Chies *et al. One Health Implement Res* 2023;3:69-76
DOI: 10.20517/ohir.2022.42

One Health & Implementation Research

Opinion

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Remembrance and oblivion in vaccine development and vaccination coverage rates in Brazil: addressing vaccinology based on the One Health perspective

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How to cite this article: Chies JAB, Ellwanger JH. Remembrance and oblivion in vaccine development and vaccination coverage rates in Brazil: addressing vaccinology based on the One Health perspective. *One Health Implement Res* 2023;3:69-76. https://dx.doi.org/10.20517/ohir.2022.42

Received: 30 Nov 2022 **First Decision:** 29 May 2023 **Revised:** 12 Jun 2023 **Accepted:** 21 Jun 2023 **Published:** 29 Jun 2023

Academic Editor: Olivier Sparagano, Jorg Heukelbach **Copy Editor**: Lin He **Production Editor:** Lin He

Abstract

Lack of funds or interest from industry delays vaccine development. In 2016, a SARS vaccine was listed among the top ten in Research & Development (R&D), but this and several other vaccines were "put in a freezer" for different reasons. This can have devastating public health consequences when a pandemic such as COVID-19 emerges. In Brazil, vaccine coverage rates have dropped significantly in recent times, facilitating the reemergence of diseases that were "forgotten" by the Brazilian population. In past years, Brazil was considered by the international community as a good example and model concerning mass immunization programs. These achievements need to be remembered and rescued as a public health strategy. Investing in vaccine R&D is fundamental to the prevention and control of infectious diseases. However, this action must be integrated into a broader strategy considering the prevention of emerging diseases by maintaining ecosystems' function and preserving human, animal and environmental health (One Health perspective). Otherwise, advances in vaccine R&D will be constantly overtaken by the emergence of new disease outbreaks. Discussion on how to accelerate vaccine development and licensure is still needed, and the One Health perspective can help us to face emerging health challenges. These and other critical points involving vaccine-related issues are addressed in this article, with a focus on the Brazilian context. Finally, some solutions to deal with these problems are suggested.

Keywords: Brazil, emerging infectious diseases, SARS, vaccination coverage, vaccine development, public health

Brazil is the largest country in Latin America, leading the scientific production in the region and occupying 14th place among countries in the world regarding the number of scientific articles published between 1996 and 2022[1]. In the fields of biomedical sciences and public health, Brazil has extensive experience and expertise in the development of vaccines for human and veterinary use. These achievements, in combination with the success of the National Immunization Program (*Programa Nacional de Imunizações*-PNI, set up in 1973), established Brazil as a benchmark in vaccinology[2-4]. Some important achievements stand out. For example, Brazil is the world's largest producer of yellow fever vaccines[5,6], making a significant contribution to the prevention of the spread of the yellow fever virus worldwide. Additionally, since 1996, the Brazilian Butantan Institute (São Paulo State) has produced the recombinant hepatitis B vaccine, which has been used for the immunization of millions of newborns and children[7]. The Butantan Institute and the Oswaldo Cruz Foundation-FIOCRUZ (Rio de Janeiro State) also have a tradition in the production of many other vaccines and immunobiologicals that hold national and international importance[7,8]. Brazil's successful history in the development and administration of vaccines contributes significantly to the maintenance of Brazilian public health, helping to control endemic diseases as well as emerging pathogens, such as SARS-CoV-2. However, this rich history in the field of vaccinology has been recently neglected and even forgotten.

