One Health 12 (2021) 100228

Contents lists available at ScienceDirect

One Health

journal homepage: www.elsevier.com/locate/onehlt

The SARS-CoV-2 pandemic: A syndemic perspective

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ARTICLE INFO

Keywords:
COVID-19
Health in all policies
One health
SARS-CoV-2
Syndemic

ABSTRACT

The SARS-CoV-2 pandemic has affected communities, populations, and countries throughout the world. As the SARS-CoV-2 pandemic developed, the extent to which the disease interacted with already existing endemic, non-communicable and infectious diseases became evident, hence deeply influencing health outcomes. Additionally, a synergistic effect has been demonstrated also with socio-economic, cultural, and contextual determinants of health which seem to contribute to poorer health and accumulating social disadvantages.

In this essay, using as a starting point the syndemic theory that translates the cumulative and intertwined factors between different epidemics, we argue that the SARS-CoV-2 is a one health issue of a syndemic nature and that the failure to acknowledge this contributes to weakened policy-making processes and public health responses and ineffective health policies and programs.

1. Background

The SARS-CoV-2 infection was declared a public health emergency of international concern on 31st January and a pandemic on 11th March 2020. The disease was first reported in China in December 2019, although there is evidence from Italy and France that it was already circulating in Europe before that time [1]. In less than four months, the virus spread to all continents (excepting Antarctica), creating multiple asynchronous national epidemics of COVID-19 [2,3].

The pandemic infection caused by SARS-CoV-2 is unquestionably a one health issue due to the high possibility that the virus has crossed the species barrier to infect humans, then causing human-to-human transmission. Thus, there is a need to recognize the interconnection between people, animals, and their shared environment, and develop appropriate, collaborative and multidisciplinary approaches for its control and mitigation [4,5].

One perspective to the one health characteristics of the SARS-CoV-2 infection pandemics is its human-focused syndemic "side".

In this essay we argue that the failure to consider the syndemic nature of this pandemic contributed to weakened policy-making processes and public health responses.

This essay is supported by a narrative review of the literature using a "synthesis of better evidence" approach [6] on syndemic theory and emerging evidence of the syndemic nature of the SARS-CoV-2 pandemic.

2. Syndemic theory

The 1990s saw the introduction of an innovative approach to comprehend health as part of a biocultural-synthesis that encompasses (i) the "determinant interconnections among pressing health problems", (ii) "sufferer and community understandings of illness(es)/disease(s)" and (iii) the "relevant social, political, and economic forces in play", as well as (iv) the environmental conditions that may lead to the development of health or disease. This dialectical thinking led to the term of

Abbreviations: NCD, Non Communicable Diseases; NTD, Neglected Tropical Diseases.; SDG, Sustainable Development Goals..

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https://doi.org/10.1016/j.onehlt.2021.100228
Received 24 November 2020; Received in revised form 10 February 2021; Accepted 11 February 2021
Available online 17 February 2021

"syndemic" as a new concept in epidemiological and public health thinking [7–12].

The syndemic model shares the ecological premises of the fields with long tradition in health research and intervention (e.g. health promotion), which claim the need to overcome dichotomic understandings of individual behavior and social determinants, and between social and natural factors and further ties the syndemic model theory in with One Health. Consequently, the model discards conventional understandings of diseases as discrete entities distinct from each other and independent of the social contexts in which they are found. The model builds on a biosocial complex of co-occurrence and synergistic interaction, or simultaneous occurrence of diseases and their determinants that promote and enhance the overall negative effects on health and other conditions experienced by individuals and populations [13]. As such, it integrates and builds on concepts emerging concurrently, namely, biosocial models of health determinants [14], salutogenesis [15,16], late life compression of morbidity [17] and life course epidemiology [18–21].

