Utilization of health care services before and after media attention about fatal side effects of the AstraZeneca vaccine

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Abstract

Objective: To assess whether utilization of health care services for newly vaccinated health care workers changed after media attention about fatal side effects of the AstraZeneca vaccine on March 11th, 2021, and whether changes differed by age, sex, or occupation.

Data sources: We utilized individual-level data on health care use, vaccination, employment, and demographics available in the Norwegian emergency preparedness register BeredtC19.

Study design: Using an event-study design with a matched comparison group and multiple time periods, we compared the change in primary and inpatient specialist care use for vaccinated health care workers from 14 days before to 14 days after the information shock on March 11th, 2021.

Data collection: Not applicable.

Principal findings: Primary health care use rose sharply by 66% (95%CI 60.7 to 71.3) the week following March 11th for those vaccinated with AstraZeneca (n = 87,632), compared with no rise for the unvaccinated comparison group (n = 175,264). Utilization of inpatient care also rose by 20% (95%CI -3.7 to 43.7) in week one and 61% (95%CI 27.1 to 94.9) in week two after March 11th. The sharpest increase in primary health care use was found for women aged 18-44 (83%, 95%CI 76.6 to 89.5) and for cleaners working in the health care sector (103 %, 95%CI 36.1 to 166.9).

Conclusions: Health care use was highly affected by the media reports of a few fatal or severe side effects of the AstraZeneca vaccine. Our results suggest that the reports did not only lead vaccinated individuals to contact primary health care more, but also that physicians referred and treated more cases to specialist care because of the new information.

Key words: COVID-19, vaccine, health care seeking behavior, drug side effects, health communication

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1 Introduction

Norwegian health authorities suspended the use of the Oxford-AstraZeneca (Vaxevria, hereafter referred to as AstraZeneca) vaccine on March 11th, 2021, after reports of fatal side effects following vaccination.[1] By then, there were reports of 30 severe and potentially fatal thromboembolic events among the five million individuals in the European Economic Area who had received the vaccine, resulting in eight other countries also pausing the administration of AstraZeneca.[2]

In Norway, AstraZeneca was administered to 121,820 health care workers (HCW, including cleaners in the health care sector) under the age of 65 from February 11th to March 11th, 2021. Multiple cases of thromboembolism and four deaths among vaccinated HCW, predominately young women, were discovered after March 11th, which eventually resulted in the permanent removal of AstraZeneca from the Norwegian COVID-19 vaccination program on May 10th, 2021.[3] Along the fatal events, recent survey studies based on self-reporting, conducted after March 11th, have also reported minor bleeding episodes such as skin and nose bleedings following vaccination with AstraZeneca.[4]

The unanticipated reporting of serious side effects on March 11th provided an opportunity to better understand how an *information shock* (high media attention and official encouragements to seek medical attention if experiencing a range of symptoms) affects the utilization of health care services. More specifically, it allowed us to study how health-literate HCW responded to reports of a very low-probability fatal outcome.

Assessing how vaccinated individuals react to sudden media coverage of vaccine-related side effects is important to ensure efficient health care services in similar situations in the future. To this end, we aimed to compare the utilization of health care services following AstraZeneca vaccination before and after the information shock on March 11th. Furthermore,

we explored variation in responses to the information shock across age, sex, and health care professions.

2 Methods

Using a pre-post study design with a comparison group and multiple time periods, we utilized data from the BEREDT C19 registry, which is a newly developed emergency preparedness register aiming to provide rapid knowledge about the COVID-19 pandemic, including how measures enforced to limit the spread of the virus affect the population's health, use of health care services and health-related behaviors.[5] From within BEREDT C19, we utilized nation-wide individual-level data originating from the following registries: The National Population Register; Norway Control and Payment of Health Reimbursement (KPR, visits to general practitioners and emergency wards); Norwegian Patient register (NPR, outpatient and inpatient hospital care); the Employer- and Employee Register (all employment contracts, used to define sample of HCW); and the Norwegian Immunization Registry (SYSVAK, vaccination date and vaccine manufacturer). Individuals could be linked across data sources and over time using an encrypted version of the unique personal identification number provided every resident of Norway at birth or upon first immigration. Additionally, we included data from the media monitoring company Retriever on the daily number of published media reports in Norway that included the words “AstraZeneca” and “side effect”.

2.1 Study sample

Our study population included all Norwegian residents, aged 18-67, who had an employment contract as HCW in the first week of January 2021, and who had received or not received the

AstraZeneca vaccine by March 11th, 2021. Persons who died or emigrated after they were vaccinated were censored from the date of death or emigration. We excluded persons who had received a different COVID-19 vaccine than AstraZeneca by March 11th, 2021.

