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**Energy, environmental, economic and social equity (4E) pressures of COVID-19
vaccination mismanagement: A global perspective**

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Highlights:

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45 The vaccination has been rolled out globally with an unprecedented scale and pace

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76 The 4E pressures of COVID-19 vaccination mismanagement have been substantial

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107 The life cycle from vaccine development to waste management is focused on

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138 Crucial lessons triggered by COVID-19 vaccination are summarised and discussed

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1629 Smart technologies with big-vaccination-data analytics have promising applications

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190 **Abstract**

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231 Vaccination now offers a way to resolve the COVID-19 pandemic. However, it is critical
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252 to recognise the full energy, environmental, economic and social equity (4E) impacts of
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2733 the vaccination life cycle. The full 4E impacts include the design and trials, order
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304 management, material preparation, manufacturing, cold chain logistics, low-temperature
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325 storage, crowd management and end-of-life waste management. A life cycle perspective
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356 is necessary for sustainable vaccination management because a prolonged immunisation
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377 campaign for COVID-19 is likely. The impacts are geographically dispersed across
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408 sectors and regions, creating real and virtual 4E footprints that occur at different
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429 timescales. Decision-makers in industry and governments have to act, unify, resolve, and
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450 work together to implement more sustainable COVID-19 vaccination management
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471 globally and locally to minimise the 4E footprints. Potential practices include using
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502 renewable energy in production, storage, transportation and waste treatment, using better
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523 product design for packaging, using the Internet of Things (IoT) and big data analytics for
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544 better logistics, using real-time database management for better tracking of deliveries and
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575 public vaccination programmes, and using coordination platforms for more equitable
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596 vaccine access. These practices raise global challenges but suggest solutions with a 4E

perspective, which could mitigate the impacts of global vaccination campaigns and prepare sustainably for future pandemics and global warming.

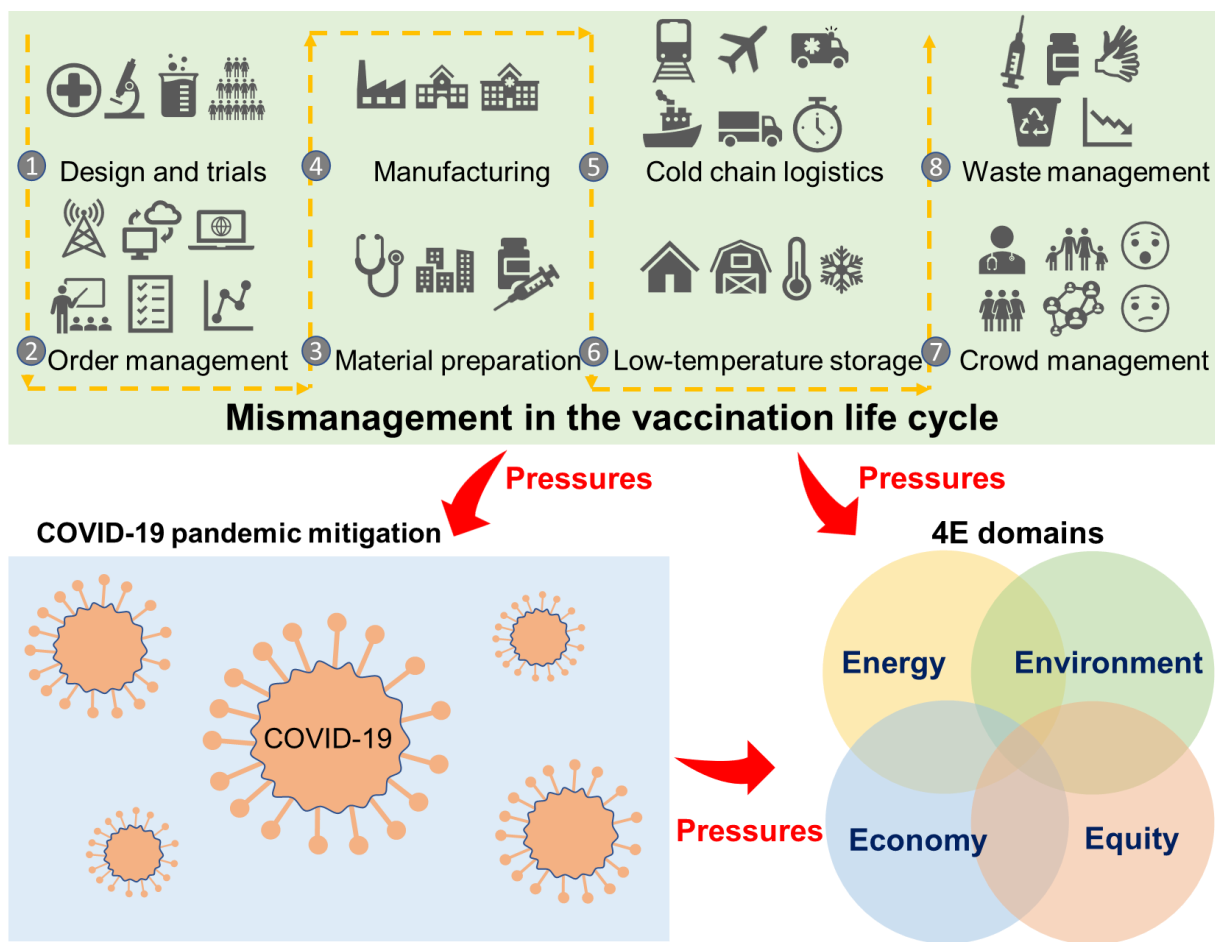
Keywords: Vaccination; Vaccines; COVID-19; Energy-Environment-Economy-Equity; Cold chain logistics; Sustainable management