Oblivion is a dangerous behavior, especially in science and public health. In this context, we would like to remember the stunning case of stalled development of scientifically feasible vaccines against major diseases due to a lack of funds or interest from the pharmaceutical industry[9]. As early as 2016, a SARS vaccine was listed among the top ten in Research & Development (R&D) priority based on feasibility and need, together with Ebola, Chikungunya, MERS, Lassa fever, Marburg, paratyphoid fever, schistosomiasis, Rift Valley fever and hookworm vaccines. Ironically, the cover picture of the journal issue in which such vaccine rank was published even depicted a vial labeled as "SARS Vaccine"[9], but all these potentially important tools, in a given stage of development, were "put in a freezer" for different reasons[9], and the COVID-19 pandemic just highlights how misguided was such decision since previous advances in SARS vaccine development could have contributed to a more rapid response to SARS-CoV-2 emergence. We recognize that issues such as low cross-immune response between SARS-CoV-2 and other coronaviruses could have limited the impact of a prior SARS vaccine on the COVID-19 pandemic (considering reductions in transmission rates). However, a SARS vaccine available early in the pandemic could have helped to lessen the disease severity in some individuals. Furthermore, the development of 'universal' pan-coronaviruses vaccines is the best option if we want to be prepared to deal with potential new outbreaks quickly and efficiently[10,11].

Moreover, it was clear as early as 2016 that if an Ebola vaccine had been available before the 2014-15 West Africa outbreak[12], many deaths would have been avoided[9]. The lack of a given vaccine is multifaceted and is reflected in indicators other than death rates. The Ebola outbreak disrupted the health system and caused a reduction in vaccine coverage for other diseases in West Africa, showing that the lack of a specific vaccine can also facilitate the occurrence of other vaccine-preventable diseases[13]. Nowadays, the COVID-19 pandemic, and a SARS vaccine, mirror this situation. Thus, in a 10-year time window, two similar huge failures could have been avoided if resources had been directed to vaccine R&D, aiming at already identified leading targets. Completely preventing the emergence of new pandemics is an unlikely achievement, even in a scenario of extensive vaccine R&D. However, as mentioned previously, robust R&D vaccine systems may significantly reduce the negative impacts of new pandemics on public health.

Neglecting the importance of actions focused on vaccine R&D is particularly important in the current global scenario where outbreaks and pandemics have become an increasing threat. In the last decades, human populations have experienced the emergence or reemergence of several disease outbreaks, many of them

caused by viral pathogens, including West Nile virus (etiological agent of West Nile fever), Zika virus (Zika fever and congenital malformations), Ebola and Marburg viruses (hemorrhagic fevers), Yellow fever virus (Yellow fever), H1N1 ("swine" flu), and Chikungunya virus (Chikungunya fever)[14,15]. It is estimated that up to 75% of emerging infectious diseases have a zoonotic origin, typically transmitted to the human population due to the imbalanced impact of human actions on ecosystems and biodiversity[16]. Wild animal hunting, loss of vegetation cover, breaking of food webs due to biodiversity loss, and climate change are just some of the human-related factors that facilitate the introduction of new pathogens into the human population and the emergence of new outbreaks. Right now, zoonotic and vector-borne diseases are spreading in developing countries, such as Brazil, with a trend that emerging infectious disease events increase as climate change, deforestation and other land-use changes intensify, especially in tropical regions [16,17].

Investing in vaccine R&D is one of the most important strategies to prevent and control infectious diseases, but it must be integrated into a broader strategy, which considers the prevention of emerging diseases by maintaining ecosystems' function, preserving human, animal and environmental health through the One Health perspective [Figure 1][16]. Otherwise, even significant advances in vaccine R&D will be constantly overtaken by the emergence of new diseases. To achieve these goals, greater scientific and technological cooperation between developed countries (where the headquarters of large pharmaceutical industries and research institutions are) and developing nations or countries with high economic power but facing social and environmental problems is necessary. This is particularly important as it is in these countries that most new infectious diseases tend to emerge. Of note, in developing countries, there are human resources equipped with expertise and readiness to deal with the challenges posed by infectious diseases in complex social contexts. However, progress in this direction has been slow due to several reasons, including underutilization of skilled labor (doctoral-level human resources), brain drain, and lack of R&D resources. For example, Brazil has been experiencing a significant brain drain in recent years due to a shortage of funds associated with political instability[18].

