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Research article

Estimating & comparing greenhouse gas emissions for existing intramuscular COVID-19 vaccines and a novel thermostable oral vaccine

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ABSTRACT

Background: Climate impacts are rarely considered in health impact and economic assessments of public health programs. This study estimates the greenhouse gas (GHG) emissions averted by a novel oral SARS-CoV-2 (COVID-19) vaccine compared with four existing intramuscular vaccines: AstraZeneca's COVISHIELD®, Pfizer/BioNTech's COMIRNATY®, Moderna's mRNA-1273, and Johnson & Johnson's Ad26.COV2.S COVID-19 vaccine.

Methods: We estimated GHG emissions averted for five vaccine modalities across nine countries. GHG emissions averted were derived from differences in cold chain logistics, production of vaccine supplies, and medical waste disposal. Countryspecific data including population coverage and electricity production mix were included in GHG emissions calculations. Results are presented in averted GHG per vaccine course and country level based on modeled vaccination demand.

Findings: Per course, an oral vaccine is estimated to avert between 0.007 and 0.024 $kgCO_2e$ compared with Johnson & Johnson, 0.013 to 0.048 $kgCO_2e$ compared with AstraZeneca, 0.23 to 0.108 $kgCO_2e$ compared with Moderna, and 0.134 to 0.466 $kgCO_2e$ compared with Pfizer/BioNTech. The total GHG averted varied across countries based upon predicted demand, mix of electrical production, and vaccination strategy with the largest emissions reductions projected for India and the United States.

Interpretation: Our results demonstrate large potential GHG emissions reductions from the use of oral vs. intramuscular vaccines for mass COVID-19 vaccination programs. Up to 82.25 million $kgCO_2e$ could be averted from utilization of an oral vaccine in the United States alone, which is equivalent to eliminating 17,700 automobiles from the road for one year.

Funding: Funding was provided by Vaxart, Inc. Vaxart, Inc. is currently developing an oral COVID-19 vaccine, the characteristics of which were utilized to define the thermostable oral vaccine discussed in this study. Apart from providing data on the characteristics of the oral vaccine under development, the funders had no influence over the study design, methods, statistical analyses, results, framing of results, decision to submit the manuscript for publication, or choice of journal.

Background

Climate change continues to be a pressing issue for policymakers as solidified during the 2021 United Nations Climate Change Conference in Glasgow, UK [1]. The meeting underpins the importance of factoring in the climate impact of publicly funded investments, both for emissions accounting and for planning mitigation efforts. However, while climate data is increasingly used to inform public health and healthcare policy, assessments of the climate impact of various delivery modalities for healthcare interventions are rare, particularly when compared to the prevalence of economic impact assessments [2–4].

Program-based emissions accounting within the healthcare sector is important because, globally, the healthcare sector is amongst the most carbon-intensive sectors, accounting for nearly 5 percent of total annual global greenhouse gas emissions and upwards of 10 percent of total annual emissions in the United States [5–8]. In the United Kingdom a recent study found that the pharmaceutical and medical supply chain was the leading source of carbon emissions within the health sector, contributing to 32 percent of total healthcare sector emissions with chemicals production, energy, and cold chain logistics representing a significant contributor to emissions [9]. As such, emissions accounting for healthcare interventions,

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particularly those requiring large pharmaceutical production and a delivery component such as mass vaccination, are important for understanding the climate externalities associated with different production and delivery modalities.

Prior to the spread of SARS-CoV-2 (COVID-19), a group of 14 countries committed to reaching net zero carbon emissions within their health systems. Furthermore, the World Health Organization acknowledged additional needs for reductions in carbon emissions from vaccine supply chains, highlighting the potential of an innovative net-zero immunization delivery platform in Tunisia [10, 11]. However, with the global rollout of vaccines to protect against COVID-19, environmental concerns have taken a backseat to emergency pandemic control considerations. While this may be appropriate given the gravity of a global pandemic, countries should consider the climate impact of more routine COVID-19 vaccination delivery going into the future or investing in systems and research to prepare for future pandemics.

