

# THE LANCET

## Digital Health

### Supplementary appendix

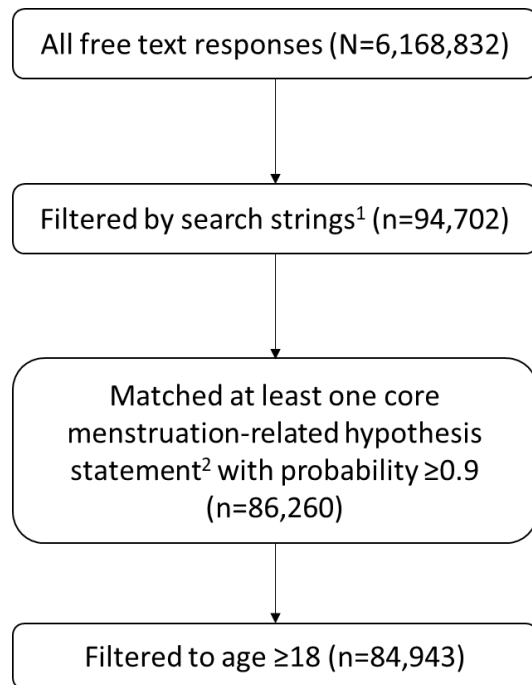
This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Wong KK, Heilig CM, Hause A, et al. Menstrual irregularities and vaginal bleeding after COVID-19 vaccination reported to v-safe active surveillance, USA in December, 2020–January, 2022: an observational cohort study. *Lancet Digit Health* 2022; published online Aug 9. [https://doi.org/10.1016/S2589-7500\(22\)00125-X](https://doi.org/10.1016/S2589-7500(22)00125-X).

## Supplementary material

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### Supplemental figure 1: Inclusion criteria



<sup>1</sup> Matches pattern 1 or both patterns 2 and 3.

Pattern 1: r'menses|menst|spotting|period(s\b\b)\bcycle\bmiscarr|menorrh|metrorrh'

Pattern 2: r'bleed|blood'

Pattern 3: r'menop\bpreg\buter|hyster|placent\bvag|breakthrough|(break through)|endomet\bgest|term\b|trimester'

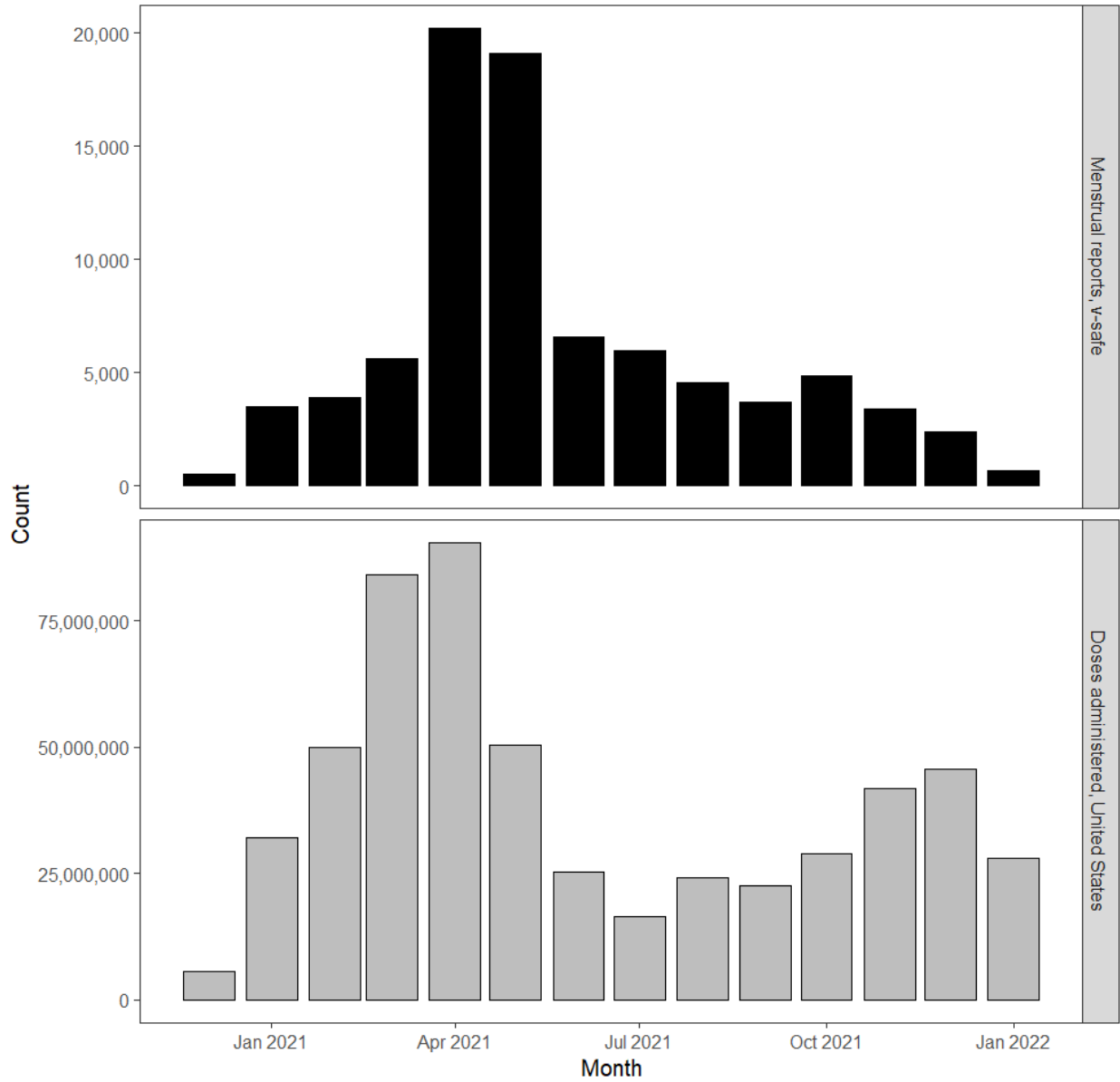
<sup>2</sup> Core menstruation-related hypothesis statements:

