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Secondary Safety Analysis of Different COVID-19 Vaccines and mRNA Products in a Cohort of 46 Million Participants in England

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Abstract

We performed a secondary safety analysis of different COVID-19 vaccines from several large UK data sets. The original published studies did not perform such analyses. We assessed confidence intervals of the ratio of hazard ratios for the following published studies: Ip et al. (45.7M participants) [1], Whiteley et al. (45.7M) [2], Horne et al. (7.6M) [3], Parker et al. (427K) [4], and Hulme et al. (2.7M) [5]. Our analysis reveals extreme and verifiable increased hazards associated with the Oxford/AstraZeneca ChAdOx1 COVID-19 vaccine ("AstraZeneca Product") relative to the Pfizer-BioNTech BNT162b2 COVID-19 mRNA product ("Pfizer Product"). Significant increased hazards for the AstraZeneca Product manifested in cardiovascular disease and death. Significant increased hazards for the Pfizer Product manifested in myocarditis and pericarditis. The published primary studies, performed during the active pandemic period, promoted the "cardiovascular safety" of the COVID-19 products. However, they neglected to compare relative safety between products, which would have revealed multiple signals contrary to that narrative. Our secondary study reveals increased hazards in each type of COVID-19 product that contradict prior safety claims. The subsequent removal of the AstraZeneca Product from the market and the now-universal recognition of myocarditis risk from the Pfizer Product are consistent with our findings. The primary studies reached false conclusions that were avoidable by making comparisons of the different products, raising concerns about investigational bias.

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Introduction

The COVID-19 era saw the fastest rollout of vaccine countermeasures in modern pharmacological regulatory history, involving multiple emergency (or exceptional) use authorizations for experimental vaccines. During this very rapid rollout, the scientific discourse in major journals consistently promoted their safety and necessity. In fact, "safe and effective" [6,7] became a worldwide catchphrase used to describe the various products in an indiscriminate manner.

In our study, we performed a secondary safety analysis of different COVID-19 vaccines and mRNA injectable products from several very large UK data sets. The original published studies of these datasets, done at the height of the COVID vaccine rollout period and with privileged access to these huge datasets, did not perform such analyses.

We assessed confidence intervals of the ratio of hazard ratios for the following published studies: Ip et al. (45.7M participants) [1], Whiteley et al. (45.7M) [2], Horne et al. (7.6M) [3], Parker et al. (427K) [4], and Hulme et al. (2.7M) [5].

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Data and Methods

Ip, et al., ("Ip") conducted a longitudinal study of health records from 45.7 million adults in England [1]. These researchers studied various indicators for cardiovascular health for the first 26 weeks after vaccination. In comparison to the unvaccinated, the AstraZeneca ChadOx1 COVID-19 vaccine ("AstraZeneca Product") posed a statistically significant hazard for intracranial venous thrombosis and thrombocytopenia. The mRNA vaccines, including the Pfizer-BioNTech BNT162b2 COVID-19 mRNA product ("Pfizer Product") were statistically significant for myocarditis and pericarditis. The authors state that "[t]hese findings support the wide uptake of future COVID-19 vaccination programs" and "[t]his England-wide study offers reassurance regarding the cardiovascular safety of COVID-19 vaccines … [w]e hope this evidence addresses public concerns, supporting continued trust and participation in vaccination programs and adherence to public health guidelines."

Whiteley, et al., ("Whiteley") was an earlier publication by largely the same research group that published Ip [2]. Whiteley conducted a similar analysis utilizing the same data, however limiting outcomes to the first 28 days post vaccination, with similar outcomes. Whiteley did address mortality, which Ip subsequently and inexplicably omitted.

By comparison, Horne et al. ("Horne"), with 7.6 million subjects [3], Parker et al. ("Parker"), with 427,000 subjects [4], and Hulme et al. ("Hulme") with 2.7 million, all assessed mortality between the AstraZeneca Product and the Pfizer Product [5].