While intramuscular vaccines delivered via syringe are the most common form of vaccination, effective oral vaccination for diseases including rotavirus, adenovirus, cholera, polio, and typhoid are also widely available [12]. When considering vaccination delivery modalities, there exist potential differences in the overall emissions impact between oral vaccines and intramuscular vaccines. The differences in carbon emissions between traditional intramuscular versus an oral vaccine are driven by three main sources of carbon emissions associated with traditional intramuscular vaccines that are absent from the lifecycle of an oral vaccine [13]. These sources include the energy required for cold chain maintenance and logistics, emission associated with the production and transportation of vaccination supplies including vials, syringes, and sanitation materials, and medical waste disposal [14]. Cold chains generate emissions due to the energy requirements of refrigerated storage and transportation of vaccine doses from a central distribution center to the fixed sites where the vaccination campaign or delivery takes place [15]. Specifically, emissions are produced for powering refrigeration units and the production of dry ice packing for transportation [16]. Vaccine supplies generate carbon emissions through the production process of syringes, alcohol prep swabs, and glass vials along with additional energy requirements for transportation of these commodities to the point of delivery [17]. Finally, medical waste disposal generates carbon emissions through the combustion disposal of used syringes as well as the disposal of administration supplies [18].

Given the potentially large climate impact of COVID-19 vaccines, this study estimates the Greenhouse Gas (GHGs) emissions averted using a novel thermostable oral recombinant protein vaccine versus four leading intramuscular vaccines for COVID-19. The four leading intramuscular COVID-19 vaccines include AstraZeneca's COVISHIELD®, Pfizer/BioNTech's COMIRNATY®, Moderna's mRNA-1273, and Johnson & Johnson's Ad26.COV2.S COVID-19 vaccine [19, 20]. The study aims to highlight relative emissions per dose between the different delivery modalities as well as to illustrate potential total emissions reductions that could be achieved in several large demand settings including Argentina, Brazil, Chile, India, Kenya, Spain, United Kingdom, United States, and Vietnam, utilizing country-specific data on projected demand and vaccination rollout.

Methods

Overview

We estimated carbon emissions per dose and per course averted for four different intramuscular COVID-19 vaccines compared with an oral vaccine as well as in aggregate across nine different countries, given their specific vaccine rollout strategies. The COVID-19 vaccines examined are: a novel oral recombinant protein COVID-19 vaccine based on Vaxart's proprietary drug delivery platform, and four leading COVID-19 intramuscular vaccines which are AstraZeneca's COVISHIELD®, Pfizer/BioNTech's COMIRNATY®, Moderna's mRNA-1273 and Johnson & Johnson's Ad26.COV2.S COVID-19 vaccine. The study followed the Greenhouse Gas Protocol for the estimation of greenhouse gas (GHGs) emissions averted between vaccine types [21]. This protocol was established by leading experts representing businesses, nongovernmental organizations, and researchers as a way to standardize accounting of GHGs. Per the protocol, GHGs were measured in kilograms of carbon dioxide equivalence ($kgCO_2e$). The protocol also stipulates the accounting of GHGs for the five stages of a product lifecycle, which are the acquisition of materials, production, distribution, use, and end of life of a product. These stages guide the calculations in this report with an emphasis on the stages with significant differences between vaccine products.

GHG emissions averted were estimated by isolating the GHGs attributable to the cold chain, vaccination supply production, and medical waste disposal of the vaccines. These sources of emissions were targeted, because they would be nearly eliminated under a shelf-stable oral delivery platform with the exception of GHG emissions for the packaging of an oral vaccine. We estimated GHGs per dose and per treatment course. We then scaled the per treatment course results up for each country based on their estimated vaccine demand for a mass immunization program against COVID-19. We assumed an all-or-nothing scenario, where the selected vaccine technology is used exclusively in nine countries including Argentina, Brazil, Chile, India, United States, United Kingdom, Spain, Kenya, and Vietnam.

Cold chain emissions

A major difference between a thermostable oral vaccine and the current leading intramuscular vaccines is the requirement of cold chain distribution for intramuscular vaccines. We estimated GHGs for the cold chain by starting with each intramuscular vaccine's refrigeration requirements. For each vaccine, we used published estimates of GHGs emitted due to leakage of coolant and kilowatt hours required to maintain proper temperatures [22]. We then applied each countries' GHG emissions per kilowatt hour to estimate heterogeneity in the GHGs emitted during refrigeration across countries with varying profiles for their energy production [23]. For example, countries relying heavily on coal-fired power plants have higher GHGs emissions per kilowatt hour than countries utilizing less carbon intensive electric production. The final component of cold chain GHGs emissions considered is the use of dry ice for last mile vaccine delivery. These were based on estimates of GHGs required to produce dry ice including the electric needs, which we again convert the kilowatt hours to country specific GHG [16, 24].

Vaccine supplies emissions

The next source for variation in GHG emissions between an oral vaccine and the four intramuscular vaccines is related to differences in the supplies utilized for vaccine administration to the end recipient. These supplies include the glass vials, syringes, packaging, and alcohol prep pads for the intramuscular vaccines compared with the packaging for oral vaccines. To estimate units of supplies used for administration, we relied on publicly available data as well as published research that identified weight of supplies used in vaccine delivery [16, 25]. For the supplies calculation, we excluded personal protective equipment (PPE), since we assumed that an equal amount of provider PPE will be used across the different vaccine types, particularly in a pandemic scenario.