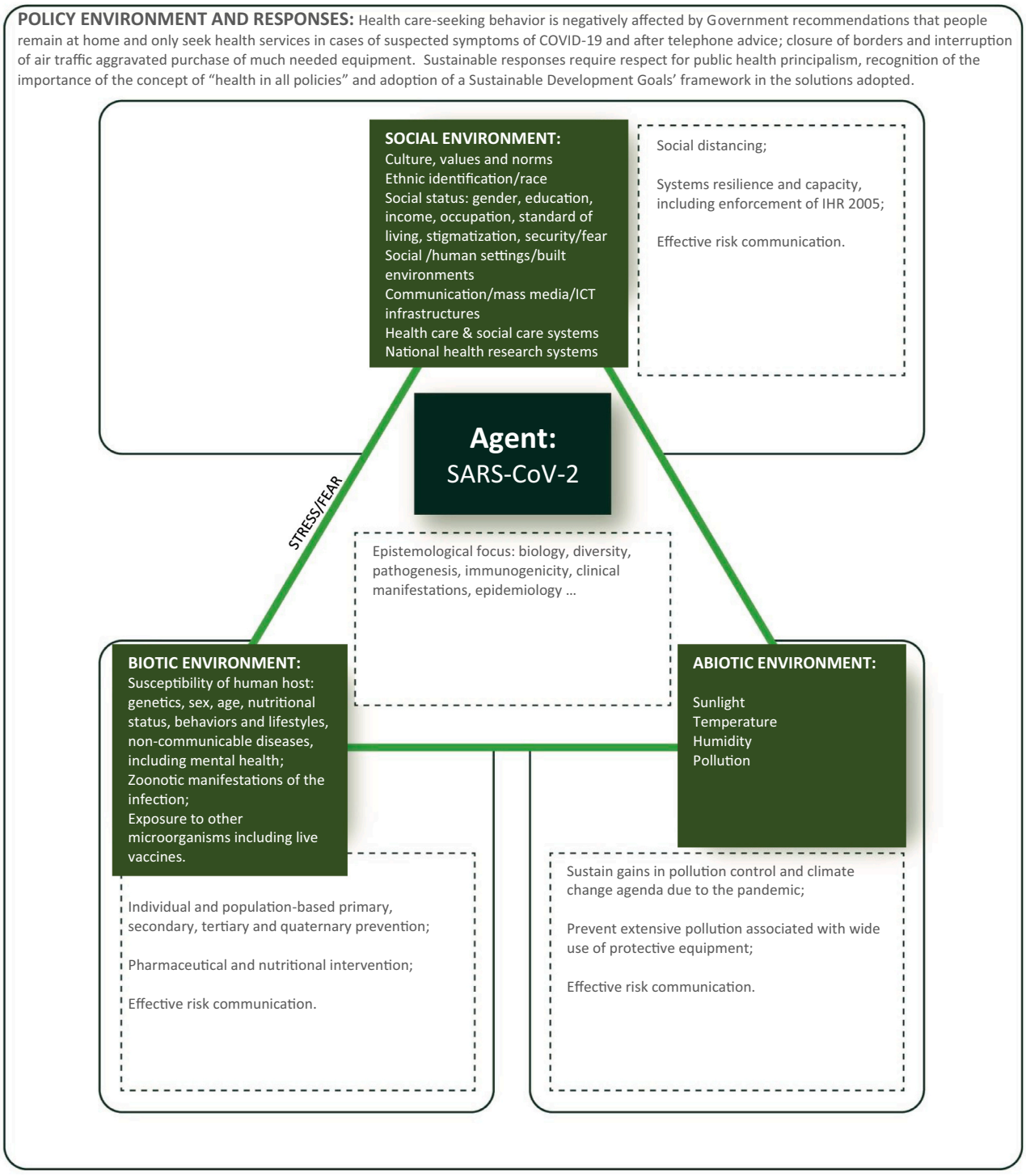

Fig. 1. Social, environmental and political determinants affect the syndemics of health and disease applied to the SARS-CoV-2 Syndemic.

