

*Invited Editorial***The response to COVID 19 across countries and the implications for future pandemics**Mainul Haque¹, Marshall Gowere², Nadia Nusrat³, Kona Chowdhury⁴, Brian Godman^{5*}Bangladesh Journal of Medical Science, Special Issue on COVID-19. 2021. Page : 7-14
DOI: <https://doi.org/10.3329/bjms.v20i5.55417>

We have previously reported that COVID-19 was first identified in Wuhan, China, in December 2019¹⁻⁴. By mid-August 2021, there were over 208 million confirmed cases worldwide with more than 4.3 million deaths giving a case fatality ratio of 2.1%⁵. Since COVID-19 is principally spread through airborne aerosols and physical contact⁶⁻⁸, and an appreciable number of patients are asymptomatic, early strategies to prevent the spread of the virus in the absence of proven effective medicines included lockdown and other preventative measures (Figure 1)^{4,9}.



Figure 1: Current situation COVID-19 including prevention strategies

Published studies have shown increased screening, quarantining and social distancing to be effective and cost-effective in preventing and controlling the prevalence of COVID-19 over the long term^{4,10-16}. However, there were appreciable differences in the rate at which lockdown and other measures were introduced across continents and countries, appreciably impacting on prevalence and mortality rates in practice^{17,18}. Instigation of early lockdown measures among a number of Asian countries including Korea, Malaysia, Taiwan and Vietnam, as well as a number of African countries, helped prevent the spread of the virus in these countries certainly initially and limited the number of deaths¹⁷⁻²². There were though appreciable unintended consequences from early lockdown measures including both clinical and economic consequences^{17,23-26}. Unintended consequences included appreciable reduced vaccinations for children especially in Africa with lack of public transport, clinic closures coupled with fears among mothers of attending clinics in case of contracting COVID-19, as well as rising rates of non-communicable diseases (NCDs) for similar reasons^{17,24,27-29} (Figure 2). The rise in mental health disorders has also been a concern across countries³⁰⁻³².

1. Unit of Pharmacology, Faculty of Medicine and Defence Health, Universiti Pertahanan Nasional Malaysia (National Defence University of Malaysia), Kem Sungai, Besi, 57000 Kuala Lumpur, Malaysia. Orcid ID: <https://orcid.org/0000-0002-6124-7993>
2. Department of Pharmacology, University of Pretoria, South Africa. Orcid ID: <https://orcid.org/0000-0003-2154-3023>
3. Delta Medical College and Hospital, 26/2, Principal Abul Kashem Road, Mirpur-1, Dhaka-1216, Bangladesh. Orcid ID: <https://orcid.org/0000-0003-0133-0303>.
4. Department of Paediatrics, Gonoshasthaya Samaj Vittik Medical College and Hospital, Dhaka, Bangladesh. Orcid ID: <https://orcid.org/0000-0002-3836-1691>
5. Division of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University South Africa; Department of Pharmacoepidemiology, Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK, and School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia. Orcid ID: <https://orcid.org/0000-0001-6539-6972>

Correspondence: Department of Pharmacoepidemiology, Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK, Email: Brian.Godman@strath.ac.uk

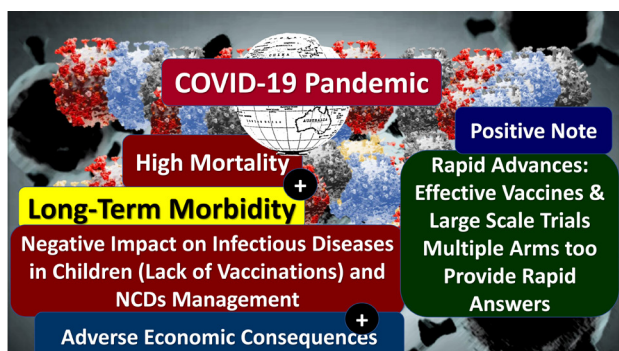


Figure 2: Clinical and economic impact of COVID-19

We have also seen an appreciable increase in the prescribing and dispensing of antimicrobials for patients with COVID-19 across sectors despite limited bacterial or fungal co-infections^{22,33-37}. This is a concern as this will increase antimicrobial resistance (AMR) rates if left unchecked increasing morbidity, mortality and costs^{4,38-40}. Several initiatives and strategies can be instigated to reduce inappropriate prescribing and dispensing of antibiotics across sectors for essentially viral infections⁴⁰⁻⁴², and we will be following these up. In hospitals, this typically involves the instigation of antimicrobial stewardship programmes (ASPs)^{40,43-45}. Whilst it is recognised that ASPs are more difficult to introduce in hospitals among low- and middle-income countries (LMICs) due to resource and personnel issues, we are seeing a growing number of ASPs introduced across LMICs providing direction for the future^{40,46-49}. Effective programmes in ambulatory care include educational initiatives among physicians as well as educational and other interventions among pharmacists^{40,42,50-52}. We have seen limited dispensing of antimicrobials without a prescription in LMICs among patients with suspected COVID-19 where there are trained pharmacists available in pharmacies, with other national activities also helping reduce the self-purchasing of antibiotics^{18-20,40,42,53}. Trained pharmacists can also help address some of the concerns arising from the COVID-19 pandemic including education especially around misinformation, helping with medicine supply especially among patients with chronic NCDs as well as increasing vaccination rates^{17,54,55}.