Table 1
Expected vaccination population.

	Argentina	Brazil	Chile	India	Kenya	Spain	United Kingdom	United States	Vietnam
Total population (2021)	45,605,816	213,993,456	19,212,360	1,393,408,896	53,771,300	47,351,567	67,215,293	329,500,000	97,338,583
Healthcare workers	541,229	3,168,360	474,455	10,971,710	144,483	633,726	1,258,012	8,540,401	400,000
Essential workers	3,544,600	12,445,977	805,469	42,370,256	2,230,586	5,021,436	9,828,792	34,483,848	5,438,250
Older adults (65+ years old)	5,246,494	21,268,322	2,440,012	144,322,064	12,537,902	9,071,995	1,349,222	54,796,260	7,656,664
Refugees and at-risk individuals	14,905,669	51,675,496	6,470,132	45,802,326	1,505,596	10,227,938	18,820,282	139,708,000	2,044,110
Children (0–14 years old)	11,087,953	44,019,351	3,677,716	361,017,585	20,750,132	6,818,373	11,881,832	60,531,991	22,576,747
All other adults (non-priority group)	10,279,871	81,415,950	5,344,576	788,924,955	16,602,601	15,578,099	24,077,153	31,439,500	59,222,812
Total Vaccination Populations	34,517,863	169,974,105	15,534,644	1,032,391,311	33,021,168	40,533,194	55,333,461	268,968,009	74,761,836
Total plus 10% wastage	37,969,649	186,971,516	17,088,108	1,135,630,442	36,323,285	44,586,513	60,866,807	295,864,810	82,238,020

Medical waste disposal emissions

The final source of differences in GHG emissions considered is the safe disposal of vaccine supplies as medical waste. This includes the disposal of the syringes, vials, packaging, and alcohol pads that are used for administering the intramuscular vaccines. Because of the biohazardous nature of the supplies, the disposal of them requires specialized treatment, which often involves incineration. To estimate GHGs associated with medical disposal, we pooled published estimates of GHG emissions per metric ton of medical waste and applied these values per metric ton of supplies used for the intramuscular vaccines [26–28]. Since medical waste disposal emissions may vary by country due to the efficiency and fuel used for incineration, we applied two estimates of GHG emissions for medical waste: one estimate used a study in the United Kingdom and this was applied to the estimates from Spain, the United Kingdom, and the Unites States; and the other estimate used a study in Pakistan, which was applied to the other countries included in this study [26, 27].

Vaccine demand

Vaccine demand was based on national immunization strategies and estimated vaccine eligible populations. The immunization strategy inputs presented in Table 1 reflect the proposed vaccination strategy of each country. Under the base case scenario, India, Argentina, Brazil, Chile, USA, United Kingdom, Spain, Vietnam, and Kenya all prioritize healthcare workers and essential workers in Phase 1. For Phase 2, countries prioritize older adults and at-risk populations. Note that India identifies older adults as age 60 and above whereas the other countries identify older adults aged 65 and above [29, 30]. For Phase 3, the remaining adult population age 15 and older is targeted for vaccination. Country-specific populations include total population, older adult population, refugee population, at-risk population, health care worker population, and essential worker population. These populations are estimated using data from The World Bank Databank and the World Health Organization's Global Health Workforce data [31–33]. Both age and obesity prevalence were used to proxy at risk populations, and data on public sector employment served as a proxy for essential worker populations. [31]

For the aggregate country-level emissions forecasts, we assume vaccination resources will be equally distributed across time such that a constant monthly effort for vaccination occurs. Lastly, we assume a target of 100% vaccination coverage for the eligible populations across Phase 1, 2, and 3. A detailed breakdown of total populations eligible for vaccination in each stage by country are provided in Table 1.

Role of the funding source

The funding for this study was provided by Vaxart, Inc., who is responsible for the development of an oral COVID-19 vaccine. The funder had no role in the research process, study design, analysis, or interpretation of results.

Results

Energy use per 100,000 doses for cold chain refrigeration for intramuscular vaccines are reported in Table 2. As expected, mRNA vaccines requiring extreme cold chain temperatures have significantly higher energy use for refrigeration than the viral vector vaccines.