HCW were defined as a priority group for SARS-CoV-2 vaccination by the Norwegian authorities from January 4th, 2021. We identified HCW following Molvik et al. by using the ISCO-08 4-digit occupation codes, in combination with standard industrial classifications from the Employer- and Employee-register (see appendix of Molvik et al. for the exact definition) [6]. We compared the healthcare use of two groups before and after March 11th, 2021:

1. HCW vaccinated with AstraZeneca up to March 11th, 2021 (the first HCW received it mid-February).
2. Comparison group of propensity-score matched unvaccinated HCW, where we matched each HCW in our treatment group to two (nearest-neighbor) HCWs who had not received any vaccine by March 11th, 2021, based on their estimated likelihood of being vaccinated with AstraZeneca via a logistic regression model (see online appendix for details). The unvaccinated HCWs in the comparison group were assigned the (hypothetical) vaccination date of its vaccinated match.

2.2 Outcomes

We studied all consultations with primary and specialist care combined, as well as separately:

1. Primary care included consultations at the general practitioner and emergency ward as well as outpatient hospital contacts.
2. Specialist care included inpatient hospital contacts (overnight hospitalization).

We focused on daily individual health care use in the first 14 days after vaccination, because the rare conditions that prompted the pausing of AstraZeneca were reported to have occurred shortly after vaccination.[7, 8] Thus, the outcomes for the workers in our sample with the latest possible vaccination date, March 11th, were observed from March 11th until March 25th. Analogously, the outcomes for the workers vaccinated on March 1st, were observed until March 15th; for the workers vaccinated on March 5th, until March 19th and so forth. This enabled us to study any rapid changes in health care use around the information shock at March 11th for all the workers in the sample.

2.3 Statistical analyses

To examine the impact of the information shock on health care use, we included all HCWs who were vaccinated with AstraZeneca from February 25th through March 11th, as well as the HCWs in the comparison group matched to the same vaccination dates. For these HCWs, we first calculated and plotted the daily rates of health care use (primary and specialist care) from February 25th to March 25th, i.e. from two weeks before to two weeks after the information shock on March 11th. We did this separately for the vaccinated HCWs and the HCWs in the comparison group. Second, we studied the impact of the information shock on primary care use and specialist care use in separate analyses using an event study design operationalized as a generalized difference-in-differences (DiD) approach with separate estimates for each week (or day, see below) after March 11th.[9] This allowed us to assess the change in health care use each week from before to after March 11th for those who had received the AstraZeneca vaccine relative to those in the comparison group. With this method

we could effectively adjust for the substantial calendar week-day variation in health care utilization.

DiD analyses evaluate the effect of an event by comparing the change in the outcome for the affected group before and after the event, to the change over the same time span in a group not affected by the event.[9-12] In this study, we compared the rate of health care use in two 7-days periods before and two after March 11th for the HCWs who were vaccinated (difference 1), to the difference in the rate of health care use in the two 7-days period before and two after the March 11th for the HCWs in the comparison group (difference 2). The DiD estimate is the difference between these two differences, estimated using linear probability models with robust standard errors and presented as a difference in percentage points. If there is no increase in health care use from before to after March 11th, the DiD estimate would be zero.

We thus generalized the traditional DiD method by extending from one period before and one after the event to two separate estimates for each 7-day period after March 11th, comparing to the health care use in the 14-day period before March 11th.[9-14] In addition to this model with separate estimates for the first and second week after March 11th, we also estimated more detailed models with separate estimates for each calendar day before and after March 11th, comparing to the health care use on March 11th. The results from such models with estimates for each calendar day were presented in plots. In addition to the presentation of results as absolute differences in percentage points, we also presented relative differences (i.e. in percent) by dividing the absolute estimate for each of the post periods by the health care use rate of the comparison group in the reference pre period (multiplied by 100).The categorical outcome variable (primary and specialist care use) was set to one if the HCW was registered using health care at least once during the given day (zero otherwise). Our outcome variables were either measured jointly as daily health care use during the first and second week after

March 11th or by calendar day. We adjusted the models for age and sex. To handle that a HCW can be present several times in the data, robust standard errors were clustered on the individual level.

To investigate group differences, we split our main sample into four mutually exclusive groups; women aged 18-44, women aged 45-67, men aged 18-44 and men aged 45-67 and ran the same regressions as above on these groups. We also conducted the same analysis on HCWs in five mutually exclusive occupational groups (physicians, health professionals, health associate professionals, personal care workers, and cleaners) based on the first digit in the ISCO-08 classification (except for physicians).[15] All analyses were run in R v.3.6.2.