Ip conducted a longitudinal study of health records from 45.7 million adults in England between December 2020 and January 2022 [1]. Supplementary Tables S8–S10 include hazard ratios that were fully adjusted ("for a wide range of comorbidities, age, sex, and prior COVID-19") and 95% confidence intervals for 13 classifications of cardiovascular, arterial, and venous thrombotic events in six time windows (week 1, week 2, weeks 3-4, weeks 5-12, weeks 13-24, and weeks 25-26) since first dose vaccination with the AstraZeneca Product, Pfizer Product, and the Moderna mRNA-1273 ("Moderna Product") respectively.

Whiteley previously had analyzed 13 vascular events in addition to lower limb fracture and death. Tables S4 and S5 contain hazard ratios for the AstraZeneca Product and Pfizer Product respectively [2]. Sub-groupings include younger than 70 years old and greater or equal to 70 years old; and events that occur in the first 28 days and after 28 days.

Horne compared eligible adult recipients of two doses of the Pfizer Product (n=1,951,866) or the AstraZeneca Product (n=3,219,349) with the unvaccinated (n=2,422,980) [3]. Supplemental Table S7 compares the adjusted non-COVID-19 death hazard ratio of the Pfizer Product vs. the AstraZeneca Product.

Parker compared two-dose AstraZeneca Product (n=257,580) recipients and two-dose Pfizer Product (n=169,205) recipients cohort analysis, additionally 130,765 are matched for analysis [4]. Supplemental Table S8 includes an AstraZeneca Product vs. Pfizer Product hazard ratio for non-COVID-19 death.

Hulme analyzed 1,406,637 individuals vaccinated with the Pfizer Product and 1,249,425 individuals vaccinated with the AstraZeneca Product. Supplemental Table S2 shows the hazard ratios of death in seven different time windows in the first 70 days after first dose [5].

Ratio of Hazard Ratios

Logarithm parameters μ and σ are used in the equations for hazard ratio (HR) and 95% confidence interval CI.

$$HR = e^{\mu} \qquad (1)$$

$$CI = e^{\mu \pm 1.96\sigma} \qquad (2)$$

The Ip et al. article does not make available μ or σ, as such we derive them from the stated hazard ratios.

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For example from Ip, et al., the week 1 arterial composite for AstraZeneca aHR is 0.84 (0.80,0.87) and for Pfizer is 0.73 (0.69,0.76). Using Equation 1 we can calculate mu as the natural log of the stated hazard ratios (AstraZeneca: $\mu = -0.174$, and Pfizer: $\mu = -0.315$).

Because the confidence intervals are rounded to two significant figures, we subtract 0.005 from the lower bound and add 0.005 to the upper bound to evaluate the maximum possible 3-significant figure confidence interval to extrapolate σ. With each end of the 95% confidence interval, we solve for σ and use the maximum value, allowing again for the greatest possible interpretation of error (AstraZeneca σ =max(0.0281, 0.0208), and Pfizer σ=max(0.032, 0.0239)).

The ratio of two independent logarithmic normal distributions is itself a logarithmic normal distribution. The ratio of hazard ratios (RHR) for two hazard ratios (a and b) and corresponding ratio of confidence intervals (RCI) are represented here:

$$RHR_{ab} = e^{(\mu a - \mu b)} \quad (3)$$

$$RCI_{ab} = e^{(\mu a - \mu b) \pm 1.96\sqrt{\sigma_a^2 + \sigma_b^2}} \quad (4)$$

Ratio of hazard ratios in data science is a secondary analysis, used when one does not have access to the primary data. Pursuant to the data availability statement, on the day of publication of Ip, Jablonowski contacted the British Heart Foundation Data Science Centre requesting the data utilized. As of this writing, they have not responded to the request.

The original study authors presented their hazard ratios and confidence intervals to only two decimal places. Secondary analysis of such low precision reporting is limited, and must consider the widest possible confidence interval. We lowered the reported lower confidence interval by 0.005 and raised the upper confidence interval by the same value to assess the largest possible interval pre-rounding. We solve for σ from both upper and lower intervals, and only entertain the maximum value of σ.