Further research on syndemics has underscored (i) a need to focus on social inequality as a root cause of syndemic interactions, and (ii) that population-level disease prevention can only occur through addressing the large-scale social forces that shape both individual and population health [22–24].

The term syndemic, at its simplest level, refers to two or more epidemics interacting synergistically and contributing, as a result of their interaction, to the clustering of excess burden of disease in a location or population, more than just the sum of both [25].

The syndemic concept also assumes biological synergisms that may vary from changes in blood biochemical markers or damage to organ systems caused by one pathogenic agent facilitating the spread of or impact on another agent, to gene mixing among pathogenic agents [25,26].

Lastly, the term syndemic also emphasizes the relevance of biological (hereditary factors, nutritional status, sex, age), social (wealth and poverty; culture and practices; networks and communities; economic, educational, dietary and leisure activities and behaviors; health care and social support systems; stigma and discrimination), environmental (natural and built environments) and political factors in the health of individuals and populations. Stress is a common pathway through which these social, environmental and political determinants affect the syndemics of health and disease (Fig. 1) [26].

The syndemic framework has been applied over the years to understand the dynamics of migrant health, health disparities, malnutrition, violence (including intimate partner violence), sexual health, substance abuse, mental health, oral health, HIV/AIDS, tuberculosis and other infectious diseases, and non-communicable diseases (NCD) (such as diabetes mellitus, cardiopulmonary conditions, obesity or kidney disease) [22,25–41].

The theory of syndemics is a conceptual tool in population health sciences that has the potential to help policymakers and program implementers in their endeavors to improve the health of populations. As originally theorized, three concepts underlie the theory: disease concentration, disease interaction, and the large-scale social forces that give rise to them. As theorized, syndemics are a complex, multilevel phenomenon. What makes the theory most noteworthy are its predictions about how interactions between different epidemics amplify the disease burden in a manner that differs if each disease would have been experienced separately. Additionally, the theory allows predictions about how public health planners can (or cannot) effectively intervene to mitigate this burden [24]. In short: syndemic translates the cumulative factors between different epidemics.

3. Evidence of the syndemic nature of the SARS-COV-2 pandemic

The SARS-CoV-2 epidemics overlaps with endemic diseases [NCD, malaria, schistosomiasis, tuberculosis, hepatitis C, HIV, dengue and other neglected tropical diseases (NTD)] and with seasonal diseases (such as influenza and other respiratory diseases), a host of cultural and social determinants (fear, stigmatization, racism, gender, economic inequalities, mis-information, risk behaviors, food and nutrition insecurity, occupation, climate, exposure to different types of pollution, supply of health and social care services, health care seeking behavior and violence, supply of drugs and addictive behaviors) and climate and environment [31,42–57] (Fig. 1).

A spatial overlap of high rates of NCD and COVID-19 suggests a broader syndemic health burden, in the sense that comorbidities intersect with nutrition, race and social determinants of health [56,58–60]. Substantial evidence points towards NCD being a major factor for poor outcomes resulting from COVID -19 [61,62] and vice-versa, COVID-19 leads to the neglect of NCD [61].

Biological interactions between SARS-CoV-2 infection and other coinfecting pathogens are also relevant. First, because of changes in host pathology related to indirect immune effects [63]. There are many examples of important interactions between malaria, NTD and other infectious diseases: malaria plays a role in Epstein–Barr virus infection, leading to Burkitt lymphoma [64]; several parasite – HIV coinfections are associated with increased HIV viral load, transmission and worsened immunosuppression [65–67]; deworming is associated with decreased HIV viral load and improved CD4+ counts among HIV-infected individuals [63].

Studies suggest that the balance between innate immunity and acquired immunity can be challenged by parasitic infections (e.g., parasite-induced disturbances to the helper cell type 1/type 2 balance and/or macrophage phenotype) and that effects of co-infections are immune-mediated. It has also been shown that these infections can affect disease susceptibility and pathogenesis and even interfere with accurate diagnose [68].