As mentioned in our previous publication, a key concern surrounding the pandemic has been the level

of misinformation with potential treatments and the adverse consequences this has produced^{4,56}. The imperative to try a range of re-purposed medicines at the start of the pandemic given rapidly rising case numbers resulted in a number of poorly controlled trials with unsatisfactory efficacy and safety data^{57,58}. This was certainly the case with hydroxychloroquine where despite concerns with initial trial designs, early endorsement by governments, medical societies, and others resulted in appreciably increased use, shortages, rising prices and deaths in a number of LMICs^{4,18,37,58-60}. However, later studies failed to show any meaningful benefit leading to recommendations not to use hydroxychloroquine for the treatment of patients with COVID-19 especially with the potential for increased cardiac events and hepatic failure^{58,61,62}. Similarly other re-purposed medicines, including lopinavir/ritonavir and remdesivir, have failed to reduce morbidity and mortality in hospitalised patients following comprehensive clinical trials leading again to recommendations not to prescribe them⁶²⁻⁶⁵. In fact, to date, only dexamethasone has been shown in large well conducted clinical trials to benefit patients on respiratory support in hospital with COVID-19⁶⁶. There is also increasing evidence to support the use of medicines such as tocilizumab⁶⁷⁻⁶⁹.

However, despite the lack of effectiveness with a number of the re-purposed medicines, the large rapidly instigated studies by the WHO (Solidarity) and the UK (Recovery) with multiple arms including hydroxychloroquine, lopinavir/ritonavir, remdesivir and dexamethasone, have shown that it is possible to rapidly assess multiple medicines simultaneously in large cohorts to provide robust answers⁶¹⁻⁶³. As a result, quickly provide treatment guidance and avoid the level of misinformation and its consequences that we have seen with medicines such as hydroxychloroquine with and without azithromycin^{18,20,58,60}. This suggests it is possible to undertake robust trials simultaneously rather than in sequence when the situation arises providing direction for the future.

We have seen a number of other positive points arise from the urgency of the pandemic. These include capacity building to rapidly test patients as well as develop new low-cost tests where there are resource

concerns^{17,21,70}. This could develop into new ways to streamline immunisation programmes where there are capacity issues both in terms of available vaccines but also support systems to administer them. Such mass monitoring could also potentially be used to rapidly track AMR rates across localities and countries through decoding the genomes of different bacteria given concerns with current surveillance methods among LMICs⁷¹. Such developments will enhance the potential for targeted interventional programmes to reduce high AMR rates among LMICs in the future. We have also seen a number of other innovations among LMICs to address concerns with identifying and managing patients with COVID-19. These include successful early sequencing of the COVID-19 genome in Ghana as well as the rapid development of different ventilators to address patients' needs among a number of African countries given shortages at the start of the pandemic^{17,21}, which also bodes well for the future.

Another positive outcome from the pandemic has been the rapid development of effective vaccines using different technologies including messenger RNA (mRNA)-based vaccines, with nanotechnologies here to stay⁷²⁻⁷⁸. This will be beneficial as more variants emerge in order to rapidly tweak vaccines⁷⁹. Studies are now emerging of the differences in effectiveness, protection and adverse events between the different vaccines to guide future management strategies in different populations, with more studies ongoing⁸⁰. We will be following this up in future research projects. However, again there have been concerns with the level of misinformation regarding the various vaccines including the level of side-effects, negatively impacting on uptake rates in practice⁸¹⁻⁸⁵. Effective communication campaigns among all key stakeholder groups alongside potentially fining companies or groups for any misinformation, which is already happening among some African countries¹⁷, are potential ways forward to address this.

Whilst children have a lower risk of COVID-19, as well as milder clinical manifestations when they are infected^{86,87}, they do experience a number of symptoms including fever, cough and diarrhoea⁸⁷. Overall, approximately 6% of COVID-19 infected children appear to experience severe symptoms

compared with an appreciable number of adults who have progressed to intensive care units to manage their condition in the absence of vaccines⁸⁸. Since a large number of children with COVID-19 are asymptomatic⁸⁹, with most others experiencing milder symptoms if they do develop COVID-19, no deaths were reported among 416 cases of COVID-19 in children aged 1 to 9 years and a single death among 549 cases aged between 10 to 19 years in a recent study in China, and COVID-19 was very rarely fatal among children and young people in the UK even among those with underlying comorbidities^{86,90}, attention across countries towards children has typically focused more on the unintended consequences of COVID-19 including concerns whether routine vaccinations are being missed^{27,40}. Alongside this, concerns with the appreciable prescribing of antibiotics in patients with COVID-19 including children⁴⁰, as well as concerns with orphanhood and caregiver deaths among children especially in LMICs and the implications for future psychosocial and economic support⁹¹. Economic hardship as a result of the pandemic is also increasing domestic violence against children especially in LMICs as well as increasing child marriages and child labour in LMICs such as Bangladesh, with concerns over child development during the coming years⁹²⁻⁹⁴. This needs to be monitored going forward.