Accordingly, we can calculate the ratio of hazard ratios (AstraZeneca/Pfizer) by Equation 3 exp(μ[AstraZeneca]-μ[Pfizer]) yielding 1.151. The confidence interval may then be calculated by Equation 4 yielding (1.058, 1.252). A statistically significant ratio of hazard ratios showing AstraZeneca is positively associated with arterial composite disease.

Results

Secondary analysis of Ip (Figure 1) assessing AstraZeneca Product vs. Pfizer Product reveals 10 of the 13 vascular diseases to have at least one significant ratio of hazard ratios. 9 of the 10 significant results show The AstraZeneca Product to be more hazardous than the Pfizer Product. Myocarditis and pericarditis is the only significant condition that is more hazardous in the Pfizer Product than the AstraZeneca Product, and peaks in weeks 13-24 with a hazard ratio (inverted from the figure) of 1.563 (1.071, 2.278).

Secondary analysis of Whiteley (Figure 2) assessing AstraZeneca Product vs. Pfizer Product reveals of 13 of the 15 classified conditions reach significance in at least one cohort. A total of 12 categories show the AstraZeneca Product to be more hazardous than the Pfizer Product. The one category where the Pfizer Product was more hazardous than the AstraZeneca Product is in other venous diseases. Remarkably, the increased hazard for death in AstraZeneca Product vs. Pfizer Product is 1.545 (1.360, 1.756).

Horne requires no secondary analysis, as the hazard ratio for the Pfizer Product vs. the AstraZeneca Product is directly computed in the paper's supplementary table. For consistency, the inverse is plotted (Figure 3) to show the significant signal for non-COVID-19 deaths in persons 65 years and older in the first four time windows, spanning weeks 3-18 after the second dose.

Parker needs no secondary analysis, as the hazard ratio for AstraZeneca Product vs. Pfizer Product is directly computed in the paper's Supplementary Table (Figure 4). Parker found significant signal for non-COVID-19 death in both forms of analysis they implemented.

Secondary analysis of Hulme found a significant ratio-of-hazard-ratios of the AstraZeneca Product vs. Pfizer Product for death in all seven-time windows recorded spanning one to 70 days after first dose (Figure 5).

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Recipients of the AstraZeneca Product have a measurable increased risk compared to the Pfizer Product of: acute myocardial infarction, intracranial venous thrombosis, ischaemic stroke, lower limb deep vein thrombosis, pulmonary embolism, subarachnoid haemorrhage and haemorrhagic stroke, thrombocytopenia, and (everywhere that it was measured) mortality. All these conditions negatively and substantially impact quality and/or length of life.

However, the discussion section of Ip, reads: "This England-wide study offers reassurance regarding the cardiovascular safety of COVID-19 vaccines." Whiteley characterizes these severe adverse events as "very small harms."

Horne (Figure 3) and Parker (Figure 4) highlight non-COVID-19 deaths where differences in efficacy of the interventions would not affect the analysis. Hulme (Figure 5) demonstrate significant all-cause mortality at every time window inspected. Whiteley (Figure 2) shows a significant death signal in both age groups and both time windows.

Discussion

Our study analyzed data from published studies to investigate an important question that the original authors neglected to address: namely, the relative safety or hazard of the various COVID-19 injectable products.

Our secondary analysis shows extreme and veritable hazards associated with AstraZeneca Product vs. Pfizer Product. Hazards manifest for the AstraZeneca Product both in multiple markers of *cardiovascular disease* and in *death*. Meanwhile, hazards associated with the Pfizer Product manifest for myocarditis and pericarditis.

These findings, which would have been readily available to the Ip authors had they chosen to perform the requisite analyses, presage the withdrawal of the AstraZeneca Product from the world market in March 2024, and with the subsequent worldwide acknowledgement of increased myocarditis risk associated with the Pfizer Product and other mRNA-based COVID injections.

Inexplicably, Ip, a follow up study to Whiteley, does not include an indicator for death. The Ip and Whiteley authors are essentially the same research group, with 10 listed authors in common in addition to the CVD-COVID-UK consortium. The datasets are largely the same, as is the analysis. However, Ip excludes mortality as an outcome when a clear increased hazard for death was apparent in the Whiteley analysis. Inclusion of death as an endpoint by Ip would have provided vital insight into the time-dependent severity of adverse vaccine outcomes.