- 'This mentions menstruation'
- 'This mentions spotting'
- 'This mentions vaginal bleeding'
- 'This mentions uterine bleeding'
- 'This specifically mentions missing or skipping a period'

**Supplemental table 1: Criteria for classifying responses into themes**

| <b>Theme</b>                | <b>Criteria</b>  |
|-----------------------------|--|
| <b>Timing</b>               | Entailment probability $\geq 0.9$ with any of the following statements: <ul style="list-style-type: none"> <li>• ‘This mentions a period that came early’,</li> <li>• ‘This mentions a period that came late’,</li> <li>• ‘This mentions spotting’,</li> <li>• ‘This mentions an irregular period specifically’,</li> <li>• ‘This specifically mentions missing or skipping a period’</li> </ul> |
| <b>Severity</b>             | Entailment probability $\geq 0.9$ with any of the following statements: <ul style="list-style-type: none"> <li>• ‘This mentions a heavy menstrual period’,</li> <li>• ‘This mentions a painful menstrual period’,</li> <li>• ‘This mentions prolonged bleeding specifically’</li> </ul>  |
| <b>Menopausal</b>           | Response contains “menop” or respondent is aged $\geq 59$ years  |
| <b>Resumption of menses</b> | Entailment probability $\geq 0.9$ with the following statement: <ul style="list-style-type: none"> <li>• ‘This mentions not having a period for years’</li> </ul>  |
| <b>Other</b>                | Does not meet criteria for any of the four other themes  |

**Supplemental figure 2: Number of v-safe reports related to menstrual irregularities and vaginal bleeding and number of COVID-19 vaccine doses administered, United States, by month**



**Supplemental table 2: Evaluation of classification performance against manually classified samples**

| Classification objective   | Sample data  | TP  | FP | TN   | FN | Sensitivity (95% CI) | Specificity (95% CI) | F1 (95% CI)          |
|--|--|-----|----|------|----|----------------------|----------------------|----------------------|
| Identify menstruation-related responses from all responses using search strings              | 2000 random responses                                  | 17  | 1  | 1982 | 0  | 1 (0.771, 1)         | 0.999 (0.997, 1)     | 0.971 (0.778, 1.0)   |
| Identify core menstruation-related responses using ZSL from search string-filtered responses | 1000 random responses matching search strings          | 912 | 1  | 71   | 16 | 0.983 (0.972, 0.990) | 0.986 (0.915, 0.999) | 0.991 (0.985, 0.994) |
| Identify timing-related responses using ZSL  | 928 random menstruation-related responses <sup>a</sup> | 690 | 83 | 125  | 30 | 0.958 (0.940, 0.971) | 0.601 (0.531, 0.667) | 0.924 (0.908, 0.937) |
| Identify severity-related responses using ZSL  | 928 random menstruation-related responses <sup>a</sup> | 510 | 88 | 281  | 49 | 0.912 (0.885, 0.934) | 0.762 (0.714, 0.803) | 0.882 (0.859, 0.899) |
| Identify responses related to resumption of menses using ZSL                                 | 928 random menstruation-related responses <sup>a</sup> | 17  | 6  | 898  | 7  | 0.708 (0.488, 0.866) | 0.993 (0.985, 0.997) | 0.723 (0.538, 0.847) |
| Identify “other” menstruation-related responses <sup>b</sup>                                 | 928 random menstruation-related responses <sup>a</sup> | 15  | 25 | 873  | 15 | 0.5 (0.332, 0.668)   | 0.972 (0.959, 0.982) | 0.429 (0.275, 0.581) |

ZSL: Zero-shot learning; TP: true positives; TN: true negatives; FP: false positives; FN: false negatives; CI: confidence interval

<sup>a</sup> Responses matching search strings deemed menstruation-related after manual review (1000 excluding 72 unrelated responses)

<sup>b</sup> Responses were categorized as “other” if they did not meet criteria for timing, severity, or resumption of menses using zero-shot classification, or for menopausal bleeding (age- and search string-based criteria). This was compared with manual classification into an “other” category.

**Supplemental table 3: V-safe female respondents aged  $\geq 18$  years by age group and vaccine received**

|                      | <b>18–49 years<br/>n=3,095,361</b> | <b>50–64 years<br/>n=1,698,520</b> | <b>65–74 years<br/>n=887,481</b> | <b>75–84 years<br/>n=249,567</b> | <b>85+ years<br/>n=44,434</b> |
|----------------------|------------------------------------|------------------------------------|----------------------------------|----------------------------------|-------------------------------|
| <b>BNT162b2</b>      | 1622348 (52.4)                     | 831395 (48.9)                      | 391331 (44.1)                    | 110824 (44.4)                    | 19540 (44)                    |
| <b>mRNA-1273</b>     | 1352143 (43.7)                     | 796965 (46.9)                      | 483701 (54.5)                    | 136861 (54.8)                    | 24344 (54.8)                  |
| <b>Ad26.COV2.S</b>   | 166818 (5.4)                       | 94905 (5.6)                        | 20054 (2.3)                      | 3241 (1.3)                       | 757 (1.7)                     |
| <b>Other/unknown</b> | 820 (<0.1)                         | 399 (<0.1)                         | 313 (<0.1)                       | 118 (<0.1)                       | 12 (<0.1)                     |

Data are n (%).