However, the focus on children is changing with potentially increased morbidity and mortality with new variants. Potential treatments that have been researched in children include hydroxychloroquine, lopinavir/ritonavir, remdesivir, interferons, steroids and tocilizumab⁹⁵⁻⁹⁹. We will be shortly consolidating our findings, as well as reviewing current treatment patterns among a range of LMICs including Bangladesh, to provide future guidance.

In conclusion, the COVID-19 pandemic has resulted in multiple deaths and long-term morbidity across countries. However, there have been concerns with the unintended consequences of COVID-19 including the impact on NCDs incorporating mental health disorders as well as economic and other consequences including a rise in domestic violence. There have also been concerns with the level of misinformation regarding both prevention

and treatment, which needs addressing going forward including the instigation of evidence-based approaches among Governments, major Healthcare societies and patient organisations. On a positive note, we have seen rapid advances including the development of effective vaccines as well as the potential to conduct large scale trials with multiple arms simultaneously to provide rapid answers (Figure 2). We have also seen society adapt to a greater use of online platforms for the management of diseases

including greater use of telemedicine and other approaches. This also includes greater use of online platforms for the teaching of pharmacy and medical students arising from early lockdown measures and closure of universities. There are though still issues of access and availability to internet bundles to address especially among LMICs to improve online teaching as well as undertaking clinical and practical teaching within a COVID-19 secure environment. This will also be the subject of future research projects.

References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *Jama*. **2020**;323(13):1239-42. doi: 10.1001/jama.2020.2648
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med*. **2020**;382(13):1199-207. doi: 10.1056/NEJMoa2001316
3. Anwar S, Nasrullah M, Hosen MJ. COVID-19 and Bangladesh: Challenges and How to Address Them. *Frontiers in Public Health*. **2020**;8(154). doi: 10.3389/fpubh.2020.00154
4. Godman B. Combating COVID-19: Lessons learnt particularly among developing countries and the implications. *Bangladesh Journal of Medical Science, Special Issue on Covid19*. 2020; S103-8. doi: <https://doi.org/10.3329/bjms.v19i0.48413>.
5. WHO. WHO Coronavirus (COVID-19) Dashboard. 18 August 2021. Available at URL: <https://covid19.who.int/>.
6. Haque M. Combating COVID-19: A Coordinated Efforts of Healthcare Providers and Policy Makers with Global Participation Are Needed to Achieve the Desired Goals. *Bangladesh Journal of Medical Science, Special Issue on Covid19*, **2020**: 1-05. DOI: <https://doi.org/10.3329/bjms.v19i0.47610>.
7. Klompas M, Baker MA, Rhee C. Airborne Transmission of SARS-CoV-2: Theoretical Considerations and Available Evidence. *Jama*. **2020**;324(5):441-2. doi: 10.1001/jama.2020.12458
8. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N Engl J Med*. **2020**;382(16):1564-7. doi: 10.1056/NEJMc2004973
9. Ayouni I, Maatoug J, Dhouib W, Zammit N, Fredj SB, Ghammam R, et al. Effective public health measures to mitigate the spread of COVID-19: a systematic review. *BMC public health*. **2021**;21(1):1015. doi: 10.1186/s12889-021-11111-1
10. Rezapour A, Souresrafil A, Peighambari MM, Heidarali M, Tashakori-Miyanroudi M. Economic evaluation of programs against COVID-19: A systematic review. *International journal of surgery*. **2021**;85:10-8. doi: 10.1016/j.ijssu.2020.11.015
11. Courtemanche C, Garuccio J, Le A, Pinkston J, Yelowitz A. Strong Social Distancing Measures In The United States Reduced The COVID-19 Growth Rate. *Health affairs*. **2020**;39(7):1237-46. doi: 10.1377/hlthaff.2020.00608
12. Nussbaumer-Streit B, Mayr V, Dobrescu AI, Chapman A, Persad E, Klerings I, et al. Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. *The Cochrane database of systematic reviews*. **2020**;4:Cd013574. doi: 10.1002/14651858.CD013574.
13. Reddy KP, Shebl FM, Foote JHA, Harling G, Scott