Such an analysis, if performed and published at the time may have saved many lives, though it would have provided much less "reassurance regarding the cardiovascular safety."

During the pandemic, the scientific community and regulatory agencies declared rapidly developed, minimally tested, and novel-designed COVID-19 injectable products to be *safe*, and they were administered to the greater human population in massive numbers and often with considerable coercion. Our secondary analysis adds to the growing literature demonstrating that those injections were in fact *unsafe*.

This secondary study also reveals an important aspect of the flawed system that produced and promoted these products: clinical studies that appear biased by design.

Ip has 17 authors [1]. Also listed is the CVD-COVID-UK/COVID-IMPACT Consortium, a group of over 400 members across more than 50 prestigious institutions. Prominently included is Oxford, which had immense proprietary interest in the AstraZeneca vaccine. Also listed is the UK Research and Innovation funded Longitudinal Health and Wellbeing COVID-19 National Core Study. Ip utilized data from the National Health Service (NHS), the second largest single-payer healthcare system in the world. The paper was published in *Nature Communications*, one of a family of high-impact journals that reaches 55 million people monthly. Ip was the product of preeminent scientific entities.

The Ip authors were granted public funds and access to an immensely powerful dataset at a critical period during the COVID-19 era [1]. As health scientists, they were entrusted to impartially and thoroughly study the safety of the COVID-19 vaccines. They had a professional and ethical

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responsibility to make a genuine contribution to human health, and they were equipped to do so. It was a golden opportunity.

Instead, they created and carried out a study that was biased by design, one that served a narrative of "cardiovascular safety" that does not fit the actual data. Ip omitted known data signals showing increased mortality [1]. They chose not to perform the obvious and necessary secondary evaluation of the different COVID-19 injections being investigated. They left that work to be done by others, long after the fact, without benefit of the primary data.

Ip serves as an object lesson in the biased-by-design nature of the state-sponsored research undertaken during the COVID-19 era. As authorities in the United States and elsewhere call for reform in medical research away from tendentious and willfully misleading study design and execution, Ip will also serve as a key example of the fatal flaws inherent in current medical research methods.

Supplementary Materials: The following supporting information can be downloaded at: Preprints.org.

Competing Interests: The authors of this publication (Jablonowski, Baker and Hooker) have no competing interests to declare outside of their affiliation with Children's Health Defense, an organization that advocates for vaccine safety.

References

1. Ip S, North T, Torabi F, Li Y, Abbasizanjani H, Akbari A, et al. Cohort study of cardiovascular safety of different COVID-19 vaccination doses among 46 million adults in England. Nat Comm 2024. 15:6085.
2. Whitely W, Ip S, Cooper J, Bolton T, Keene S, Walker V, et al. Association of COVID-19 vaccines ChAdOx1 and BNT162b2 with major venous, arterial, or thrombocytopenic events: A population-based cohort study of 46 million adults in England. Plos Med 2022. 19(2):e1003926.
3. Horne E, Hulme W, Keogh R, Palmer T, Williamson E, Parker E, et al. Waning effectiveness of BNT162b2 and ChAdOx1 covid-19 vaccines over six months since second dose: OpenSAFELY cohort study using linked electronic health records. BMJ 2022. 377:e071249.
4. Parker E, Horne E, Hulme W, Tazare J, Zheng B, Carr E, et al. Comparative effectiveness of two- and three-dose COVID-19 vaccination schedules involving AZD1222 and BNT162b2 in people with kidney disease: a linked OpenSAFELY and UK Renal Registry cohort study. The Lancet Regional Health – Europe 2023. 30:100636.
5. Hulme W, Williamson E, Horne E, Green A, McDonald H, Walker A, et al. Challenges in Estimating the Effectiveness of COVID-19 Vaccination Using Observational Data. Ann Intern Med. 2023. doi:10.7326/M21-4269.
6. COVID-19 advice for the public: Getting vaccinated https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice
7. CDC Website: Safety of COVID-19 Vaccines Updated Mar. 7, 2023 https://archive.cdc.gov/www_cdc_gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html