2.4 Ethics

The establishment of an emergency preparedness register forms part of the legally mandated responsibilities of The Norwegian Institute of Public Health (NIPH) during epidemics. Institutional board review was conducted, and the Ethics Committee of South-East Norway confirmed (June 4th, 2020, #153204) that external ethical board review was not required.

3 Results

Among 363,750 persons registered with an employment contract as HCW in week 1, 2021, we studied 87,632 persons who had received the AstraZeneca vaccine in the time period from February 19th to March 11th and their 175,264 unvaccinated matches (Table 1). As intended, there were only small differences on variables predicting AstraZeneca vaccination between those vaccinated and the unvaccinated comparison group. Both groups consisted of a

majority of younger, Norwegian-born women working as personal care assistants or in academic professions (Table 1).

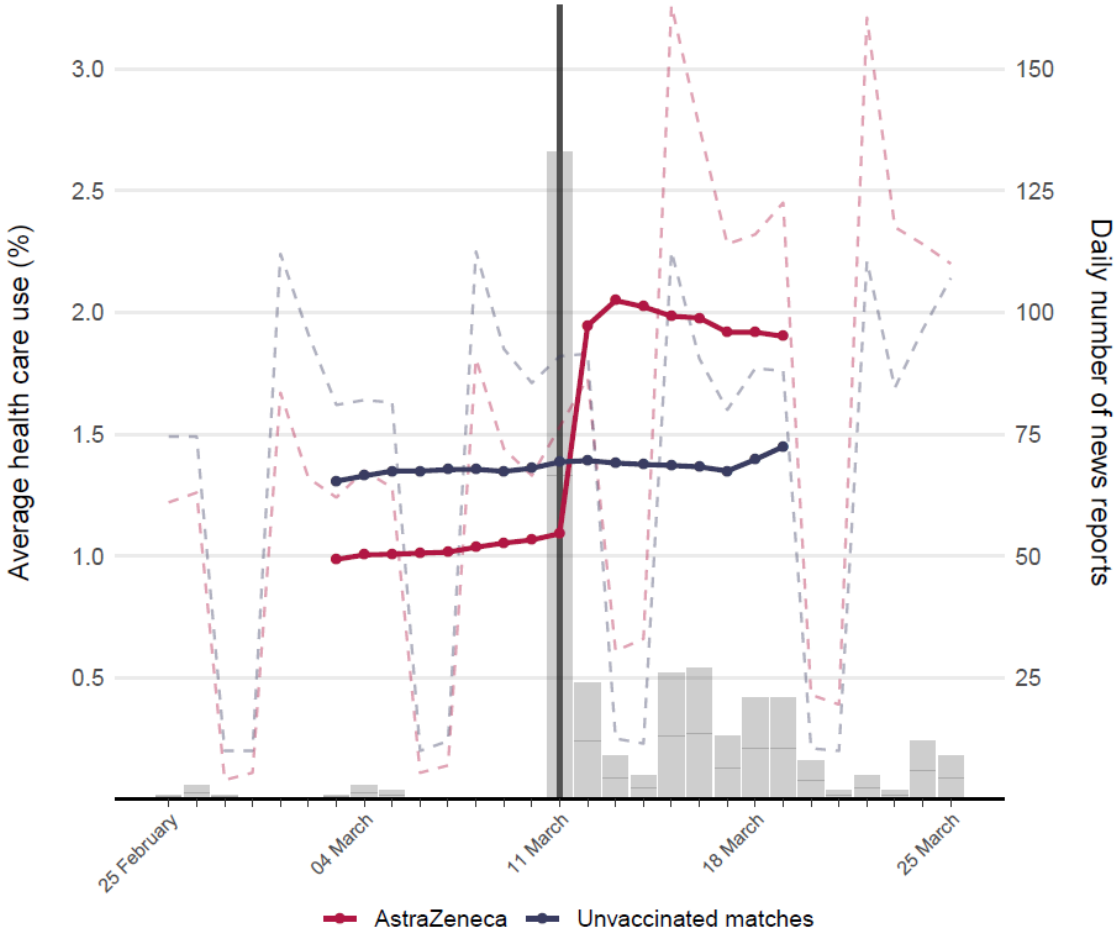
The mean health care utilization rate in the period prior to the information shock was 1.1 % for those vaccinated with AstraZeneca, while the corresponding numbers for March 12th-18th and March 19th-25th were 1.9 and 1.9 % (Table 1). The information shock started on March 11th, with more than 125 news articles covering AstraZeneca-related side effects (Fig. 1). The following day, we observed a sharp increase in health care use for those vaccinated with AstraZeneca (Fig. 1). While the comparison group had slightly higher average health care use prior to March 11th, the comparison group had no increase in health care utilization after March 11th (Table 1, Fig. 1), which indicates that the increase for individuals vaccinated with AstraZeneca was not due to any other acute events occurring around the same date.