- JA, Panella C, et al. Cost-effectiveness of public health strategies for COVID-19 epidemic control in South Africa: a microsimulation modelling study. *The Lancet Global health*. **2021**;9(2):e120-e9. doi: 10.1016/S2214-109X(20)30452-6
14. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet*. **2020**;395(10242):1973-87. doi: 10.1016/S0140-6736(20)31142-9
 15. Ng Y, Li Z, Chua YX, Chaw WL, Zhao Z, Er B, et al. Evaluation of the Effectiveness of Surveillance and Containment Measures for the First 100 Patients with COVID-19 in Singapore - January 2-February 29, 2020. *MMWR*. **2020**;69(11):307-11. doi: 10.15585/mmwr.mm6911e1
 16. Mendez-Brito A, El Bcheraoui C, Pozo-Martin F. Systematic review of empirical studies comparing the effectiveness of non-pharmaceutical interventions against COVID-19. *J Infect*. **2021** (EPrint). doi: 10.1016/j.jinf.2021.06.018
 17. Ogunleye OO, Basu D, Mueller D, Sneddon J, Seaton RA, Yinka-Ogunleye AF, et al. Response to the Novel Corona Virus (COVID-19) Pandemic Across Africa: Successes, Challenges, and Implications for the Future. *Frontiers in Pharmacology*. **2020**;11(1205). doi: 10.3389/fphar.2020.01205
 18. Godman B, Haque M, Islam S, Iqbal S, Urmi UL, Kamal ZM, et al. Rapid Assessment of Price Instability and Paucity of Medicines and Protection for COVID-19 Across Asia: Findings and Public Health Implications for the Future. *Frontiers in Public Health*. **2020**;8(744). doi: 10.3389/fpubh.2020.585832
 19. Kibuule D, Nambahu L, Sefah IA, Kurdi A, Phuong TNT, Kwon H-Y, Godman B. Activities in Namibia to Limit the Prevalence and Mortality from COVID-19 Including Community Pharmacy Activities and the Implications. *Sch Acad J Pharm*. **2021**; 10(5): 82-92. DOI: 10.36347/sajp.2021.v10i05.001
 20. Sefah I, Ogunleye O, Essah D, Opanga S, Rizvi N, Wamaitha A, et al. Rapid assessment of the potential paucity and price increases for suggested medicines and protection equipment for COVID-19 across developing countries with a particular focus on Africa and the implications. *Front Pharmacol*. **2021**;11(2055). doi: 10.3389/fphar.2020.588106
 21. Afriyie DK, Asare GA, Amponsah SK, Godman B. COVID-19 pandemic in resource-poor countries: challenges, experiences and opportunities in Ghana. *J Infect Dev Ctries*. **2020**;14(8):838-43. doi: 10.3855/jidc.12909
 22. Haque M, Islam S, Iqbal S, Urmi UL, Kamal ZM, Shuvo SA et al. Availability and price changes of potential medicines and equipment for the prevention and treatment of COVID-19 among pharmacy and drug stores in Bangladesh; findings and implications. *Bangladesh Journal of Medical Science* **2020**; 19 Special Issue on Covid19: S36-S50 DOI:https://doi.org/10.3329/bjms.v19i0.48106
 23. Sharma A, Ghosh D, Divekar N, Gore M, Gochhait S, Shireshi SS. Comparing the socio-economic implications of the 1918 Spanish flu and the COVID-19 pandemic in India: A systematic review of literature. *Int Soc Sci J*. **2021**. (EPrint). doi: 10.1111/issj.12266
 24. Kluge HHP, Wickramasinghe K, Rippin HL, Mendes R, Peters DH, Kontsevaya A, et al. Prevention and control of non-communicable diseases in the COVID-19 response. *Lancet*. **2020**;395(10238):1678-80. doi: 10.1016/S0140-6736(20)31067-9
 25. Turcotte-Tremblay A-M, Gali Gali IA, Ridde V. The unintended consequences of COVID-19 mitigation measures matter: practical guidance for investigating them. *BMC Med Res Methodol*. **2021**;21(1):28. doi: 10.1186/s12874-020-01200-x
 26. Chiesa V, Antony G, Wismar M, Rechel B. COVID-19 pandemic: health impact of staying at home, social distancing and 'lockdown' measures-a systematic review of systematic reviews. *J Public Health*. **2021** (EPrint). doi: 10.1093/pubmed/fdab102
 27. Abbas K, Procter SR, van Zandvoort K, Clark A, Funk S, Mengistu T, et al. Routine childhood immunisation during the COVID-19 pandemic in Africa: a benefit-risk analysis of health benefits versus excess risk of SARS-CoV-2 infection. *Lancet Glob Health*. **2020**;8(10):e1264-e72. doi: 10.1016/S2214-109X(20)30308-9
 28. Basu S. Non-communicable disease management in vulnerable patients during Covid-19. *Indian J Med Ethics*. **2020**;V(2):103-5. doi: 10.20529/IJME.2020.041
 29. Lim MA, Huang I, Yonas E, Vania R, Pranata R. A wave of non-communicable diseases following the COVID-19 pandemic. *Diabetes Metab Syndr*. **2020**;14(5):979-80. doi: 10.1016/j.dsx.2020.06.050
 30. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain Behav Immun*. **2020**;89:531-42. doi: 10.1016/j.bbi.2020.05.048
 31. Henssler J, Stock F, van Bohemen J, Walter H, Heinz A, Brandt L. Mental health effects of infection containment strategies: quarantine and isolation-a systematic review and meta-analysis. *Eur Arch Psychiatry Clin Neurosci*. **2021**;271(2):223-234. doi: 10.1007/s00406-020-01196-x.
 32. Cénat JM, Blais-Rochette C, Kokou-Kpolou CK, Noorishad PG, Mukunzi JN, McIntee SE, et al. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. *Psychiatry Res*. **2021**;295:113599. doi: 10.1016/j.psychres.2020.113599
 33. Langford BJ, So M, Raybardhan S, Leung V, Soucy JR, Westwood D, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clin Microbiol Infect*. **2021**;27(4):520-31. doi: 10.1016/j.cmi.2020.12.018
 34. Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal co-

- infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* **2020**;71(9):2459-2468. doi: 10.1093/cid/ciaa530
35. Mah EMS, Hassan MZ, Biswas M, Rahman F, Akhtar Z, Das P, et al. Use of Antimicrobials among Suspected COVID-19 Patients at Selected Hospitals, Bangladesh: Findings from the First Wave of COVID-19 Pandemic. *Antibiotics.* **2021**;10(6). doi: 10.3390/antibiotics10060738
 36. Iwu CJ, Jordan P, Jaja IF, Iwu CD, Wiysonge CS. Treatment of COVID-19: implications for antimicrobial resistance in Africa. *Pan Afr Med J.* **2020**;35(Suppl 2):119. doi: 10.11604/pamj.supp.2020.35.23713
 37. Haque M, Abubakar A, Ogunleye O, Sani I, Sefah I, Kurdi A, et al. Changes in availability, utilization, and prices of medicines and protection equipment for COVID-19 in an Urban population of Northern Nigeria. *J Res Pharm Pract.* **2021**;10(1):17-22. doi: 10.4103/jrpp.JRPP_20_92
 38. Hsu J. How covid-19 is accelerating the threat of antimicrobial resistance. *BMJ.* **2020**;369:m1983. doi: 10.1136/bmj.m1983
 39. Hofer U. The cost of antimicrobial resistance. *Nat Rev Microbiol.* **2019**;17(1):3. doi: 10.1038/s41579-018-0125-x
 40. Godman B, Ekwuenu A, Haque M, Malande OO, Schellack N, Kumar S, et al. Strategies to Improve Antimicrobial Utilization with a Special Focus on Developing Countries. *Life.* **2021**;11(6):528. doi: 10.3390/life11060528
 41. Godman B, Fadare J, Kwon HY, Dias CZ, Kurdi A, Dias Godói IP, et al. Evidence-based public policy making for medicines across countries: findings and implications for the future. *J Comp Eff Res.* **2021**;10(12):1019-52. doi: 10.2217/ce-2020-0273
 42. Godman B, Haque M, McKimm J, Abu Bakar M, Sneddon J, Wale J, et al. Ongoing strategies to improve the management of upper respiratory tract infections and reduce inappropriate antibiotic use particularly among lower and middle-income countries: findings and implications for the future. *Curr Med Res Opin.* **2020**;36(2):301-27. doi: 10.1080/03007995.2019.1700947
 43. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. *Antimicrob Resist Infect Control.* **2019**;8:35. doi: 10.1186/s13756-019-0471-0
 44. Fadare JO, Ogunleye O, Iliyasu G, Adeoti A, Schellack N, Engler D, et al. Status of antimicrobial stewardship programmes in Nigerian tertiary healthcare facilities: Findings and implications. *J Glob Antimicrob Resist.* **2019**;17:132-6. doi: 10.1016/j.jgar.2018.11.025
 45. Haque M, Godman B. Potential Strategies to Improve Antimicrobial Utilisation in Hospitals in Bangladesh Building on Experiences Across Developing Countries. *Bangladesh Journal of Medical Science.* **2021**; 19 (3): 355-7. DOI: <https://doi.org/10.3329/bjm>.
 46. Cox JA, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas MV, et al. Antibiotic stewardship in low- and middle-income countries: the same but different? *Clin Microbiol Infect.* **2017**;23(11):812-8. doi: 10.1016/j.cmi.2017.07.010