Are we waiting for developed countries to be significantly affected to make a move? Apparently, this seems to be the leitmotiv. Hookworm, also listed as a top-ten in R&D priority[9], and affecting millions of people in low- and middle-income countries[19], is still not perceived as a priority by the pharmaceutical industry. Monkeypox only reached the News after leaving Africa and affecting wealthy non-endemic countries[20], raising global concern about our ability to deal with this new outbreak. As a sad song, are we doomed to repeat the same mistakes again? Further discussion on how to accelerate vaccine development and licensure is still needed.

The development and production of vaccines in Brazil work satisfactorily in some situations. The participation of the Butantan Institute in the phase III clinical trial of a Dengue vaccine[21], and the recent contribution of both the Oswaldo Cruz Foundation and the Butantan Institute with foreign research institutions and the pharmaceutical industry for the mass production of COVID-19 vaccines demonstrate the national capacity in these fields, despite the existence of many Brazilian political and logistical challenges[22,23]. Nevertheless, advances in vaccine R&D are still needed in Brazil. For example, vaccines to deal with diseases of huge public health importance in the Brazilian territory are still lacking, such as Chagas disease[24]. Brazil's dependence on the foreign pharmaceutical industry for vaccine R&D could also be lessened by strengthening public research institutes in the country. In this context, we stress that international collaboration is a key strategy to advance vaccine R&D in Brazil. The country should receive foreign researchers and send Brazilians abroad on scientific missions focused on vaccine R&D. Of note, Brazil should not only aim to collaborate with developed countries but also cooperate scientifically and

Figure 1. Challenges and solutions involving vaccine-related issues in brazil. Currently, Brazilian problems involving vaccination are diverse, ranging from the drop in vaccine coverage rates and reduced investment in vaccine R&D to limited preparedness to control and prevent emerging infectious diseases (panel A). Solutions to address these problems include greater investment in vaccine R&D, reduction of vaccine hesitancy, and prevention of new infectious disease outbreaks through the One Health perspective (panel B). This figure was created using templates from MapChart (https://mapchart.net/) and Servier Medical Art (https://smart.servier.com/).

technologically with developing countries, especially other Latin American nations. These measures will help Brazil to enhance its competitiveness in the global vaccine market. However, the country must create favorable conditions for proper vaccine R&D within the national territory, valuing its scientific independence. This strategy can make a strong contribution to reducing public health costs in a situation of health emergency, in addition to creating jobs for highly qualified professionals, jointly benefiting public health and Brazil's scientific and economic development. However, currently, the challenges faced by Brazil in the field of vaccination are not limited to R&D but also affect vaccination coverage.

Around 85% of the general population of Brazil received at least one dose of SARS-CoV-2 vaccine, although the demand for booster doses was lower, especially as the pandemic was brought under control[25,26]. At the moment, the most worrying problem in Brazil is probably the drop in vaccination coverage rates for diseases that were no longer a major concern in the country. As mentioned previously, the Brazilian National Immunization Program has already been considered a model internationally, with Brazil showing extensive experience in carrying out mass vaccination campaigns[22]. However, a robust body of evidence shows a significant decrease in vaccine coverage for poliomyelitis, measles, mumps, rubella, rotavirus, hepatitis B, and yellow fever, among others[27-31]. For example, the vaccination coverage rate for hepatitis B

dropped from 90.9% in 2015 to 62.8% in 2020[31]. For tuberculosis, the vaccination coverage rate, which stood at 100% in 2015, decreased to 73.3% by 2020[31]. The vaccine coverage rate for measles, mumps and rubella (triple viral vaccine) dropped from 96.1% to 79.5% in the same period[31]. This scenario of low vaccination coverage opens space for the reemergence of known, but forgotten, diseases in Brazil. In 2019, Brazil lost the measles elimination certificate due to measles outbreaks that occurred in recent years[28]. The problem involving vaccine-preventable diseases is exacerbated by the presence of environmental disturbances (e.g., deforestation, habitat fragmentation, biodiversity loss) and socio-demographic problems, which are intensifying in the country and facilitating the spread of yellow fever and other infectious diseases[32,33].