Hence it is possible that preexisting infection with tropical parasites and other NTDs may also lead to changes in susceptibility and/or severity of COVID-19, but it is unclear whether the resulting immune response will be beneficial or harmful when hosts are coinfected with SARS-CoV-2. It is worth mentioning the line of research that is looking at the nonspecific effects of BCG by studying the interplay between the prevalence of COVID-19 and the BCG vaccination and the hypothetical immunomodulatory effect of the BCG vaccine applied to the infection by the SARS-CoV-2 [69].

Actually, the low intensity and lethality of the national epidemics in most African countries suggest hypothetical protective interactions of the high burden of tuberculosis (and/or BCG coverage) and tropical parasitic diseases, along with the lack of health-care infrastructure capable of clinically detecting and confirming COVID-19 cases, the implementation of social distancing and hygiene, international air traffic flows, the climate, the relatively young and rural population, the genetic polymorphism of the angiotensin-converting enzyme 2 receptor, cross-immunity and the use of antimalarial drugs [70–80]. However, the detection of a new variant of the SARS-CoV-2 in South Africa (variant 501Y·V2) in middle December 2020 with preliminary studies suggesting that the variant is associated with a higher viral load, which may suggest potential for increased transmissibility, might challenge the low transmissibility, low lethality trend observed so far in most African Countries [81].

There are significant concerns that the emergence of COVID-19 is currently overlapping with other circulating viruses, particularly dengue, in various *endo*-epidemic regions across South America, South East Asia and Africa. The situation warrants observations and monitoring as both conditions may potentially lead to fatal outcomes, especially in patients with chronic comorbidities. Also, overlapping infections and co-occurrence may increase the number of patients requiring intensive care and mechanical ventilation, overwhelming the capacity of health services [82,83].

On the other hand, there is also evidence that non-pharmaceutical control measures (e.g., social distancing, school closures, travel restrictions, use of masks) being taken may prevent or postpone the occurrence of seasonal infections caused by virus such as influenza and respiratory syncytial virus. A buildup of susceptibility during these control periods may result in out of season peaks or in larger outbreaks in the coming years [84].

Non-pharmaceutical interventions also negatively affect many economic sectors, particularly in the informal economic sector (e.g., street vendors, informal traders), proximity economic activities, liberal workers and economic activities where the value chain is most dependent on the mobility of goods and people [85]. These include, for example, animal production and its related industries. Indeed, with the cessation of imports and exports between countries, it is not possible to provide feeds that are considered as basic raw materials in livestock raising. This situation impairs animal movements, decreases production inputs availability and negatively affects animal welfare. The sustainability of animal production is also affected by a shortage of workers due to the lockdown/curfew and the strong decrease in the purchasing power of the consumer. The result of the impact of non-pharmaceutical

interventions, namely, lockdown, restrictions to movement of people and goods and physical distancing, among others, may result in economic collapse, increased unemployment, poverty deterioration and widespread famines, as food security becomes a global concern [86–99].

Stress and fear are likely to potentiate many of the interactions already cited. The epidemic of fear is well described by Delgado et al. and by Robalo et al. [100,101]. Fear in association with epidemics and pandemics has been acknowledged for centuries [102]. The peculiar aspect in relation to COVID-19 is that fear is as much caused by the novelty of the SARS-CoV-2 as it stems from the lack of preparedness of scientific communities and policymakers to help the populations to manage it [103,104].

Fear can lead to denial, including of scientific knowledge, and violence against neighbors and health care workers [105–107]. Fear is associated with social isolation, which is desirable to curtail the transmission of the infectious agent but impacts negatively the mental health of individuals [107] and facilitates intimate partner and child violence: social isolation contributes to unprotecting the victim and making escape, requesting help and reporting of violence difficult [27,30,32]. Fear is behind much of the stigmatization observed in association with infected persons and their contacts [108]. Fear influences health-seeking behavior in a negative way, resulting in avoidance of contact with health care facilities for preventive, promotive and treatment health care [61,109]. Fear leads also to the abandonment of the household [110,111] and to disruptive consumption patterns: one of the most immediate impacts of COVID-19 was a wave of panic buying by the public as lockdowns were announced [112].