Given the variation in the GHG emissions associated with the production methods for electricity, we apply country-specific estimates for emissions per kwh for cold chain, including dry ice production and utilization requirements for las-mile delivery [16, 23]. Table 3 displays the per-country production mix as well as the anticipated GHG per 100,000 doses of each vaccine. Of the countries examined, Kenya and India have the highest weighting factors, reflecting low levels of clean energy in their production mix whereas Spain, the United Kingdom, and Brazil lead in terms of clean energy as a proportion of their overall energy production mix.

Input factors for computing the GHGs associated with vaccine supply production, by country are presented in Table 4 for glass vials, syringes, and alcohol prep pads while Table 5 displays the GHG emissions per 100,000 doses for medical waste disposal process by country derived from estimates in the existing literature. [4, 6, 11, 16, 18, 26–28]

Utilizing the inputs presented in Tables 1-5, we estimate that a novel oral recombinant protein COVID-19 vaccine would avert between 0.007 and 0.024 $kgCO_2e$ per course compared with Johnson & Johnson, between 0.013 and 0.048 $kgCO_2e$ per course compared with AstraZeneca, between 0.23 and 0.108 $kgCO_2e$ per course compared with Moderna, and between 0.134 and 0.466 $kgCO_2e$ per course compared with Pfizer/BioNTech, depending on the setting. The total $kgCO_2e$ averted varied widely across countries based upon predicted demand, mix of electrical production, and vaccination strategies with the largest emissions reductions projected for India and United States.

The emissions attributed to vaccine supplies varied depending on the number of consumables required per course, such as syringes,

TABLE 2
Refrigeration Characteristics of Intramuscular Vaccines (per 100,000 doses).

Vaccine	Cold Room Temperature (°C)	Cooling Factor (kW)	Equipment Total Equivalent Warming Impact per year [1]	Energy Use for Refrigeration per year (kWh/yr)
Pfizer	−70	2.23	4,111.99	18,904.65
Moderna	−25	1.38	876.97	4968
AstraZeneca	2	1.02	598.45	2,023.06
J&J	2	1.02	598.45	2,023.06

[1] Equipment Total Equivalent Warming Impact is based on estimated leaks of refrigerant[16].

TABLE 3
Refrigeration and Dry Ice GHGs emissions (per 100,000 doses).

Country	Production Electricity Mix ($kgCO_2e$ per kWh)[23]	Dry Ice ($kgCO_2e$)[1]	Refrigeration ($kgCO_2e$)[2]			
			Pfizer	Moderna	AstraZeneca	J&J
Argentina	0.313	162	10,029	2,432	1,232	1,232
Brazil	0.074	109	5,511	1,245	748	748
Chile [3]	0.194	135	7,770	1,838	990	990
India	0.708	249	17,496	4,394	2,031	2,031
Kenya [4]	0.928	298	21,656	5,487	2,476	2,476
Spain	0.22	141	8,271	1,970	1,044	1,044
United Kingdom	0.253	148	8,895	2,134	1,110	1,110
United States	0.453	193	12,676	3,127	1,515	1,515
Vietnam[5]	0.497	202	13,508	3,346	1,604	1,604

[1] Dry Ice is based on needing 615.4 kg of dry ice, with each kg emitting 0.15 $kgCO_2e$ and requiring 0.36 kWh for production.[16].
[2] Refrigeration is based on data from table 2 and country specific fuel mix[16,23].
[3] Chile is based on the average production electricity mix of Brazil and Argentina.
[4] Kenya is based on South Africa's production electricity mix.
[5] Vietnam is based on Thailand's production electricity mix.

TABLE 4
Vaccine Supply GHGs emissions in $kgCO_2e$ per 100,000 doses [1].

	Production Fuel Mix ($kgCO_2e$ per kWh)	Glass vials (1 g/dose)	Packaging (Paper)	Syringes	Alcohol Prep	Total
Argentina	0.313	157	61	300	154	672
Brazil	0.074	92	61	300	154	607
Chile	0.194	125	61	300	154	640
India	0.708	265	61	300	154	780
Kenya	0.928	325	61	300	154	840
Spain	0.22	132	61	300	154	647
United Kingdom	0.253	141	61	300	154	656
United States	0.453	195	61	300	154	711
Vietnam	0.497	207	61	300	154	723

[1]GHG inputs and electricity requirements for Glass vials, packaging, syringes, and alcohol prep are based on Kurzweil et al. (2021) and measured in kilograms of carbon dioxide equivalence ($kgCO_2e$)[16].

alcohol swabs, glass vials, and gloves as well as the refrigeration requirements for each type of vaccine. AstraZeneca's ChAdOx1-S (COVISHIELD®), Pfizer-BioNTech's BNT162b2 (COMIRNATY®), and Moderna's mRNA-1273 all require two doses delivered for one vaccination course, while Johnson & Johnson's Ad26.COV2.S only requires one dose, thus halving the vaccine supplies required per course. Estimates derived from scaling the emissions data to reflect the recommended treatment course are presented in Table 6, by country.