Promoting animal health in Brazil is also a critical measure for multiple reasons. For example, controlling animal rabies through vaccination prevents zoonotic cases of human rabies[34]. Moreover, maintaining the health of livestock animals, which involves vaccination and other sanitary control measures, ensures animal welfare and exports of animal products from Brazil to various countries, contributing significantly to the Brazilian economy[35,36]. Controlling infectious diseases in domestic and livestock animals through vaccination also prevents pathogens from being transmitted from these animals to the wildlife, avoiding conservation issues and negative impacts on ecosystems species [37-39]. In brief, vaccines for veterinary use directly promote animal health and indirectly human health and ecosystems, also bringing benefits to the Brazilian economy.

The advances that Brazil has achieved in the areas of immunization and public health are being neglected and falling into oblivion. This situation is due to various reasons, including social inequalities[40], anti-vaccine movements[41], vaccine hesitancy[31,42], the impact of COVID-19 pandemic on the Brazilian health system and National Immunization Program[30,40,43], dissemination of misinformation (fake news)[31,44], difficulty in accessing vaccination sites[44], forgetting the importance of vaccination and lack of concern for diseases considered "rare"[44], and reduced investment in science[45].

In a broad sense, the drop in vaccine coverage rates and the reemergence of "forgotten" diseases in Brazil must be addressed by improving vaccine R&D. Considering the particularities and variety of causes of setbacks in the Brazilian vaccination system, we summarized in Table 1 the major problems and potential solutions concerning these vaccine-related issues. These strategies can help society overcome confidence, complacency and convenience barriers linked to vaccine hesitancy (the 3C-Confidence, Complacency and Convenience Model of Vaccine Hesitancy)[46,47]. We stress that although many of the strategies described in Table 1 are considered commonplace, they need to be highlighted so that they do not fall into oblivion. Brazil needs to expand its participation in vaccine R&D and recover its leading role in terms of public health and vaccination campaigns. Finally, measures focusing on the maintenance of human, animal and environmental health [Figure 1] can help to reduce the pressure on the vaccination system by preventing the emergence of new infectious diseases. These measures include promotion of environmental sanitation, vector control, urban planning, food security and proper nutrition, control of deforestation, climate change and biodiversity loss, reduction of human contact with wild species (hunting and bushmeat practices), improvements in the living conditions of vulnerable populations, and better infectious disease surveillance[16]. Finally, we emphasize that to achieve these goals, cross-disciplinary collaboration is essential, involving scientists and decision makers from different fields. Coordinated collaboration is critical for Brazil to achieve a solid vaccine R&D system and promote human, animal, and environmental health in a more sustainable society.

Table 1. Problems and potential solutions concerning vaccine development and vaccination coverage rates in Brazil

Major problems	Potential solutions	Considering the 3C Model of Vaccine Hesitancy[46,47], what barriers can these solutions help overcome?
Lack of funding for vaccine Research & Development	Increase financial and logistical support to the Brazilian National Immunization Program	Confidence; Convenience; Complacency (considering the strengthening of Brazil's vaccination system in a broad sense)
	Increase the federal budget for science and technology	
	Secure basic budget and public funding for research institutions, including universities	
	Encourage public-private partnerships focused on the immunobiological industry	
	Politically strengthen national research funding agencies, such as CAPES (*Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*) and CNPq (*Conselho Nacional de Desenvolvimento Científico e Tecnológico*)	
Social inequalities and difficulty in accessing vaccines	Target vaccine awareness strategies to the most vulnerable groups of the population	Confidence; Convenience
	Facilitate access to vaccination through "vaccination days", free public transport on mass vaccination days, and mobile vaccination sites in places of wide public circulation	
Poor adherence to vaccination campaigns and reduced vaccination coverage	Promote media campaigns (print media, television and internet) popularizing and encouraging vaccination (this could even involve artists and digital influencers, who have a great influence on the Brazilian population)	Confidence
	Strengthening health education programs in schools, universities and communities with a focus on infectious disease prevention	
	Encouraging and funding scientific and professional journalism as a way to control the spread of fake news	
	Give voice to public health historians, highlighting and popularizing the gains that vaccines have already brought to society	
	Clearly state the benefits as well as any potential risks or adverse effects associated with vaccines	Confidence; Complacency*
	Target vaccine awareness strategies to health professionals who are hesitant to recommend vaccination	
	Clearly state the risks associated with vaccine-preventable diseases (considering individual and community health)	