1. Introduction

Coronavirus disease 2019 (COVID-19) continues to ravage the world after already infecting 171 M people and causing over 3.6 M deaths between the initial outbreak in late 2019 to June 2021 [1]. Worries about impacts on the energy, environmental, economic and social equity (4E) domains of the planet have been raised [2]. As the energy, environmental and economic domains have natural intersections [3], and social equity is broadly associated with the other three domains; the impacts of COVID-19 on energy [4], the environment [5], economy [6] and social equity [7] should not be analysed in isolation.

The rapid development of multiple vaccines has led to an evolving global vaccination campaign that is bringing hope to the fight against COVID-19. By 1 June 2021, there were eight vaccines approved for full use, seven vaccines in limited use, 30 vaccines in Phase III testing, 34 vaccines in Phase II testing and 51 vaccines in Phase I testing [8]. A town in Brazil that was hardest hit by COVID-19 has demonstrated that even a vaccine with relatively low efficacy could control the outbreak [9]. As of the beginning of June 2021, a massive vaccination with 1.98 billion (10^9) doses was rolled out in 209 countries or regions [10]. It is believed that a large number of vaccine doses is required in a short window to immunise 55% to 85% of the world's population [11]. However, the current

number of vaccinated people is still far from this target. If managed properly, significant health and economic outcomes are apparent after introducing COVID-19 vaccination [12]. Rapid scale-up of vaccination could pose serious sustainability challenges to various sectors, e.g. the pharmaceutical sector [13], the biotech manufacturing sector [14], the logistics sector [15] and the waste management sector [16]. Due to the gravity of the pandemic, the need to deploy vaccines has taken priority over sustainability considerations. This perspective paper brings attention to the 4E pressures of vaccination mismanagement. As visualised in Figure 1, such pressures come from multiple pathways, including the vaccination life cycle itself and the pandemic mitigation effects.



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Figure 1. The 4E pressures related to vaccination mismanagement upon the fight against COVID-19.

2. Unpreparedness for vaccination and 4E domains

For sustainable vaccination management, it is critical to recognise the 4E impacts of the vaccination life cycle (Figure 1). The life cycle includes design and trials, order management, material preparation, manufacturing, cold chain logistics, low-temperature storage, crowd management, and end-of-life waste management. These impacts are geographically dispersed across sectors and regions, creating significant long-lasting footprints. Just for the air transport-related cold chain logistics, 15 million cooling boxes, 200,000 pallets, and 15,000 flights are needed to deliver 10 billion (10^9) vaccine doses [17]. The energy and greenhouse gas footprints can vary significantly amongst the available alternatives. Vaccines with ultra-freezing temperature storage requirements are estimated to have an environmental impact 35 times higher than that of normal medical freezer storage [18]. Much of this impact can be attributed to the inherent energy and environmental pressures of cold chain logistics for newly developed high-efficacy vaccines. This drawback is the result of vaccination-related energy consumption not being optimised during vaccine development [19]. Under the current health crisis conditions, the 4E domains are not getting the priority they should have from decision-makers in government and industry. This position highlights the lack of preparedness for the current pandemic, vaccination and even future outbreaks [20]. It also bodes badly for the future management of uncertain global warming events related to anthropogenic climate change, as predicted over the next decades [21].