 47. Akpan MR, Isemin NU, Udoh AE, Ashiru-Oredope D. Implementation of antimicrobial stewardship programmes in African countries: a systematic literature review. *J Glob Antimicrob Resist.* **2020**;22:317-24. doi: 10.1016/j.jgar.2020.03.009
 48. van den Bergh D, Messina AP, Goff DA, van Jaarsveld A, Coetzee R, de Wet Y, et al. A pharmacist-led prospective antibiotic stewardship intervention improves compliance to community-acquired pneumonia guidelines in 39 public and private hospitals across South Africa. *Int Journal Antimicrob Agents.* **2020**;56(6):106189. doi: 10.1016/j.ijantimicag.2020.106189
 49. Ahmed SA, Kumar A, Sethi P, Kapil A, Pandey RM, Wig N. Effectiveness of education and antibiotic control programme at All India Institute of Medical Sciences, New Delhi. *Natl Med J India.* **2018**;31(5):262-7. doi: 10.4103/0970-258X.261176
 50. Dyar OJ, Beovic B, Vlahovic-Palcevski V, Verheij T, Pulcini C. How can we improve antibiotic prescribing in primary care? *Expert Rev Anti infect Ther.* **2016**;14(4):403-13. doi: 10.1586/14787210.2016.1151353
 51. Jacobs TG, Robertson J, van den Ham HA, Iwamoto K, Bak Pedersen H, Mantel-Teeuwisse AK. Assessing the impact of law enforcement to reduce over-the-counter (OTC) sales of antibiotics in low- and middle-income countries; a systematic literature review. *BMC Health Serv Res.* **2019**;19(1):536. doi: 10.1186/s12913-019-4359-8
 52. Haque M, Godman B. Potential strategies to reduce inappropriate prescribing and dispensing of antimicrobials in Bangladesh building on the experiences in other developing countries. *Bangladesh Journal of Medical Science.* **2021**; 20 (4): 700-6. DOI: <https://doi.org/10.3329/bjms.v20i4.54123>.
 53. Opanga SA, Rizvi N, Wamaitha A, Sefah IA, Godman B. Availability of Medicines in Community Pharmacy to Manage Patients with COVID-19 in Kenya; Pilot Study and Implications. *Sch Acad J Pharm.* **2021**; 10(3): 36-42. DOI: 10.36347/sajp.2021.v10i03.001
 54. Cadogan CA, Hughes CM. On the frontline against COVID-19: Community pharmacists' contribution during a public health crisis. *RSAP.* **2021**;17(1):2032-5. doi: 10.1016/j.sapharm.2020.03.015
 55. Hedima EW, Adeyemi MS, Ikunaiye NY. Community Pharmacists: On the frontline of health service against COVID-19 in LMICs. *RSAP.* **2021**;17(1):1964-6. doi: 10.1016/j.sapharm.2020.04.013
 56. Chowdhury N, Khalid A, Turin TC. Understanding misinformation infodemic during public health emergencies due to large-scale disease outbreaks: a rapid review. *Z Gesundh Wiss.* **2021**;1-21. doi: 10.1007/s10389-021-01565-3
 57. Goodman JL, Borio L. Finding Effective Treatments for COVID-19: Scientific Integrity and Public Confidence