*"Vaccine complacency exists where perceived risks of vaccine-preventable diseases are low and vaccination is not deemed a necessary preventive action"[47].

DECLARATIONS

Authors' contributions

Conceived the article: Chies JAB
Wrote and edited the text: Chies JAB, Ellwanger JH
Both authors approved the final manuscript.

Availability of data and materials

Not applicable.

Financial support and sponsorship

J. A. B. Chies receives a research fellowship from Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq (Bolsa de Produtividade em Pesquisa - Nível 1A, CNPq, Brazil) and has research project funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES (AUXPE 686/2020, Brazil). J. H. Ellwanger receives a postdoctoral fellowship from CAPES (Programa Nacional de Pós-Doutorado - PNPD/CAPES, Brazil).

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Scimago Journal & Country Rank. 2023. Available from: https://www.scimagojr.com/countryrank.php. [Last accessed on 26 June 2023].
2. Paim J, Travassos C, Almeida C, Bahia L, Macinko J. The Brazilian health system: history, advances, and challenges. *Lancet* 2011;377:1778-97. DOI PubMed
3. Homma A, Tanuri A, Duarte AJ, et al. Vaccine research, development, and innovation in Brazil: a translational science perspective. *Vaccine* 2013;31 Suppl 2:B54-60. DOI
4. Peres KC, Buendgens FB, Prates EA, et al. Vaccines in Brazil: historical analysis of the Sanitary registration and vaccine availability in the Brazilian Unified Health System. *Cien Saude Colet* 2021;26:5509-22. DOI PubMed
5. Benchimol J. How Brazil joined the quest for a yellow fever vaccine. Interview by Claudia Jurberg and Julia D'Aloisio. *Bull World Health Organ* 2013;91:165-6. DOI PubMed PMC
6. Xeyla R. Brasil retoma exportação de vacina contra febre amarela. 2019. Available from: https://portal.fiocruz.br/noticia/brasil-retoma-exportacao-de-vacina-contra-febre-amarela. [Last accessed on 26 June 2023].
7. Ho PL, Miyaji EN, Oliveira ML, et al. Economical value of vaccines for the developing countries--the case of Instituto Butantan, a public institution in Brazil. *PLoS Negl Trop Dis* 2011;5:e1300. DOI PubMed PMC
8. Raw I, Higashi HG. Auto-suficiência e inovação na produção de vacinas e saúde pública. *Estud av* 2008;22:155-70. DOI
9. Cohen J. Unfilled vials. *Science* 2016;351:16-9. DOI PubMed
10. Koff WC, Berkley SF. A universal coronavirus vaccine. *Science* 2021;371:759. DOI PubMed
11. Murray SM, Ansari AM, Frater J, et al. The impact of pre-existing cross-reactive immunity on SARS-CoV-2 infection and vaccine responses. *Nat Rev Immunol* 2023;23:304-16. DOI PubMed PMC
12. Walker NF, Whitty CJ. Tackling emerging infections: clinical and public health lessons from the West African Ebola virus disease outbreak, 2014-2015. *Clin Med* 2015;15:457-60. DOI PubMed PMC
13. Elston JW, Cartwright C, Ndumbi P, Wright J. The health impact of the 2014-15 Ebola outbreak. *Public Health* 2017;143:60-70. DOI PubMed
14. Morens DM, Fauci AS. Emerging pandemic diseases: how we got to COVID-19. *Cell* 2020;182:1077-92. DOI PubMed PMC
15. Trovato M, Sartorius R, D'Apice L, Manco R, De Berardinis P. Viral emerging diseases: challenges in developing vaccination strategies. *Front Immunol* 2020;11:2130. DOI PubMed PMC
16. Ellwanger JH, Veiga ABG, Kaminski VL, Valverde-Villegas JM, Freitas AWQ, Chies JAB. Control and prevention of infectious diseases from a One Health perspective. *Genet Mol Biol* 2021;44:e20200256. DOI PubMed PMC
17. Ellwanger JH, Kulmann-Leal B, Kaminski VL, et al. Beyond diversity loss and climate change: Impacts of Amazon deforestation on infectious diseases and public health. *An Acad Bras Cienc* 2020;92:e20191375. DOI
18. Brazil's brain drain is getting worse. *The Economist*. 2021. Available from: https://www.economist.com/the-americas/2021/07/24/brazils-brain-drain-is-getting-worse?utm_medium=cpc.adword.pd&utm_source=google&ppccampaignID=19495686130&ppcadID=&utm_campaign=a.22brand_pmax&utm_content=conversion.direct-response.anonymous&gclid=EAIaIQobChMI0vyOuqPg_wIVwWmLCh2tIw4lEAAYASAAEgIn4PD_BwE&gclsrc=aw.ds. [Last accessed on 26 June 2023].
19. Loukas A, Hotez PJ, Diemert D, et al. Hookworm infection. *Nat Rev Dis Primers* 2016;2:16088. DOI
20. Lancet Infectious Diseases. Monkeypox: a neglected old foe. *Lancet Infect Dis* 2022;22:913. DOI PubMed PMC
21. Instituto Butantan. Vacina contra a dengue desenvolvida pelo Butantan entra na reta final de estudos clínicos. 2021. Available from: https://butantan.gov.br/noticias/vacina-contra-a-dengue-desenvolvida-pelo-butantan-entra-na-reta-final-de-estudos-clinicos. [Last accessed on 26 Jun 2023].
22. Domingues CMAS. Challenges for implementation of the COVID-19 vaccination campaign in Brazil. *Cad Saude Publica* 2021;37:e00344620. DOI PubMed