3. Observations on vaccination mismanagement

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Unsustainable vaccination management has already been observed in the vaccination life cycle. These situations will only worsen and increase the 4E pressures while the global immunisation campaigns continue, possibly until 2024 [22] or even longer, considering virus variants [23], possible vaccine failure [24], and the strategy of third-dose vaccination following the initial vaccination campaigns for enhanced protection in some countries [25].

Some of the notable 4E pressures of the vaccination campaign are:

(i) The initial design of syringe size causes the wastage of two extra doses per vial [26], i.e. about 16.7% (Pfizer-BioNTech vaccines) to 28.6% (Moderna vaccines codenamed mRNA-1273) wastage at the early stage of vaccination campaigns.

Due to the low-temperature storage requirement and mismanagement in the multimodal cold chain logistics, the wastage rate of vaccines could be up to 30%, even in some developed countries [27]. The need for excess production and reallocation to compensate for the massive wastage would significantly inflate the 4E impacts and prolong the global recovery, entailing unnecessary depletion of resources.

(ii) The last-mile logistics has already been problematic in the USA [28], and wastage would be even worse in lower-income countries. For example, less than 50% of respondents have positive perceptions in terms of power back-up (39%), cold chain capacity (49%), cold chain storage (36%), and distribution plan (44%) in Africa [29]. Many countries have limited readiness for mass vaccination. For example, only 59% of respondents agreed or strongly agreed that a logistics management information system that supports vaccination effectively needs vaccine demand forecasting [29].

(iii) Several virus variants have been threatening the world population, such as the B.1.617 and B.1.351 variants [30]. Under such situations, increasing numbers of

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young persons are being [31] or going to be vaccinated in a growing number of countries [32]. After extending the vaccination to the youth, the consumption of vaccines is likely to grow considerably, and related energy, emissions and economic costs would increase as well. However, with the vaccination opened for younger adults, there have been increasing "no show" cases due to vaccine hesitancy. In addition, the anti-vaccination beliefs compound the misallocation problem. Overall, poor crowd management of social dimensions leads to the wastage of already scarce vaccines.

(iv) The environmental impact of the sudden surge in plastics [33], medical waste [16] and single-use personal protective equipment (PPE) [34] has been severe since the start of the pandemic. Without proper management guidelines, the vaccination campaigns could be followed by a looming waste crisis from syringes, needles, sharps containers, vaccine vials, and packing materials [35].

(v) The long-term unsustainable financial and economic implications of the vaccination campaign should not be ignored [36]. Vaccination is necessary to end the pandemic; however, the economic pressure related to vaccination mismanagement is bound to persist and spread to not only 4E domains but also other aspects of society. The pandemic and the imbalanced vaccine deployment threaten the achievement of the Sustainable Development Goals by 2030, particularly in the least developed countries [37]. One of the studies suggests the global economy stands to lose US\$ 9.2 trillion (10^{12}) if it fails to ensure developing economies' access to COVID-19 vaccines [38]. Çakmaklı et al. [39] proposed that if vaccines are unequally distributed between advanced economies and emerging and developing economies in 2021, the global economic costs could reach up to US\$ 1.84 to 3.8 trillion (10^{12}). Çakmaklı

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4 et al. [39] concluded that the whole gross domestic product (GDP) loss of not
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6 vaccinating all countries, compared to a global vaccination, could be much higher
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8 than the total cost of global vaccine manufacturing and distribution. These
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10 observations emphasise the importance of the equitable distribution of vaccines and
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12 that "no economy is an island". Economic drag in one country has consequences
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14 for others. The mitigation of pandemic economic losses requires multilateral
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16 coordination, ensuring vaccine access and proper vaccination management.
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20 (vi) Some countries have over-booked vaccines [36] as a result of initial uncertainties
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22 on the efficacy of vaccine products and the effects of pandemic control. These
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24 actions have led to insufficient supply in other parts of the world due to the still limited
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26 production capacity worldwide. As of 2 June 2021, the number of doses purchased
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28 in high income countries was 5,929,777,500 (i.e. 52.25%), upper-middle-income
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30 countries 1,825,678,075 (i.e. 16.09%), lower-middle-income countries 961,328,000
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32 (i.e. 8.47%), low income countries 270,200,000 (i.e. 2.38%) and the COVID-19
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34 Vaccines Global Access (COVAX) 2,361,000,000 (i.e. 20.81%) [40]. Based on data
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36 from World Health Organization (WHO) [41], as of 9 April 2021, an average of one
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38 in four persons was vaccinated in high-income countries, but this proportion in low-
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40 income countries was just one in five hundred. The imbalanced distribution would
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42 cause variations in levels of population immunity in different countries and regions,
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44 which can exacerbate 4E pressures, in particular the social equity pressure, due to
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46 the need for redistribution and reallocation.
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54 55 **4. Lessons triggered by COVID-19 vaccination** 56 57 58 59 60 61 62 63 64 65