Scaling the per-course data by anticipated demand from Phase I-III rollout guidance outlined in each of the examined countries, we estimate total GHG emissions reductions for covering the eligible population within each setting with a complete course of each vaccine. The results are presented in Table 7 with emissions averted from an oral vaccine delivery platform ranging in magnitude from 385,406,311 $kgCO_2e$ compared with the same level of coverage utilizing Pfizer/BioNTech's COMIRNATY® in India to 149,136 $kgCO_2e$ representing the lower observed bound on emissions reduction potential being compared with a hypothetical complete J&J Ad26.COV2.S vaccine rollout out in Chile.

Table 8 displays the estimated breakdown of GHG emissions averted by vaccine, source, and country. In terms of contributors to overall emissions averted compared with a thermostable oral vaccine, cold chain refrigeration was the largest driver of GHG emissions averted, accounting for between 71%–90% of total emissions averted when compared with Pfizer, 42%–72% of total emissions averted when compared with Moderna, and 28%- 53% of total emissions averted when compared with AstraZeneca and J&J.

TABLE 5
Medical Waste Disposal GHGs emissions (per 100,000 doses).

	Kilograms of waste per 100,000 doses	kg CO2 for disposal per 1000 kg of waste (LMIC)	kg CO2 for disposal per 1000 kg of waste (OECD)	Total GHGs (kg) Per 100,000 doses
Argentina	400	1,492	1,074	597
Brazil	400	1,492	1,074	597
Chile	400	1,492	1,074	597
India	400	1,492	1,074	597
Kenya	400	1,492	1,074	597
Spain	400	1,492	1,074	430
United Kingdom	400	1,492	1,074	430
United States	400	1,492	1,074	430
Vietnam	400	1,492	1,074	597

TABLE 6
Estimates of GHGs Averted ($kgCO_2e$) per Treatment Course.

	COMIRNATY® (Pfizer/BioNTech)	mRNA-1273Moderna	COVISHIELD® (AstraZeneca)	Ad26.COV2.SJ&J / Janssen
Argentina	0.227	0.047	0.023	0.012
Brazil	0.134	0.023	0.013	0.007
Chile	0.181	0.035	0.018	0.009
India	0.38	0.086	0.039	0.020
Kenya	0.466	0.108	0.048	0.024
Spain	0.191	0.037	0.019	0.010
United Kingdom	0.201	0.041	0.020	0.010
United States	0.278	0.061	0.028	0.014
Vietnam	0.299	0.065	0.03	0.015
Low Value	0.134	0.023	0.013	0.007
High Value	0.466	0.108	0.048	0.024

Notes: [1]GHGs averted is in comparison to a novel oral vaccine.
[2]One vaccine course (1 or 2 doses) is assumed for all vaccines.
[3]GHGs include emissions resulting from cold chain requirements, vaccination commodities (syringes, vials, and alcohol prep pads), and medical waste disposal.

TABLE 7
Estimates of Total GHGs Averted ($kgCO_2e$) for Mass Immunization.

	COMIRNATY® (Pfizer/BioNTech)	mRNA-1273Moderna	COVISHIELD® (AstraZeneca)	Ad26.COV2.SJ&J / Janssen
Argentina	8,188,960	1,695,512	829,719	414,860
Brazil	24,533,161	4,210,915	2,380,082	1,190,041
Chile	2,999,290	579,973	298,272	149,136
India	385,406,311	87,223,534	39,554,858	19,777,429
Kenya	16,926,650	3,922,914	1,743,517	871,759
Spain	8,516,024	1,649,701	847,144	423,572
United Kingdom	12,234,228	2,495,539	1,217,336	608,668
United States	82,250,417	18,047,753	8,284,214	4,142,107
Vietnam	24,589,168	5,345,471	2,467,141	1,233,571

Notes: [1]GHGs averted is in comparison to a novel oral vaccine.
[2] Assumes 100% coverage of all populations in Phases 1, 2, & 3.
[3] Assumes 10% wastage.

TABLE 8
Breakdown of GHG Emissions Averted by Source ($kgCO_2e$ per 100,000 doses).