23. FIOCRUZ - Fundação Oswaldo Cruz. Vacinas contra a Covid-19. 2022. Available from: https://portal.fiocruz.br/vacinascovid19. [Last accessed on 6 Jun 2023].
24. Camargo EP, Gazzinelli RT, Morel CM, Precioso AR. Why do we still have not a vaccine against chagas disease? *Mem Inst Oswaldo Cruz* 2022;117:e200314. DOI PubMed PMC
25. Mapa da vacinação contra Covid-19 no Brasil. 2023. Available from: https://especiais.g1.globo.com/bemestar/vacina/2021/mapa-brasil-vacina-covid/. [Last accessed on 26 June 2023].
26. Ministério da Saúde - Brasil. Vacinômetro COVID-19. 2023. Available from: https://infoms.saude.gov.br/extensions/SEIDIGI_DEMAS_Vacina_C19/SEIDIGI_DEMAS_Vacina_C19.html. [Last accessed on 26 June 2023].
27. Fujita DM, Gomes da Cruz TC, Ferreira EM, Henrique da Silva Nali L. The continuous decrease in Poliomyelitis vaccine coverage in Brazil. *Travel Med Infect Dis* 2022;48:102352. DOI PubMed PMC
28. Nunes L. Cobertura Vacinal do Brasil 2020, Panoramas IEPS, Os relatórios do IEPS. Instituto de Estudos para Políticas de Saúde, 2021. Available from: https://ieps.org.br/wp-content/uploads/2021/05/Panorama_IEPS_01.pdf. [Last accessed on 26 Jun 2023].
29. Silva TMRD, Nogueira de Sá ACMG, Prates EJS, et al. Yellow fever vaccination before and during the covid-19 pandemic in Brazil. *Rev Saude Publica* 2022;56:45. DOI PubMed PMC
30. Silveira MM, Conrad NL, Leivas Leite FP. Effect of COVID-19 on vaccination coverage in Brazil. *J Med Microbiol* 2021:70. DOI PubMed
31. Fernandez M, Matta G, Paiva E. COVID-19, vaccine hesitancy and child vaccination: challenges from Brazil. *Lancet Reg Health Am* 2022;8:100246. DOI PubMed PMC
32. Ilacqua RC, Medeiros-Sousa AR, Ramos DG, et al. Reemergence of yellow fever in brazil: the role of distinct landscape fragmentation thresholds. *J Environ Public Health* 2021;2021:8230789. DOI PubMed PMC
33. Ellwanger JH, Fearnside PM, Ziliotto M, et al. Synthesizing the connections between environmental disturbances and zoonotic spillover. *An Acad Bras Cienc* 2022;94:e20211530. DOI
34. World Health Organization. Rabies. 2023. Available from: https://www.who.int/health-topics/rabies#tab=tab_1. [Last accessed on 26 June 2023].
35. Ferraz JB, Felício PE. Production systems--an example from Brazil. *Meat Sci* 2010;84:238-43. DOI PubMed