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With 4E pressures, disruptions to the UN Sustainable Development Goals [42] could be exacerbated by unsustainable vaccination management. Despite the considerably fast development of COVID-19 vaccines, the world still has a long way to go, as (i) the global average vaccination rate was still low as 10.91% as of 1 June 2021 [10], in particular, for the low- and middle-income countries, (ii) the acceptance of COVID-19 vaccines is not high (i.e. 71.5%), which also presents significant spatial differences [43], and (iii) regular re-vaccination will be necessary if vaccine-induced immunity is not permanent. Since 2020, the world has had to scale the steep learning curve of pandemic management to draw crucial lessons:

a) The challenges of COVID-19 vaccination were summarised by several authors, e.g. by Forman et al. [44] into seven aspects, including maintaining incentives of research and development, running population trials, approvals and authorisations, surveillance in the post-market, manufacturing and distribution, worldwide dissemination, and system adaption of the clinical environments. They also emphasised that policy-makers should prioritise those strategies and solutions implementing at scale to address the challenges. For the 4E domains, policy-makers are recommended to systematically implement solutions with an international outlook that accounts for the global network of interdependencies.

b) Behavioural disinhibition (e.g. abandoning masks and social distancing) after immunisation has been widely observed [45]. Such behaviour is risky, as there is no definitive evidence yet of the transmission-blocking capacity of the approved vaccines, and even immunised persons might still be disease vectors. Using mathematical modelling with the epidemiological data, the UK seems unlikely to achieve herd immunity by vaccination even though the vaccine efficacy is as high

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as 88% on the basis of filed data in the UK [46]. Although several vaccines have been approved, vaccination should not be regarded as the final defence. Proper non-pharmaceutical interventions alongside the vaccination could still guarantee the progress of COVID-19 fighting. In other words, although non-pharmaceutical interventions would postpone economic recovery, the measures could be dominant strategies in the medium term to control the pandemic and ease 4E pressures.

c) Pfizer-BioNTech vaccines were required to be stored at temperatures between -80°C and -60°C [47]. The initial conclusion on valid duration was up to 5 days for the Pfizer-BioNTech vaccine at the standard refrigerator temperatures between 2°C and 8°C (i.e. 36°F and 46°F) in December 2020 [48]. This duration was updated as 14 days in February 2021. It was again updated to be 31 days at regular refrigerator temperatures by the US Food and Drug Administration on 19 May 2021. Since the extended duration and refrigerator conditions could guide more flexible transportation/distribution and storage, the new standard has been implemented promptly in other countries, such as Singapore [48], Canada [47], and the UK [49]. From the environmental impact perspective, the dynamic standard improvement based on the process data related to vaccines could reduce energy usage and air emissions.

d) The vaccination pace in most countries is limited by the pace of the supply arriving. Many countries, e.g. France and the UK, have delayed dispensing the second vaccine dose, trying to provide protection to the vast population as soon as possible [50]. Experts are still debating about giving two doses between the regular period (usually 3-4 weeks) or space out between the first and second doses. This is also an open optimisation question about vaccination cost and effect. However, it takes

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240 time to answer which one is better between one vaccine jab with more population
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201 and two jabs to fewer people. The 4E pressures have to be considered for the
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282 optimal answer.