Table 1. Descriptive statistics

	AstraZeneca	**Unvaccinated matches**
N	87,632	175,264
Person-days	1,840,121	3,678,316
Mean (SD) age	42.3 (13)	42.2 (13)
Women, N (%)	72,750 (83)	148,139 (84.5)
Norwegian born, N (%)	72,020 (82.2)	138,595 (79.1)
Occupational groups		
Physicians, N (%)	4,414 (5.0)	8,974 (5.1)
Health professionals, N (%)	27,693 (31.6)	53,443 (30.5)
Health associate professionals, N (%)	4,577 (5.2)	8,188 (4.7)
Personal care workers, N (%)	50,092 (57.2)	102,954 (58.7)
Cleaners, N (%)	856 (1.0)	1,705 (1.0)
Average daily health-care use		
Two weeks prior to March 11th (%)		
All health care	1.06	1.37
Primary care	1.03	1.26
Inpatient specialist care	0.03	0.12
First week after March 11th (%)		
All health care	1.90	1.36
Primary care	1.85	1.24
Inpatient specialist care	0.07	0.14
Second week after March 11th (%)		
All health care	1.85	1.33
Primary care	1.79	1.23
Inpatient specialist care	0.09	0.11

SD: Standard deviation

Figure 1. Average daily health care utilization and the information shock on March 11th



Notes: Daily (dashed lines) and 7-day rolling average of (solid lines) daily health care use after vaccination. For days prior to and including March 11th the 7-days rolling average equals the mean of the rate the given day and the six preceding days, while it for days after Match 11th equals the mean of the rate the given day and the six subsequent days. Bars indicate daily number of news reports mentioning “AstraZeneca” and “side effect”.

3.1 Impact of the information shock on health care use after AstraZeneca vaccination

Primary health care use for those recently vaccinated with AstraZeneca increased by 0.83 percentage points in the first week after March 11th when compared to those unvaccinated. This corresponded to a 66 % increase compared to levels prior to March 11th (Table 2). A similar increase of 0.78 percentage points (62 %) was observed in the second week after March 11th (Table 2). Estimates of the daily difference between use of primary care for those vaccinated vs. those not vaccinated rose from the first day after March 11th, peaking after around 4-5 days (Fig. 2). We also observed a 0.2 percentage point (20 %) increase in inpatient specialist care visits the first week, and a 0.07 percentage point (61 %) increase in the second week after March 11th (Table 2, Fig. 2).