Country	Pfizer			Moderna			AstraZeneca			J&J		
	Cold Chain	Supplies	Disposal	Cold Chain	Supplies	Disposal	Cold Chain	Supplies	Disposal	Cold Chain	Supplies	Disposal
Argentina	10,191	672	597	2,594	672	597	1,394	672	597	1,394	672	597
Brazil	5,511	607	597	1,245	607	597	748	607	597	748	607	597
Chile	7,770	640	597	1,838	640	597	990	640	597	990	640	597
India	17,496	780	597	4,394	780	597	2,031	780	597	2,031	780	597
Kenya	21,656	840	597	5,487	840	597	2,476	840	597	2,476	840	597
Spain	8,271	647	597	1,970	647	597	1,044	647	597	1,044	647	597
United Kingdom	8,895	656	430	2,134	656	430	1,110	656	430	1,110	656	430
United States	12,676	711	430	3,127	711	430	1,515	711	430	1,515	711	430
Vietnam	13,508	723	597	3,346	723	597	1,604	723	597	1,604	723	597

Interpretation

A thermostable oral COVID-19 vaccine offers large potential for lower GHG emissions compared to the four leading intramuscular COVID-19 vaccines. This benefit is primarily driven by the requirement of a cold chain refrigeration system for the distribution of existing intramuscular vaccines. Secondary to the cold chain requirement, an oral vaccine would also necessitate fewer vaccination supplies in the form of syringes, vials, and alcohol prep pads which all generate GHG emissions for their production and disposal. An oral COVID-19 vaccine would have particularly favorable environmental impacts in settings with large eligible populations and a lower proportion of energy generated through clean sources, including India and Kenya, who would see the largest emissions reductions per 100,000 doses. Putting the reduction estimates into scale, the 39.5 million $kgCO_2e$ averted in a setting such as India when using a novel oral vaccine versus the COVISHIELD® by AstraZeneca would be equivalent to the removal of approximately 8500 passenger vehicles from the road for one year and in the United Stated compared with COMIRNATY® by Pfizer/BioNTech would result in 82.25 million $kgCO_2e$ averted, or approximate equivalence of removing 17,700 passenger vehicles from the road for one year.

This study has several limitations. First, we have limited our examination of GHG emissions reductions to only production of vaccine delivery supplies, cold chain requirements, and waste disposal. Production of the vaccine itself is not included due to a paucity of information on the true production costs of each specific vaccine, including the oral comparator. However evidence suggests that, in general, oral vaccines may be likely to require even lower chemical and energy needs during production due to lower requirements for

aseptic techniques and sterilization during the production process [34]. Given that precise data on the energy requirements for production were unavailable at the time of this study, we assumed the difference in production emissions between oral and intramuscular vaccines to be zero, and as a result our estimates are likely to underestimate the potential emissions reduction from a full lifecycle perspective.

A second limitation is related to estimating the hypothetical scenarios for vaccine rollout in each country. While we utilize data from country reports on vaccination rollout strategies as well as data on the size of eligible populations from The World Bank and WHO, we still assume full vaccination coverage with only one vaccine in each scenario and at a constant rate over time. In reality most countries have rolled out multiple vaccines at once and often in a staggered manner with ebbs and flows in vaccine doses delivered depending on supply constraints [33]. While these are not reflected in the above scenarios, we believe that the evidence presented offers insights into the relative magnitude of emissions reduction potential at scale compared with different vaccine delivery modalities, which can be used by decisionmakers in future planning, rather than in trying to assess the actual level of emissions averted by changes to their current vaccination program. Similarly, the scenario presented in this analysis is based on rollouts that occurred before the widespread introduction of booster doses. While booster doses have not been rolled out in all settings, we expect our estimates to underestimate the GHG emissions averted by a comparably effective oral vaccine as more doses per course are added to immunization recommendations.

A third limitation is that the literature on medical waste disposal emissions and emissions related to vaccine supply production across settings was limited. As such, assumptions were made to allocate emissions per 100,000 dose estimates from countries observed in the literature to the countries in our study with the most similar levels of clean energy production mix. This is an imperfect solution and the comparison in any specific setting could be improved with the collection of more specific data on the medical waste disposal energy requirements in that setting.

A final limitation concerns the assumption over comparable vaccine effectiveness per course and the omission of the environmental impacts of COVID-19 treatment. Given that the per-dose efficacy at preventing a case of severe COVID-19 varies over time based upon a number of factors including dominant variant in circulation, current transmission rates, level of population immunity, and population demographic and geographic characteristics, we have chosen to assume roughly equal effectiveness per course across all vaccines, based on early clinical data. This allows us to assume comparable emissions averted due to reductions in hospitalizations cross all vaccines, after completing a full course. While this was true for early variants of COVID-19, it may not be true for all future variants. As such, the relative clinical effectiveness of future oral vaccines and intramuscular vaccines should be considered as variant and modality-specific effectiveness data become more readily available across settings.