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223 e) Given the availability of multiple vaccines that were rapidly developed in response
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133 to the crisis, optimal allocation of available doses would be critical to finally bringing
144 the pandemic under control. Maximising the possible number of avoided COVID-19
15 205 cases per unit of vaccine administered can yield significant 4E co-benefits through
17 196 avoided hospitalisation and death. The available vaccine options have all been
19 217 demonstrated to protect people from serious illness, but there is still limited evidence
22 228 of their transmission-blocking capability. When such capability is fully proven, the
24 229 allocation of COVID-19 vaccines can be rationalised with optimisation models used
25 26 for influenza vaccines to suppress the spread of the virus [51]. Vaccines with higher
27 280 transmission-blocking characteristics can be prioritised for younger, more mobile
29 31 adults to reduce their propensity to act as disease vectors [52]. Mixed-vaccination
32 33 strategies can maximise benefits that result from any given number of doses while
34 353 also relieving supply chain bottlenecks [53]. Such optimised allocation can help
36 384 bring the pandemic under control more efficiently and with reduced total 4E
39 405 footprints.
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47 238 f) Some high-income countries have been criticised for their roles in the unequal
48 49 distribution of vaccines. However, their efforts in investing resources and funding in
50 209 developing COVID-19 vaccines are undeniable [54]. A favourable solution can be
51 521 found through negotiation between different stakeholders at the international level.
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54 241 For example, COVAX [55], funded by WHO and United Nations, CEPI and Gavi, is
56 57 one channel to mitigate social inequality and discrepancy issues. Distributing
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4 vaccines to more than 100 low-income countries, cost-sharing mechanisms (funded
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6 by multilateral development banks) [56], and free vaccines are amongst the major
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8 strategies for tackling this global immunity, humanity and resource issues that could
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10 not be viewed as isolated under globalisation. The optimal distribution following the
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12 herd immunity threshold and a more in-depth understanding of the single-dose
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14 vaccine efficacy could better facilitate the distribution under supply chain constraints
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16 [56], further easing the 4E pressures. For example, the data based on population
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18 trials suggested that a new single-dose nasal spray vaccination technology could
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20 save 80% of vaccines, with no requirements of special glass vials and cold-chain
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22 storage and transport [57]. Such new vaccines would significantly reduce energy,
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24 environmental and economic footprints if successfully applied to vaccination.
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31 **5. Outlooks**

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35 This disease follows no borders, age, ethnicity, wealth, political and religious beliefs, or
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37 indeed nationality. Although vaccination worldwide has been around for some places and
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39 some time, e.g. polio, tuberculosis, dengue and regular flu, it has not been as that short
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41 time window and mass scale. Decision-makers in industry and governments have to act,
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43 unify, and resolve together to design more sustainable vaccine development,
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45 manufacturing and deployment solutions (including the new low-footprint broad-spectrum
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47 vaccines [58]) globally and locally to minimise the 4E footprints. In addition, real-time
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49 vaccination tracking [59], rapid assessment of vaccination hesitancy at scale [60], natural
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51 language processing-enabled social media analysis [61], longitudinal analysis of the
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53 changing acceptance [62], Big Data analytics, Internet of Things (IoT) and blockchain
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55 technologies could be used to optimise production, transport, cold chain logistics and
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4 storage and waste management and reducing the global 4E impacts of this COVID-19
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6 pandemic and enhancing preparedness for future pandemics [63], as well as climate
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8 change [64]. The worldwide vaccination campaign has been still fast-evolving, and the
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10 energy and emissions impacts are emerging and should be closely followed [65].
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14 This perspective paper recommends substantial attention to the 4E pressures and the
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16 related efforts of promoting proper vaccination management, which would contribute to
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18 successfully managing the current and future pandemics. More research with quantitative
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20 assessment incorporating the 4E framework is urgently needed to draw a more precise
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22 picture for consistent decision making and road mapping worldwide.
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45 46 47 **Competing interests** 48

49
50 The authors declare that they have no known competing financial interests or personal
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52 relationships that could have appeared to influence the work reported in this paper.
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55 56 57 **CRedit authorship contribution statement**

58
59 **Peng Jiang:** Conceptualisation, Writing-original draft, Formal Analysis, Writing-review
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4 and editing, Visualisation, Funding Acquisition; **Jiří Jaromír Klemeš**: Conceptualisation,
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6 Writing-review and editing, Supervision and Management, Funding Acquisition; **Yee Van**
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8 **Fan**: Conceptualisation, Writing-review and editing, Formal Analysis; **Xiuju Fu**:
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10 Conceptualisation, Writing-review and editing; **Raymond R. Tan**: Conceptualisation,
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12 Writing-review and editing; **Siming You**: Conceptualisation, Writing-review and editing;
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14 **Aoife M. Foley**: Conceptualisation, Writing-review and editing.
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