**Virus Monitoring in Denmark: a community based self-sampling system to surveil respiratory viruses and associated symptoms**

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**Abstract**

Objectives:  
This study presents findings captured in the first 1.5 years of the Virus Monitoring in Denmark (VMD) surveillance system. It describes trends in respiratory viruses, related symptoms, and participant demographics and behaviors.

Methods:  
VMD used self-swabbing and self-reported symptoms to monitor respiratory viruses in the general population. Participants were recruited via digital invitations to a representative sample of the population or through workplaces. Symptomatic participants could self-swab and register their samples and report their symptoms via a dedicated smartphone web app.

Results:  
With 30,627 participants and 12,642 samples analyzed, VMD had broad demographic representation. SARS-CoV-2 was the most frequently detected virus, with positivity rates peaking at over 50% in late 2023. Participants commonly self-swabbed because of fever, cough, and rhinorrhea with influenza A linked to the highest median number of symptoms. Participants only provided samples after reaching a specific symptom threshold and participation affected health-seeking behaviors and work attendance of few individuals.

Conclusions:  
VMD continuously provided real-time insights into respiratory virus trends and symptomatology in the general non-healthcare seeking population. Its accessibility – available to anyone with a Danish identification number, a smartphone and an invitation – highlights its potential as a mass testing preparedness tool.

**Key words**

eHealth; symptom assessment; self-testing; pandemic preparedness; public health surveillance; respiratory tract infections;

**Introduction**

National surveillance systems are essential for tracking infectious disease spread and shaping public health policies, as seen during the COVID-19 pandemic. Conventional surveillance systems primarily capture data from individuals seeking medical care, leaving infections in the general population undetected1,2. Therefore, the COVID-19 response in Denmark included extensive population testing facilitated by dedicated testing centers and personnel3. As free public testing began to scale back in the months leading up to its cessation in March 2023, surveillance efforts reverted to conventional methods4, raising concerns about accurately assessing population-level incidence.

Continuous self-sampling systems can fill this gap without burdening healthcare resources. Population-based home-sampling systems were actively in place in some countries during the COVID-19 pandemic, e.g., the Office for National Statistics’ COVID-19 Infection Survey, which was considered the “gold standard” for SARS-CoV-2 surveillance during the pandemic in the United Kingdom (UK)5,6. In the summer of 2022, a pilot study was conducted in Denmark to monitor SARS-CoV-2 through home-based self-sampling7. While promising, it lacked sufficient power to detect changes in weekly trends. Additionally, it remained unclear what information it could provide beyond data captured by already existing surveillance systems.

To address these uncertainties, and to sustain continuous monitoring of SARS-CoV-2 after the discontinuation of free testing, Denmark launched Virus Monitoring in Denmark (VMD), a novel surveillance system which is based on self-swabbing. Participants in VMD register samples and report symptoms using a smartphone web application. VMD aims to complement existing systems, improve respiratory virus surveillance, detect community transmission, and enhance pandemic preparedness. This paper examines the first 1.5 years of VMD, focusing on its design, challenges, and findings on respiratory virus trends and symptoms within its cohort.

**Methods**

Virus Monitoring in Denmark (VMD) surveillance system

VMD comprises a national cohort, a smartphone web application, standardized test kits, two logistical setups, high-throughput laboratory analyses, and automated outputs which are included in the Danish national surveillance8.

**Study Design**: Recruitment started in week 24, 2023, in phases to build a cohort large enough for trend analysis. The study spans weeks 24, 2023, to 46, 2024, with analyses focused on data from weeks 40, 2023, to 46, 2024.

**Participants**: Individuals aged 5+ were eligible. Household members were encouraged to enroll as well. Participants swabbed when symptomatic. Adults performed combined oropharyngeal and mid-turbinate swabs9, and children under 15 swabbed the mid-turbinate with assistance if necessary.

**Recruitment and logistical setup:**

* The workplace cohort: Eight workplaces and educational institutions participated. Employees collected kits and returned samples to designated drop-off locations at their workplace. Samples were collected daily and transported to Statens Serum Institut (SSI). Participants also had the option to instead mail samples using prepaid envelopes provided.
* The Digital Post cohort: From week 37, 2023, a random sample of the Danish population aged 18 to 65 was invited to participate via Digital Post, a secure digital mailbox system. Invitations for individuals aged 65 and above began in week 13, 2024. By the end of the study period, approximately 230,000 individuals had been sent an invitation. Testing materials were sent to participants by mail after sign-up and following each sample registration. Participants sent samples to SSI in prepaid envelopes by regular mail.

**Web application:** a custom-designed smartphone web application (hereon referred to as web app) provided the following functions:

* Sign-up: Anyone with a Danish CPR number (a unique personal identification number in Denmark) can log in to the system. However, to enroll in VMD, individuals also had to scan a QR code provided in the invitation letter. The web app also enabled participants to withdraw from the study at any time.
* Sample registration: Participants registered a sample by scanning a unique 2D code on the bottom of the test tube, thereby linking the sample to the participant. Detailed instructions for sample collection and submission, including infographics and an instructional video, were also available on the web app.
* Symptom questionnaire: A brief questionnaire (see supplementary material S1) could be answered in relation to each sample registration, detailing the symptoms that prompted the sample collection. Participants could also report themselves as asymptomatic or skip the questionnaire entirely.
* Analysis result: Once the samples were analyzed, participants could see their results in the web app. Additionally, the web app provided a link to a website with a brief description of each virus and its associated symptoms.
* Follow-up symptom questionnaire: A follow-up questionnaire (see supplementary material S2), was introduced on the web app to evaluate symptom progression within the period 7 to 28 days after each sample registration.