- in a Time of Crisis. *Jama*. **2020**;323(19):1899-900. doi: 10.1001/jama.2020.6434
58. Ferner RE, Aronson JK. Chloroquine and hydroxychloroquine in covid-19. *BMJ*. **2020**;369:m1432. doi: 10.1136/bmj.m1432
 59. International Society of Antimicrobial Chemotherapy. Official Statement from International Society of Antimicrobial Chemotherapy (ISAC)-Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial (Gautret P et al. PMID 32205204). Available at URL: <https://www.isac.world/news-and-publications/official-isac-statement>.
 60. Abena PM, Decloedt EH, Bottieau E, Suleman F, Adejumo P, Sam-Agudu NA, et al. Chloroquine and Hydroxychloroquine for the Prevention or Treatment of COVID-19 in Africa: Caution for Inappropriate Off-label Use in Healthcare Settings. *Am J Trop Med Hyg*. **2020**;102(6):1184-8. doi: 10.4269/ajtmh.20-0290
 61. Horby P, Mafham M, Linsell L, Bell JL, Staplin N, Emberson JR, et al. Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19. *N Engl J Med*. **2020**;383(21):2030-40. doi: 10.1056/NEJMoa2022926
 62. WHO. WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19. 4 July 2020. Available at URL: <https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19>.
 63. RECOVERY Collaborative Group. Lopinavir-ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. **2020**;396(10259):1345-52. doi: 10.1016/S0140-6736(20)32013-4
 64. Dyer O. Covid-19: Remdesivir has little or no impact on survival, WHO trial shows. *BMJ*. **2020**;371:m4057. doi: 10.1136/bmj.m4057
 65. Charan J, Kaur RJ, Bhardwaj P, Haque M, Sharma P, Misra S, et al. Rapid review of suspected adverse drug events due to remdesivir in the WHO database; findings and implications. *Expert Rev Clin Pharmacol*. **2021**;14(1):95-103. doi: 10.1080/17512433.2021.1856655
 66. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med*. **2021**;384(8):693-704. doi: 10.1056/NEJMoa2021436
 67. Abubakar AR, Sani IH, Godman B, Kumar S, Islam S, Jahan I, et al. Systematic Review on the Therapeutic Options for COVID-19: Clinical Evidence of Drug Efficacy and Implications. *Infect Drug Resist*. **2020**;13:4673-95. doi: 10.2147/IDR.S289037
 68. Viswanatha GL, Anjana Male C, Shylaja H. Efficacy and safety of tocilizumab in the management of COVID-19: a systematic review and meta-analysis of observational studies. *Clin Exp Rheumatol*. 2021 (EPrint). PMID: 34251307
 69. Zhao M, Lu J, Tang Y, Dai Y, Zhou J, Wu Y. Tocilizumab for treating COVID-19: a systemic review and meta-analysis of retrospective studies. *Eur J Clin Pharmacol*. **2021**;77(3):311-9. doi: 10.1007/s00228-020-03017-5
 70. HAQUE M, Kumar S, Charan J, Bhatt R, Islam S, Dutta S, et al. Utilisation, availability and price changes of medicines and protection equipment for COVID-19 in India: findings and implications Short title: COVID-19 and price changes of treatments in India. *Front Pharmacol*. **2021**;11(1822). doi: 10.3389/fphar.2020.582154
 71. Iskandar K, Molinier L, Hallit S, Sartelli M, Hardcastle TC, Haque M, et al. Surveillance of antimicrobial resistance in low- and middle-income countries: a scattered picture. *Antimicrob Resist Infect Control*. **2021**;10(1):63 doi: 10.1186/s13756-021-00931-w
 72. Malande OO, Musyoki MM, Meyer JC, Godman BB, Masika J. Understanding the Pathophysiology of COVID-19: A Review of Emerging Concepts. *EC Paediatrics* **2021**; 10 (4): 22-30.
 73. Harder T, Koch J, Vygen-Bonnet S, Külper-Schiek W, Pilic A, Reda S, et al. Efficacy and effectiveness of COVID-19 vaccines against SARS-CoV-2 infection: interim results of a living systematic review, 1 January to 14 May 2021. *Euro Surveill*. **2021**;26(28):2100563. doi: 10.2807/1560-7917.ES.2021.26.28.2100563
 74. Xing K, Tu XY, Liu M, Liang ZW, Chen JN, Li JJ, et al. Efficacy and safety of COVID-19 vaccines: a systematic review. *Zhongguo dang dai er ke za zhi*. **2021**;23(3):221-8. doi: 10.7499/j.issn.1008-8830.2101133
 75. Ling Y, Zhong J, Luo J. Safety and effectiveness of SARS-CoV-2 vaccines: A systematic review and meta-analysis. *J Med Virol*. 2021. (EPrint). doi: 10.1002/jmv.27203
 76. Knoll MD, Wonodi C. Oxford-AstraZeneca COVID-19 vaccine efficacy. *Lancet*. **2021**;397(10269):72-4. doi: 10.1016/S0140-6736(20)32623-4
 77. Shinde V, Bhikha S, Hoosain Z, Archary M, Bhorat Q, Fairlie L, et al. Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant. *NEJM*. **2021**;384(20):1899-909. doi: 10.1056/NEJMoa2103055
 78. Cavanaugh AM, Fortier S, Lewis P, Arora V, Johnson M, George K, et al. COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility After Vaccination Program - Kentucky, March 2021. *MMWR*. **2021**;70(17):639-43. doi: 10.15585/mmwr.mm7017e2
 79. Kupferschmidt K. Vaccine 2.0: Moderna and other companies plan tweaks that would protect against new coronavirus mutations. 2021. Available at URL: <https://www.sciencemag.org/news/2021/01/vaccine-20-moderna-and-other-companies-plan-tweaks-would-protect-against-new>.
 80. Pouwels KB, Pritchard E, Matthews PC, Stoesser N, Eyre DW, Karina-Doris Vihta K-D et al. Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. EPrint August 2021. Available at URL: <https://www.ndm.ox.ac.uk/files/coronavirus/covid->