Conclusion

Our results demonstrate the possibility for large GHG emissions reductions from the use of a thermostable oral vaccine compared with commonly administered intramuscular vaccines for mass COVID-19 vaccination programs. Results range from 0.007 $kgCO_2e$ averted per course to 0.466 $kgCO_2e$ per course depending on the cold chain requirements of the comparator vaccine. The total GHG averted varied widely across countries based upon predicted demand, mix of electrical production, and vaccination strategies with the largest emissions reductions projected in India and the United States. Given the overall impact of the pharmaceutical sector on global greenhouse emission, understanding the environmental impact of a large-scale immunization program is critical information for policymakers to plan for the minimization and mitigation of expected greenhouse gas emissions.

Declaration of Competing Interest

The authors received funding for this study from Vaxart, Inc. Vaxart, Inc. is currently developing an oral COVID-19 vaccine, the characteristics of which were utilized to define the thermostable oral vaccine discussed in this study. Apart from providing data on the characteristics of the oral vaccine under development, the funders had no influence over the study design, methods, statistical analyses, results, framing of results, decision to submit the manuscript for publication, or choice of journal.

CRediT authorship contribution statement

Bryan Patenaude: Conceptualization, Methodology, Data curation, Writing – original draft. **Jeromie Ballreich:** Conceptualization, Methodology, Data curation, Writing – review & editing.

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References

[1] United Nations Framework Convention on Climate Change. COP26 Reaches Consensus on Key Actions to Address Climate Change | UNFCCC [Internet]. 2021 [cited 2021 Dec 3]. Available from: https://unfccc.int/news/cop26-reaches-consensus-on-key-actions-to-address-climate-change
[2] Salas RN, Friend TH, Bernstein A, Jha AK. Adding a climate lens to health policy in the United States. Health Aff 2020 Dec 1;39(12):2063–70.
[3] Mahmud A.S., Martinez P.P., He J., Baker R.E. The impact of climate change on vaccine-preventable diseases: insights from current research and new directions. curr environ health rep. 2020 Dec;7(4):384–91.
[4] Guo B, Naish S, Hu W, Tong S. The potential impact of climate change and ultraviolet radiation on vaccine-preventable infectious diseases and immunization service delivery system. Expert Rev Vaccines 2015;14(4):561–77 Apr.
[5] Shankar Dhruv, Ahsanuddin Sofia. It's Time For The Health Care System To Reckon With The Human Costs Of Climate Change | Health Affairs Blog [Internet]. Health Affairs Blog 2019 [cited 2021 Dec 3]. Available from https://www.healthaffairs.org/do/10.1377/hblog20191011.432819/full/.
[6] Eckelman MJ, Huang K, Lagasse R, Senay E, Dubrow R, Sherman JD. Health care pollution and public health damage in the united states: an update, 39. Health Affairs; 2020 Dec 1. p. 2071–9.
[7] Lenzen M, Malik A, Li M, Fry J, Weisz H, Pichler P-P, et al. The environmental footprint of health care: a global assessment. The Lancet Planetary Health 2020 Jul 1;4(7):e271–9.
[8] Teghammar A, Sand Lindskog H, Fagerberg B, Berko L. Climate impact of healthcare. Lakartidningen 2019 Feb 26;116:FH9W.
[9] Tennison I, Roschnik S, Ashby B, Boyd R, Hamilton I, Oreszczyn T, et al. Health care's response to climate change: a carbon footprint assessment of the NHS in England. The Lancet Planetary Health 2021 Feb 1;5(2):e84–92.
[10] Wilkinson E. Reaching net zero carbon emissions in health systems. The Lancet 2021 Nov 27;398(10315):1953–4.
[11] PATH. Green Supply Chains: a Glimpse into the Future? [Internet]. 2013 [cited 2021 Dec 3]. Available from: https://www.path.org/resources/green-supply-chains-a-glimpse-into-the-future/
[12] Zhang L, Wang W, Wang S. Effect of Vaccine Administration Modality on Immunogenicity and Efficacy. Expert Rev Vaccines 2015;14(11):1509–23.
[13] De Smet R, Allais L, Cuvelier CA. Recent advances in oral vaccine development. Hum Vaccin Immunother 2014 May 8;10(5):1309–18.
[14] Klemeš JJ, Jiang P, Fan YV, Bokhari A, Wang X-C. COVID-19 pandemics Stage II – Energy and environmental impacts of vaccination. Renew Sustain Energy Rev 2021 Oct;150:111400.
[15] Sun X, Andoh EA, Yu H. A simulation-based analysis for effective distribution of COVID-19 vaccines: a case study in Norway. Transp Res Interdiscip Perspect 2021 Sep;11:100453.
[16] Kurzweil P, Müller A, Wahler S. The ecological footprint of COVID-19 mRNA vaccines: estimating greenhouse gas emissions in Germany. Int J Environ Res Public Health 2021 Jul 12;18(14):7425.
[17] Hasija V, Patial S, Raizada P, Thakur S, Singh P, Hussain CM. The environmental impact of mass coronavirus vaccinations: a point of view on huge COVID-19 vaccine waste across the globe during ongoing vaccine campaigns. Sci Total Environ 2021 Nov 23:151881.
[18] Phadke R., dos Santos Costa A.C., Dapke K., Ghosh S., Ahmad S., Tsagkaris C., et al. Eco-friendly vaccination: tackling an unforeseen adverse effect. The Journal of Climate Change and Health. 2021 Mar;1:100005.