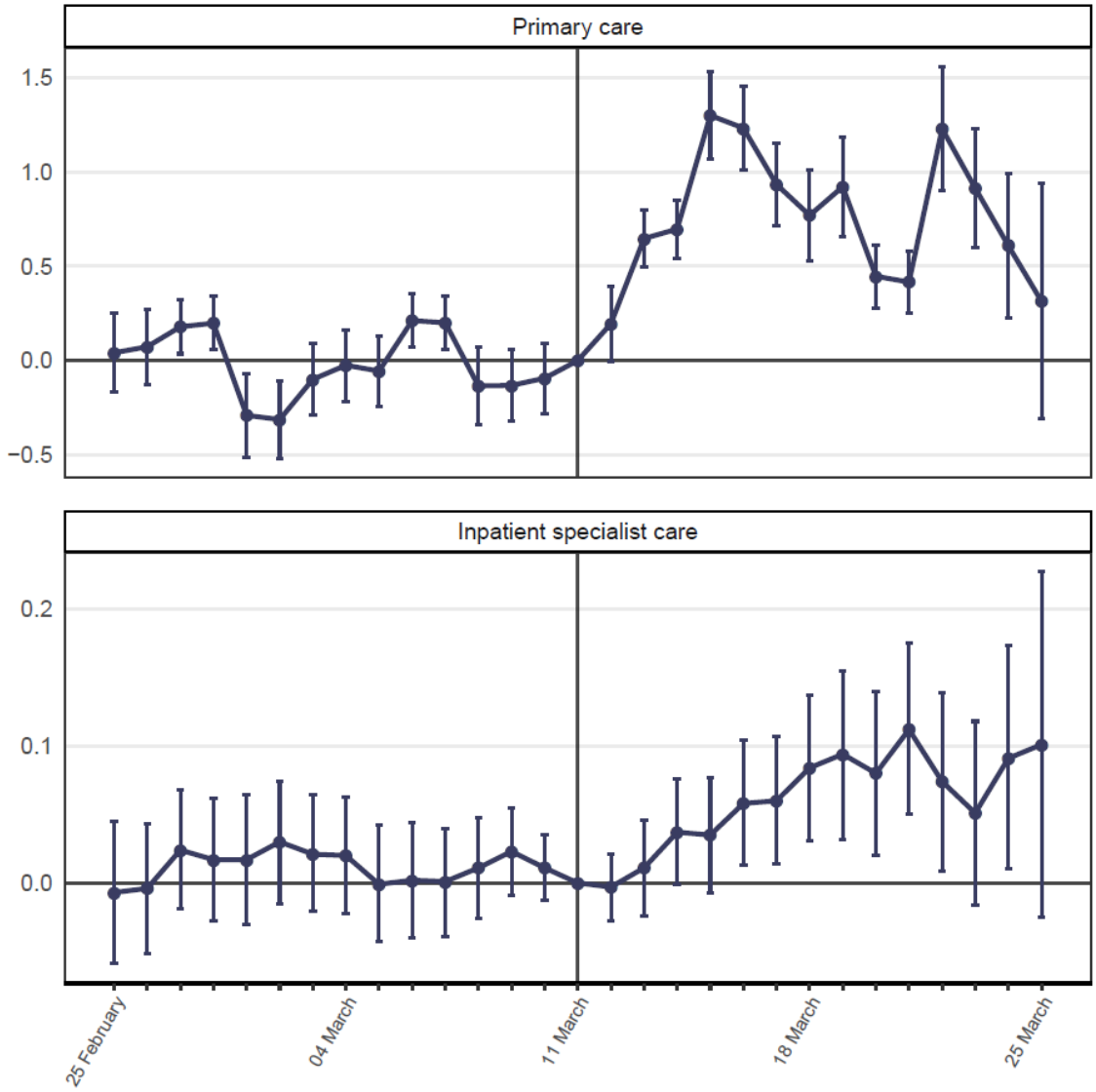
Table 2. Impact of the information shock on health care use

	Primary Care				**Inpatient specialist care**			
Period after March 11th	β	St. err.	% Relative diff (β)	Relative diff (St. err.)	β	St. err.	% Relative diff (β)	Relative diff (St. err.)
First week	0.83***	0.035	66	2.7	0.02*	0.015	20	12.1
Second week	0.78***	0.053	62	4.2	0.07***	0.021	61	17.3

Notes: Differences-in-differences estimates (in percentage points) for the change in health care use for different health care services before and after March 11th for individuals vaccinated the past 14 days. In primary care reimbursement codes 2ad, 2ak, 2ae is used to identify consultations at general practitioner or emergency ward. All models control for age and sex. Standard errors (St. err.) are clustered on individuals. The pre-period (health care utilization after vaccination the two weeks prior to March 11th) is reference period in all regressions. In addition to the presentation of results as absolute differences in percentage points, we also presented relative differences (i.e. in percent) by dividing the absolute estimate (and corresponding standard error) for each of the post periods by the health care use rate of the comparison group in the pre period (and multiplying with 100).

Significance levels: * <0.1; ** <0.05; *** <0.01

Figure 2. Impact of the information shock on utilization of primary and inpatient care