36. Alves AJ, Rocha F, Amaku M, et al. Economic analysis of vaccination to control bovine brucellosis in the States of Sao Paulo and Mato Grosso, Brazil. *Prev Vet Med* 2015;118:351-8. DOI
37. Morgan E, Lundervold M, Medley G, Shaikenov B, Torgerson P, Milner-gulland E. Assessing risks of disease transmission between wildlife and livestock: the saiga antelope as a case study. *Biol Conserv* 2006;131:244-54. DOI
38. Randall D, Marino J, Haydon D, et al. An integrated disease management strategy for the control of rabies in Ethiopian wolves. *Biol Conserv* 2006;131:151-62. DOI
39. Ellwanger JH, Chies JAB. The triad "dogs, conservation and zoonotic diseases" - an old and still neglected problem in Brazil. *Perspect Ecol Conserv* 2019;17:157-61. DOI PubMed PMC
40. Silveira MF, Tonial CT, Goretti K Maranhão A, et al. Missed childhood immunizations during the COVID-19 pandemic in Brazil: analyses of routine statistics and of a national household survey. *Vaccine* 2021;39:3404-9. DOI PubMed PMC
41. Oliveira IS, Cardoso LS, Ferreira IG, et al. Anti-vaccination movements in the world and in Brazil. *Rev Soc Bras Med Trop* 2022;55:e05922021. DOI PubMed PMC
42. Sato APS. What is the importance of vaccine hesitancy in the drop of vaccination coverage in Brazil? *Rev Saude Publica* 2018;52:96. DOI PubMed PMC
43. Moura C, Truche P, Sousa Salgado L, et al. The impact of COVID-19 on routine pediatric vaccination delivery in Brazil. *Vaccine* 2022;40:2292-8. DOI PubMed PMC
44. Milani LRN, Busato IMS. Causas e consequências da redução da cobertura vacinal no Brasil. *R Saúde Públ Paraná* 2021;4:157-71. DOI
45. Goldenberg S, Rodrigues ML, Savino W. Brazilian science: towards extinction? *Mem Inst Oswaldo Cruz* 2022;116:e210357. DOI PubMed PMC
46. Confidence, complacency, convenience model of vaccine hesitancy. 2022. Available from: https://www.local.gov.uk/our-support/coronavirus-information-councils/covid-19-service-information/covid-19-vaccinations/behavioural-insights/resources/3Cmodel-vaccine-hesitancy. [Last accessed on 26 Jun 2023].
47. Report of the SAGE Working Group on vaccine hesitancy. 2014. Available from: https://www.asset-scienceinsociety.eu/sites/default/files/sage_working_group_revised_report_vaccine_hesitancy.pdf. [Last accessed on 26 Jun 2023].