The perception of a medical urgency is affected, leading to avoidance of emergency health care services [109]. This is further aggravated by the redeployment of scarce resources to the medical care of COVID-19 patients and to the reinforcement of public health teams involved with case finding, contact tracing and enforcement of non-pharmaceutical public health interventions [113,114].

Neglect of routine and emergency care is a reality that potentiates the negative effects of the SARS-CoV-2 pandemic. Government regulations, particularly at the beginning of the epidemics, usually recommended that people remained at home and only seek healthcare services, preferably through an initial telephone contact. With these restrictions, negative impacts on health were soon felt: endemic diseases such as malaria were neglected; chronic conditions worsened; women were left without access to family planning services, prenatal surveillance consultations, vaccinations or nutritional counseling, and institutional births were reduced considerably, associated in many developing countries with lack of public transport, leading to increases in mortality amenable to health care [24,29]. This situation, which accentuated the weaknesses of health systems and compromised the provision of services, is like a “triple burden of disease” [26] and contributed for an unwelcome “third wave” [29].

The relationship between COVID-19 and environmental factors is complex [78,115]. Recent studies have demonstrated a positive correlation between spread and decay of SARS-CoV-2 and temperature, absolute humidity and population density [116] and a positive correlation between the transmissibility of the SARS-CoV-2 and lower UV radiation, lower latitudes, lower elevation, and smaller populations with historical air pollution exposure [117]. No association was detected between deaths and country temperature or precipitation [118]. There are also preliminary findings attributing a significant fraction of worldwide COVID-19 mortality to anthropogenic air pollution [57]. On the other, a strong reduction of air pollution was identified in many locations during the lockdown measures [119–122]. Studies measuring changes in air pollution and mortality have been related to a reduction in excess deaths due to air pollution (>4600 deaths in China, [119]. This can be viewed as a health co-benefit from the containment measures, which may reduce air pollution-induced COVID-19 mortality. Such benefits could also be achieved after the COVID-19 lockdown. Both perspectives of air pollution during the pandemic underscore the important role of fossil fuel-related and other anthropogenic emissions.

There is also evidence of SARS-CoV-2 viral RNA detectable in the inflow but not in the outflow wastewaters and its infectivity seems null [123].

An infodemic of fake news campaigns have significantly contributed for all the above, by disseminating misleading information and risk communication strategies, incoherent messages between politicians, public health authorities and scientists and an information overload that reduces trust and confidence, compromise economic activities and fail to mobilize the wider level of public support needed to enforce control measures effectively [30,31,124].

4. Conclusions

SARS-CoV-2 brought back to the forefront of the health policy debate significant issues already identified in past pandemics. Pledges were made then that we would learn from previous outbreaks and be better prepared when faced with another. That such has not happened and we are once again discussing predictable issues previously identified - such as health systems fragility and lack of resilience, inadequate surge capacities, and poor communication - is on the one end a moral failure [125] and, on the other, a reflection of the inadequate framework used to understand and respond to pandemics demonstrating the lack of preparedness for globally catastrophic risks [126]. It also identifies that the lack of capacity for governance is not a problem limited to low- and middle-income countries but widespread at all levels of development, highlighting the inability to correspond to the expectations created by the Sustainable Development Goals (SDG), of ministries exercising leadership beyond narrow sectoral boundaries, in pluralistic and multisectoral milieus, and also to predict and be prepared for emergent and future challenges while continuing to manage public services and institutions [127].

The interconnectivity of humans, animals and the social and abiotic environment (Fig. 1) is also highlighted by the current pandemic and it is most relevant in understanding and tackling any threats to food systems, agricultural production and other systems of economic livelihood. This is particularly important in economic systems where animals play an important role for society and food security – providing, income, transport, fuel and clothing as well as food, highlighting the relevance of a One-Health understanding of the pandemic [128].