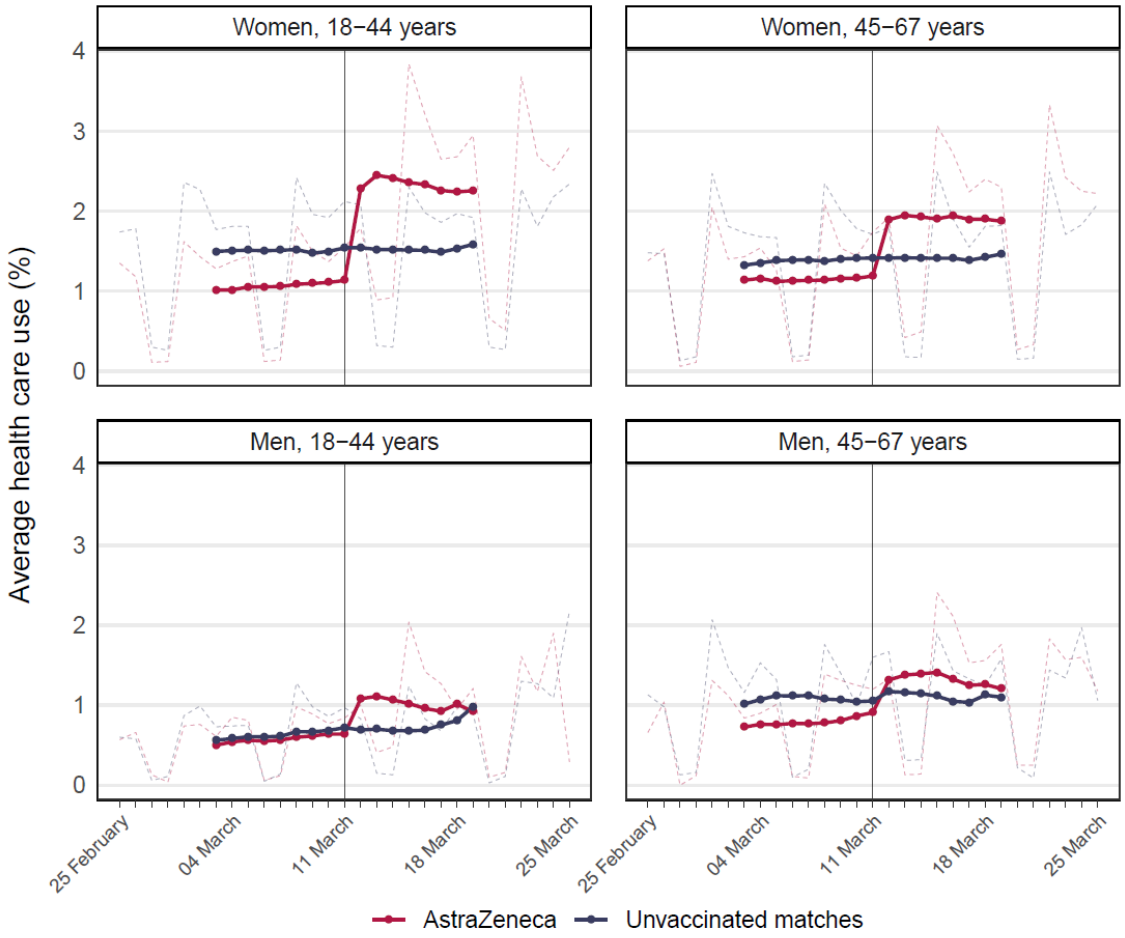
Notes: Estimated difference in health care use (95% CI) for those vaccinated with AstraZeneca compared to the unvaccinated comparison group, prior to and after the information shock on March 11th. Estimates are adjusted for age and sex. Standard errors are clustered on individual.

3.2 Information shock and health care use by age and sex

Health care use, both before and after March 11th, was found to differ by age and sex for those vaccinated with AstraZeneca (Fig. 3, Table A-A1). Prior to March 11th, women had higher utilization rates of primary and specialist care than men (Fig. 3). Compared to utilization rates prior to March 11th, primary health care use among women aged 18-44 increased with 1.14 percentage points (82 %) during the first week after March 11th and by 1.13 percentage points (82 %) during the second week (Table A-A1). For women aged 45-67, the corresponding increase was 0.65 percentage points (49 %) in the first week and 0.62 percentage points (47 %) in the second week (Table A-A1).

A similar increase in use of primary care of 0.44 percentage points (71 %) was found for men aged 18-44 the first week after March 11th, and 0.2 percentage point (31 %) in the second week, compared to the pre-period (Table A-A1). For men aged 45-67, the corresponding increases were 0.43 percentage points (44 %) and 0.23 percentage points (24 %) (Table A-A1). However, the overall average use of health care after March 11th was lower among men than women in both age groups (Fig. 3).

Figure 3. Average health care utilization after the information shock by age and gender

