for public health awareness and policy-
18	making. In this context, it is especially important to highlight that changes in nature, such as
19	zoonotic spillover events, are often irreversible, and that humans, while deeply embedded in
20	ecosystems, are intricate ecosystems themselves. A better recognition of the complex biology
21	and evolution of human-parasite interactions will assist our understanding of such zoonoses.
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23	Keywords: One Health, COVID-19, spillover, host-parasite coevolution
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26 Main text

Undoubtedly, the current COVID-19 pandemic is one of the greatest health crises humanity has
faced. To better understand and mitigate this global crisis, and to be better prepared for similar
epidemics in the future, it has been suggested to view the COVID-19 outbreak within the One
Health (OH) framework (e.g. [1]). The OH concept aims at achieving optimal health for people,
non-human organisms, and the environment via inter- and transdisciplinary collaborations
across health and environmental sciences [2].

Given the zoonotic origin of SARS-CoV-2 that spilled over to humans from wildlife, 33 such an approach is certainly warranted. And without doubt, linking human, animal and 34 35 ecosystem health within the OH framework is a powerful approach in predicting, tackling and preventing disease outbreaks [3]. However, even though OH and related concepts such as 36 EcoHealth have expanded beyond an initial narrow focus on human and veterinary health and 37 38 now include wider ecological perspectives [2], we find that the framing of the COVID-19 pandemic within OH misses a crucial perspective: the evolutionary ecology of this host-parasite 39 system. Rather, in the literature, the stated importance of OH in the COVID-19 context often 40 seems limited to recognizing and detecting zoonotic origins, understanding the human-animal-41 environment interface, and avoiding the circumstances of transmission. Hence, integrative 42 43 approaches appear especially useful in preventing future zoonotic epidemics, while less attention is given to their potential for dealing with the ongoing pandemic. 44

Although vaccination efforts will likely be a great success in tackling the pandemic [4], the virus and COVID-19 are expected to persist, potentially with regular seasonal outbreaks occurring during the coming years [5]. SARS-CoV-2 has therefore become, and will in the foreseeable future remain, part of the human pathobiome [6]. From the viruses' point of view, the human host represents a resource-rich ecosystem that the virus has spilled over to and inhabits, and in which it thrives, replicates and evolves [7]. The emergence of new SARS-CoV-2 variants carrying different mutations highlights the pathogen's rapid evolution within its human host system [8]. This should caution against any hopes of returning to the *status quo ante* and 'back to normal', once this crisis has been overcome. In evolutionary processes, there is no going back, and a solution that aims at restoring a pre-outbreak situation simply does not exist. Accordingly, the 'new normal' [9] in social contexts comes along with a new biological normality in a long-term host-parasite association with continuous coevolution.

Moreover, after the initial wildlife-to-human transmission of SARS-CoV-2, the virus 57 has continued to spill over to other mammals, most notably American mink *Neovison vison* in 58 Danish and Dutch fur farms, and it has the potential to infect a wide range of domesticated and 59 wild animals [10]. Having been co-introduced around the world by its cosmopolitan human 60 61 host, there is little reason to assume that no further cross-species transmission events will occur in the future. Such spillovers are largely driven by increased exposure events and the acquisition 62 of genetic variations that allow host switching [11], both of which are common features of the 63 64 current outbreak. It is therefore well likely that the human host system can serve as a 'stepping stone' for the virus to find its way into yet other host species, which might be the starting point 65 of an ever-changing host range of SARS-CoV-2 throughout its evolutionary history. To fully 66 understand and predict the risks this entails, input from ecological and evolutionary 67 parasitology that focuses on host-pathogen interaction will be crucial. 68

69 Considering human, animal and ecosystem health together under the OH umbrella can greatly benefit our understanding of zoonotic diseases, but will require investigating them as 70 novel and potentially persistent host-parasite systems including an eco-evolutionary 71 72 perspective. In this context, it is especially important to point out that changes in nature, such as zoonotic spillover events, are often irreversible, and that humans, while deeply embedded in 73 ecosystems, are complex ecosystems themselves. Human health, rather than a state of well-74 75 being with the mere absence of disease, encompasses the ability to adapt and self-manage in the face of physical, social, and emotional challenges [12]. A better recognition and public 76 awareness of the complex biology and evolution of human-parasite interactions could help our 77

78	understanding of this pandemic, assist the public in framing often poorly known phenomena
79	like viral mutations, zoonotic spillovers or biological invasions [13], and lead to more
80	autonomous and responsible behaviour in light of current and future health challenges.
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89	C.S. conceived the paper and led the writing with primary inputs from M.P.M.V. and K.N.M.
90	
91	Corresponding author
92	Correspondence to christian.selbach@bios.au.dk
93	
94	Competing interests
95	The authors declare no competing interests.
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