[19] Ashraf MU, Kim Y, Kumar S, Seo D, Ashraf M, Bae Y-S. COVID-19 vaccines (revisited) and oral-mucosal vector system as a potential vaccine platform. Vaccines (Basel) 2021 Feb 18;9(2):171.
[20] Vaxart, Incorporated. Oral Vaccines [Internet]. 2021 [accessed 2021 Dec 3]. Available from: https://vaxart.com/tablet-vaccines/
[21] World Business Council for Sustainable Development, World Resource Institute. Greenhouse Gas Protocol [Internet]. 2017 [accessed 2021 Dec 3]. Available from: https://ghgprotocol.org/
[22] Santos AF, Gaspar PD, de Souza HJL. Refrigeration of COVID-19 Vaccines: ideal Storage Characteristics, Energy Efficiency and Environmental Impacts of Various Vaccine Options. Energies 2021 Jan;14(7):1849.
[23] Carbon Footprint Ltd. carbonfootprint.com - International Electricity Factors [Internet]. Int Electricity Factors 2021 [cited 2021 Dec 3]. Available from https://www.carbonfootprint.com/international_electricity_factors.html.
[24] Nadimuthu LPR, Victor K. Environmental friendly micro cold storage for last-mile Covid-19 vaccine logistics. Environ Sci Pollut Res Int 2021 Nov 23:1–12.
[25] World Health Organization. Global vaccine market report. Geneva, Switzerland: World Health Organization; 2019. [Internet][cited 2021 Dec 2] p. 14. Report No.: WHO/IVB/19.03. Available from https://apps.who.int/iris/handle/10665/311278.
[26] Rizan C, Bhutta MF, Reed M, Lillywhite R. The carbon footprint of waste streams in a UK hospital. J Clean Prod 2021 Mar 1;286:125446.
[27] Khan BA, Khan AA, Ali M, Cheng L. Greenhouse gas emission from small clinics solid waste management scenarios in an urban area of an underdeveloping country: a life cycle perspective. J Air Waste Manag Assoc 2019 Jul;69(7):823–33.
[28] Oteri J, Bawa S, Christopher E, Nsubuga P, Dieng B, Braka F, et al. Potential for improving routine immunisation waste management using measles vaccination campaign 2017 in Kebbi State, Nigeria. Vaccine 2021 Nov 17;39(3):C60–5 Suppl.
[29] World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. 2021 [cited 2021 Dec 3]. Available from: https://covid19.who.int
[30] Coronavirus Registration for next phase of vaccination on Co-WIN 2.0 portal to open on March 1. The Hindu [Internet]. 2021 Feb 28 [cited 2021 Dec 3]; Available from: https://www.thehindu.com/sci-tech/health/coronavirus-registration-for-next-phase-of-vaccination-on-co-win-20-portal-to-open-on-march-1/article33955656.ece
[31] The World Bank. Population ages 0-14, total | Data [Internet]. DataBank. 2021 [cited 2021 Dec 3]. Available from: https://data.worldbank.org/indicator/SP.POP.0014.TO
[32] World Health Organization. Global Health Workforce statistics database [Internet]. The 2021 update, Global Health Workforce Statistics. 2021 [cited 2021 Dec 3]. Available from: https://www.who.int/data/gho/data/themes/topics/health-workforce
[33] World Health Organization. COVID-19 vaccine tracker and landscape [Internet]. 2021 [cited 2021 Dec 3]. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
[34] Vela Ramirez JE, Sharpe LA. Peppas NA. Current state and challenges in developing oral vaccines. Adv Drug Deliv Rev 2017 May 15;114:116–31.