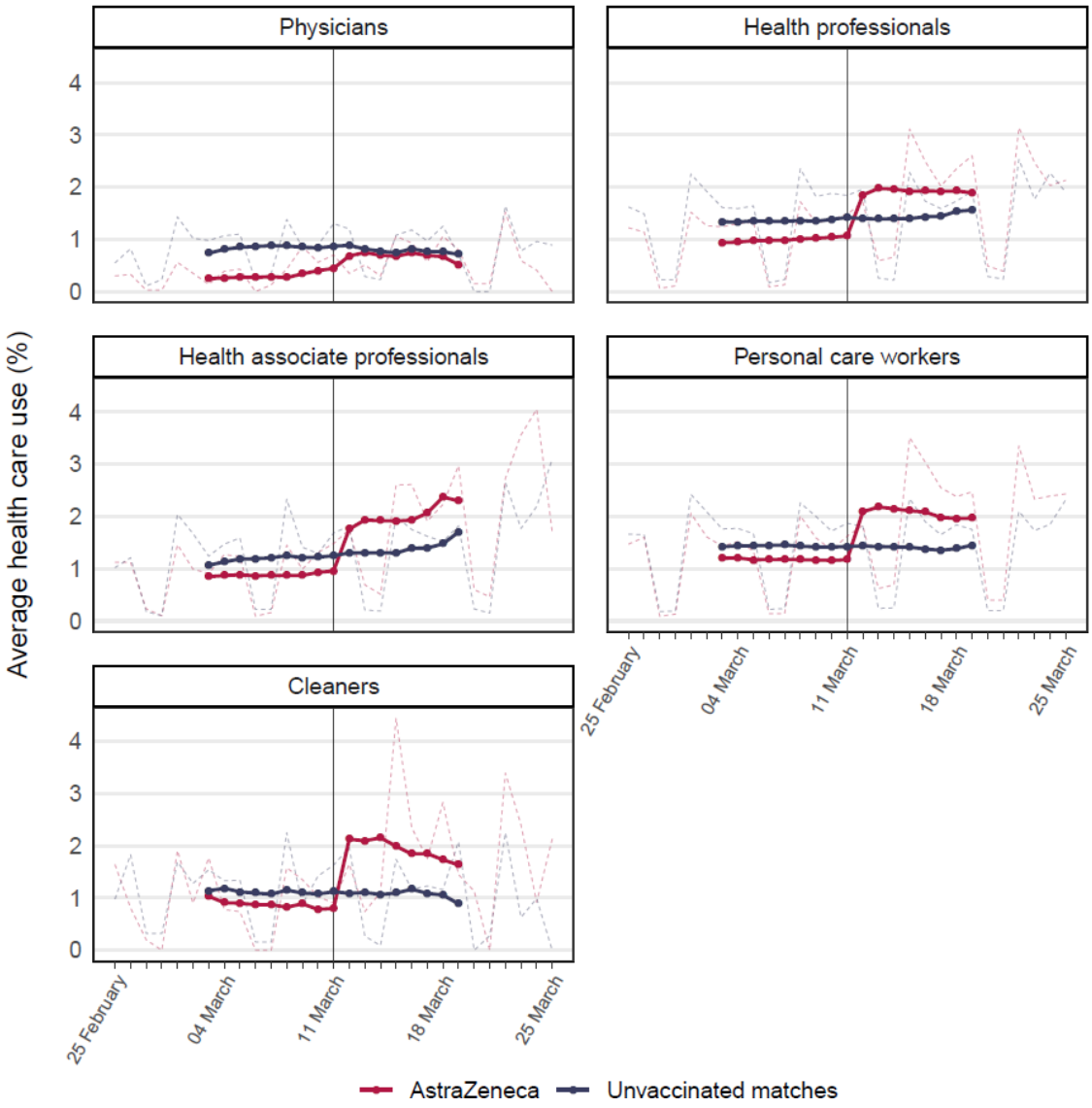


Notes: Daily (dashed lines) and 7-day rolling average of (solid lines) daily health care use before and after the pausing of AstraZeneca. For days prior to and including March 11th, the 7-days rolling average equals the mean of the rate for the given day and the six preceding days, while it for days after March 11th equals the mean of the rate for the given day and the six subsequent days.

3.3 Information shock and health care use by occupation

The impact of the information shock on health care use was also found to differ across HCW occupational groups (Fig. 4, Table A-A2). While primary health care use for physicians increases by 0.21 percentage points (33 %) in the first week after March 11th, the corresponding increase for HCWs working as cleaners were 1.03 percentage points (103 %) (Table A-A2). Health professionals, health associate professionals and personal care workers had similar increases in primary care the first week after March 11th, ranging from 64 % to 69 %. The results for inpatient specialist care were more inconsistent, however cleaners again had the greatest increase of 0.15 percentage points (123 %) (Table A-A2).

Figure 4. Average health care utilization after the information shock by occupational groups



Notes: Daily (dashed lines) and 7-day rolling average of (solid lines) daily health care use before and after March 11th for occupations with different work tasks, based on the first digit in ISCO-08 classification (except for physicians). For days prior to and including March 11th, the 7-days rolling average equals the mean of the rate the given day and the six preceding days, while it for days after March 11th equals the mean of the rate the given day and the six subsequent days.

4 Discussion

Our study of 87,632 health care workers (HCWs) who had recently received the AstraZeneca vaccine shows that the use of primary care increased by 66 % and inpatient specialist care increased by 20 % during the first week after the information shock of potentially fatal side-effects on March 11th, 2021 (Table 2). The largest increases in primary consultations were found for young women and cleaners working in the health care sector, while older men and physicians were found to be the least affected by the information shock (Table A-A1, Table A-A2). Additional analyses (not reported) show that the increases in health care use from the information shock on March 11th by far exceed the minor or nonexistent increases in health care use for HCWs in the days after vaccination, as evaluated solely in the weeks before the information shock (Table A-B1, see Appendix for details).