The focus on finding a response to the COVID-19 pandemics, which should have been thought of previously (since for a long time, it was a given fact that a new epidemic would strike) led to a blurred approach to all other prevalent health issues and problems reflecting the “curse of piecemeal perspectives” and “siloed frameworks” [129,130].

Co-existent endemicendemic, and epidemic, NCD, NTD, and other (human and animal) infectious diseases as well as social systems’ fragilities, long neglected environmental challenges, the level of health literacy and cultural issues were not considered and, now, the challenges loom larger than before as COVID-19 interacts syndemicaly with all these issues.

Understanding the impact of this syndemic requires first and foremost learning from documented experiences. Second, it requires the use of theoretical frameworks that can sufficiently conceptualize its multilevel, interacting and dynamic nature. It implies a need for assessment of how the public health system and communities can better respond to syndemics. Thus, we advocate for the adoption of a syndemic policy approach that enables a holistic and distinctive understanding of the intersection of prevalent (endemic) diseases and COVID-19-specific vulnerabilities and disparities experienced by individuals, populations, communities and societies. Syndemic-informed approaches can then, supported by insightful application of public health principalism [103], lead to impactful multi-level prevention strategies that simultaneously tackle both (endemic) diseases and their determinants, and COVID-19-specific factors and outcomes that lead to the clustering of health vulnerabilities and disparities over time (Fig. 1). This more holistic

approach would integrate other conceptual frameworks such as "one health", "health in all policies" and assume a SDG framework in the solutions adopted [113,131–134].

These frameworks would contribute to (i) an approach which transcends geopolitical boundaries, based on good science, transparent communication and widespread global solidarity: (ii) tackle the transition out of market closures and lockdowns; (iii) more integrated and transparent surveillance infrastructures and monitoring of the occurrence of infectious diseases in humans, animals; (iii) environmental surveillance as an early warning system that monitors the levels of pathogens circulating in the population, identifies outbreaks, even before cases are notified to the healthcare system, and agents sharing similar genotypes across species as well as spatio-temporal spread of such infections; (iv) scrutiny of data, information, models and the processes by which the decisions are made and their rationale; (v) improve coordination and active collaboration among stakeholders representing diverse and apparently incompatible domains; (vi) highlight the need for an effective institutional landscape (national, regional and global), facilitating adequate regulation of hotspots for transmission of infectious agents among abiotic environment, animals and humans – regional Blocs such as the European Union, African Union, Association of Southeast Asian Nations, Caribbean Community and *Mercado Común del Sur* (MERCOSUR) should increase their role in health; (vii) emphasize the need for equitable solutions to infectious disease challenges, ensuring that policy response mechanisms and interventions are reflective of the disproportionate disease burdens borne by vulnerable and marginalized populations, or by persons providing health care and other essential services to those sick; (viii) further blur the border between infectious and NCD and between human and animal health encouraging an integrated approach to planetary health aligned with the SDG; and (ix) combine the short term approach in response to the crisis with a long term vision provided by the SDG.

Despite the widely recognition that the SARS-CoV-2 pandemic has become a learning opportunity, as we enter the "second epidemiological wave" much is still to be learned and one wonders if the way society deals with co-existing health problems is ever going to change. The SARS-CoV-2 has unraveled the complex dynamics between a novel, challenging health problem, co-existing, chronic and endemic ones and the capital of knowledge, competencies and practices of people all over the world and stressed its fundamental syndemic nature. As such, in this and incoming epidemics a syndemic understanding of health and disease is needed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Paula Saraiva for the support with bibliography. Fundação para a Ciência e Tecnologia for funds to GHTM UID/04413/2020. CTDR is supported by CNPq, Brazil, through a Productivity Research Fellowship and is a "Cientista do Nosso Estado" by Faperj, Rio de Janeiro, Brazil.

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