- 19-infection-survey/finalfinalcombinedve20210816.pdf.
81. Islam MS, Kamal AM, Kabir A, Southern DL, Khan SH, Hasan SMM, et al. COVID-19 vaccine rumors and conspiracy theories: The need for cognitive inoculation against misinformation to improve vaccine adherence. *PloS one*. **2021**;16(5):e0251605. doi: 10.1371/journal.pone.0251605
 82. Lin C, Tu P, Beitsch LM. Confidence and Receptivity for COVID-19 Vaccines: A Rapid Systematic Review. *Vaccines*. **2020**;9(1). doi: 10.3390/vaccines9010016
 83. Sallam M, Dababseh D, Eid H, Al-Mahzoum K, Al-Haidar A, Taim D, et al. High Rates of COVID-19 Vaccine Hesitancy and Its Association with Conspiracy Beliefs: A Study in Jordan and Kuwait among Other Arab Countries. *Vaccines*. **2021**;9(1). doi: 10.3390/vaccines9010042
 84. Jeet Kaur R, Dutta S, Charan J, Bhardwaj P, Tandon A, Yadav D, et al. Cardiovascular Adverse Events Reported from COVID-19 Vaccines: A Study Based on WHO Database. *Int J Gen Med*. **2021**;14:3909-27. doi: 10.2147/IJGM.S324349
 85. Burn E, Roel E, Pistillo A, Fernandez-Bertolín S, Aragón M, Reyes C et al. Thromboembolic Events and Thrombosis With Thrombocytopenia After COVID-19 Infection and Vaccination in Catalonia, Spain. 2021. Available at URL: <http://dx.doi.org/10.2139/ssrn.3886421>
 86. Mehta NS, Mytton OT, Mullins EWS, Fowler TA, Falconer CL, Murphy OB, et al. SARS-CoV-2 (COVID-19): What Do We Know About Children? A Systematic Review. *Clin Infect Dis*. **2020**;71(9):2469-79. doi: 10.1093/cid/ciaa556
 87. Mantovani A, Rinaldi E, Zusi C, Beatrice G, Saccomani MD, Dalbeni A. Coronavirus disease 2019 (COVID-19) in children and/or adolescents: a meta-analysis. *Pediatr Res*. **2021**;89(4):733-7. doi: 10.1038/s41390-020-1015-2
 88. Singh T, Heston SM, Langel SN, Blasi M, Hurst JH, Fouda GG, et al. Lessons From COVID-19 in Children: Key Hypotheses to Guide Preventative and Therapeutic Strategies. *Clin Infect Dis*. **2020**;71(8):2006-13. doi: 10.1093/cid/ciaa547
 89. Bhuiyan MU, Stiboy E, Hassan MZ, Chan M, Islam MS, Haider N, et al. Epidemiology of COVID-19 infection in young children under five years: A systematic review and meta-analysis. *Vaccine*. **2021**;39(4):667-77. doi: 10.1016/j.vaccine.2020.11.078
 90. Smith C, Odd D, Harwood R, Ward J, Linney M, Clark M et al. Deaths in Children and Young People in England following SARS-CoV-2 infection during the first pandemic year: a national study using linked mandatory child death reporting data. Research Square 2021. Available at URL: <https://assets.researchsquare.com/files/rs-689684/v1/3e4e93fb-4e98-4081-9315-16143c2bbd2b.pdf?c=1625678600>.
 91. Hillis SD, Unwin HJT, Chen Y, Cluver L, Sherr L, Goldman PS, et al. Global minimum estimates of children affected by COVID-19-associated orphanhood and deaths of caregivers: a modelling study. *Lancet*. **2021**;398(10298):391-402. doi: 10.1016/S0140-6736(21)01253-8
 92. The Alliance of Child Protection in Humanitarian Action. Technical Note: Protection of Children during the Coronavirus Pandemic. May 2020. Available at URL: https://reliefweb.int/sites/reliefweb.int/files/resources/the_alliance_covid_19_tn_version_2_05.27.20_final.pdf.
 93. United Nations Children's Fund UNICEF). COVID-19: A threat to progress against child marriage. 2021. Available at URL: <https://data.unicef.org/resources/covid-19-a-threat-to-progress-against-child-marriage/>.
 94. DW Asia. COVID-19 lockdown increases domestic violence in Bangladesh. 2020. Available at URL: <https://www.dw.com/en/covid-19-lockdown-increases-domestic-violence-in-bangladesh/a-53411507>.
 95. Maharaj AR, Wu H, Hornik CP, Balevic SJ, Hornik CD, Smith PB, et al. Simulated Assessment of Pharmacokinetically Guided Dosing for Investigational Treatments of Pediatric Patients With Coronavirus Disease 2019. *JAMA Pediatr*. **2020**;174(10):e202422. doi: 10.1001/jamapediatrics.2020.2422
 96. Patel NA. Pediatric COVID-19: Systematic review of the literature. *Am J Otolaryngol*. **2020**;41(5):102573. doi: 10.1016/j.amjoto.2020.102573
 97. Deniz M, Tapısız A, Tezer H. Drugs being investigated for children with COVID-19. *Acta Paediatr*. **2020**;109(9):1905-6. doi: 10.1111/apa.15399
 98. Siemieniuk RA, Bartoszko JJ, Ge L, Zeraatkar D, Izcovich A, Kum E, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ*. **2020**;370:m2980. doi: 10.1136/bmj.m2980
 99. Li M, Wang Y, Xu H, Liu C, Shi L, Ye Q, et al. Existing drug treatments cannot significantly shorten the clinical cure time of children with COVID-19. *J Infect Dev Ctries*. **2020**;14(9):963-7. doi: 10.3855/jidc.13491