This study both confirms and sheds new and important light on previous studies of the communication of vaccine-related side effects. A randomized experimental study on 292 individuals in Canada found that the individuals who were presented with advantages of influenza vaccination reported fewer systemic side effects than the individuals who were communicated negatively framed vaccine-related side effects.[16] Similarly, Trogstad et al. [4] also found that 5,132 AstraZeneca vaccinated individuals in Norway were more likely to report skin bleeding in surveys than 3,416 individuals vaccinated with mRNA-vaccines, and the authors discuss that the difference may be due to awareness bias after March 11th when the fatal side effects of AstraZeneca vaccination were communicated. In line with previous studies, we demonstrated a major increase in health care use immediately following negatively framed communication of side effects (Table 2). Hence, our findings may indicate that the information shock introduced vaccine-related awareness and that future studies of side effects and health-seeking behavior need to take negatively framed media coverage into account – and this is likely true for any type of vaccine.

To our knowledge, this study is the first to explore changes in utilization of primary and specialist care for vaccinated individuals after such an information shock concerning vaccine-related side effects. For health authorities, our findings imply that both primary and specialist health care services may need to be upscaled in situations of high media attention on possible severe side effects, even though the risk of experiencing the severe side effect is extremely low. The excess thrombolytic events after AstraZeneca vaccination were estimated to be 11 per 100 000 [17], and our results thus add to an intriguing literature on humans' responsiveness to negative events of very low probabilities.[18] The largest increase in primary care use was found among young women which supports existing theory arguing that women are more risk averse than men.[19] The second largest increase in primary care consultations was found among young men, while the third largest increase was found among older women (Table A-A1). The perceived risk may have been high for all three groups as the public was informed that a majority of the most serious cases of suspected vaccine-related side effects occurred among young individuals, mostly women.

Furthermore, our results for the first week after March 11th showed a larger and more consistent increase in primary care consultations than hospital admissions (Table 2, Fig. 2), which may be explained by the former acting as a gatekeeper to specialist care. However, the following week, we observed an increase in overnight hospital stays in all groups, except young men (Table A-A1). While this may indicate that a larger share of those vaccinated required specialist care in this period, it may also indicate that primary care physicians' threshold for referring vaccinated patients to specialist care was lowered due to the information shock, even though the vaccinated physicians' own health care use was little affected (Figure 4, Table A-A2).

Important strengths of our study are the prospective design and use of nation-wide registry data that included daily information on health care use for all HCWs regardless of vaccination status. However, there are also, certain limitations to our analysis. First, we do not attempt to shed any light on whether the increase in health care use led to better health, and to what cost. To assess this, further research should strive to quantify the health gain and costs of increases in health care utilization under such information shocks. Second, our data only contains registered consultations and hospital admissions. This may have led to an underestimation of the results as our study population consisted solely of HCWs who could potentially have received second opinions from colleagues, particularly in periods of greater pressure on the health care services. In addition, due to our specific study population, the external validity of our results may not go beyond HCW. Accordingly, our stratified analysis showed different impacts of the information shock for different occupations, with occupations not requiring formal health education, such as cleaners, having a larger increase in health care use than other occupations working in the health care sector. This may imply that the individual level of health literacy could have been a mediating factor when responding to the information shock, and hence that our estimates of the impact of the information shock again may be underestimated compared to the general population.

The observed increase in health care use is driven, at least partly, by behavioral responses to information shocks, which implies that general utilization data may be more suitable as an indicator of an individual's overall health rather than somatic health. In these situations, only hard outcomes, eventually mainly death, can be trusted to reflect relevant information about the latent health of the patient. In the current debate about side effects of AstraZeneca, it is thus interesting that a study based on utilization data found an increase in milder diagnoses, but a *decrease* in mortality.[17] As our results have shown, using these utilization data for real-time monitoring and evaluation of previously unknown vaccine side effects may be biased

without carefully considering information shocks and awareness bias on individual health-seeking behavior.

By studying HCWs who had recently been vaccinated with the AstraZeneca vaccine, we have shown that the unexpected reports of fatal vaccine-related side effects on March 11th, 2021, led to a large increase in utilization of primary and specialist care. Our study sheds important light on how health authorities should be prepared to respond to future information shocks about negative events with low probabilities, like possible vaccine-related side effects. The large increase in health care use, especially in primary health care, for recently vaccinated individuals implies that health care services may need to be upscaled due to negatively framed media attention.

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