**Evaluation questionnaire**: in November 2023, an evaluation questionnaire (see supplementary material S3) was distributed to all participants in VMD aged 18+ to assess participant adherence, influence of test results on health-seeking behaviors etc. A similar questionnaire was distributed in November 2024, in which they were further asked whether, in the event of a future pandemic, they would prefer being tested at a testing center or through the home-based approach utilized in VMD.

Laboratory analysis  
**RT-PCR panels:** The multiplex RT-PCR panel included influenzavirus A, influenzavirus B, RSV A/B, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from week 24, 2023 to week 7, 2024. The RT-PCR panel was expanded in week 8, 2024 to include: human adenovirus, human enterovirus, human rhinovirus, endemic human coronaviruses types HKU1, NL63, OC43, 229E, human parainfluenzavirus (PIV) types 1, 2, 3, 4, and human metapneumovirus (hMPV). Swabs were shipped dry without transport- or stabilizing media (FLOQswab, Meditec) and analyzed on the day of arrival or the following workday. Samples that did not arrive within 12 days of sample registration, or were damaged upon arrival, were given an inconclusive test result per default, and excluded from epidemiological analyses. Residual sample materials in 1xPBS were stored at -80°C at the National Danish Biobank.

**Reanalysis:** Samples from week 39, 2023 to week 7, 2024 were retrieved form the DNB, thawed and reanalyzed in autumn 2024 with the extended RT-PCR panel for the purpose of this study. Reanalysis results for influenzavirus A, influenzavirus B, RSV A/B, and SARS-CoV-2 were consistent with the original analyses, suggesting that the quality was comparable to that of samples tested immediately.

**RNA extraction:** On the day of analysis, 700 µL of 1xPBS (Phosphate Buffered Saline pH 7.2, Gibco) were added to the swabs. Samples were left agitating on a shaker for 10 minutes (700 rpm) to elute the sample material from the swab. Viral RNA was extracted using Beckman Coulter RNAdvance Viral Reagent Kit with 200 µL sample in 1xPBS as input and 50 µL nuclease-free water for elution on Beckman Coulter i7 automated workstations. Positive controls consisted of 200 µL Exact Diagnostics RP Positive Run Control (RPPOS, Bio-Rad). Sterile 1xPBS was used as negative control. Positive and negative controls were run in parallel with samples throughout RNA isolations and RT-PCR.

**RT-qPCR assays:** The primers and probes listed in the supplementary material (supplementary material S4) were synthesized by Biosearch Technologies, Denmark, except for the MGB-conjugated probes, which were synthesized by Eurogentec, Belgium, and the Zen- or TAO-conjugated probes, which were synthesized by Integrated DNA Technologies, Belgium. All oligoes were HPLC-purified.

The reaction mixture for the RT-qPCR:

* From week 24, 2023 to week 7, 2024: For each 20 µL reaction, 5 µL extracted RNA was added to a 15 µL reaction mix containing 10 µL Luna® Universal Probe One-step RT-qPCR reaction buffer (New England Biolabs Inc), 1.0 µL Luna® Warmstart RT Enzyme mix, primers and probes (100 µM, see volumes in Table S4), brought up to 20 µL with nuclease-free water. The PCR program consisted of reverse transcription at 55°C for 10 min., initial denaturation at 95°C for 3 min., followed by 45 cycles of denaturation and annealing/extension at 95°C for 15 sec., and 58°C for 30 sec., respectively.
* From week 8, 2024 to week 42, 2024 and reanalysis: consisted of five multiplex RT-PCR run in parallel using the same extracted viral RNA material.

Mastermixes A, C and E contained 10 µL Luna® Universal Probe One-step RT-qPCR reaction buffer, 1.0 µL Luna® WarmStart RT Enzyme mix, primers and probes (100 µM, volumes in Table S4), DNase/RNase-free water and 5 µL extracted RNA to a total volume of 20 µL. Cycling conditions: Reverse transcription at 55 °C for 10 min., initial denaturation at 95 °C for 1 min., followed by 45 cycles of denaturation and annealing/extension at 95 °C for 10 sec. and 60 °C at 30 sec., respectively.

Mastermix B and F contained 5 µL 4x Reliance One-step Multiplex Supermix, primers and probes (100 µM, volumes in Table S4), DNase/RNase-free water and 5 µL template to a total volume of 20 µL. Cycling conditions: Reverse transcription at 50 °C for 10 min., initial denaturation at 95 °C for 10 min., followed by 45 cycles of denaturation and annealing/extension at 95 °C for 10 sec. and 55 °C at 30 sec., respectively.

All RT-qPCR assays were performed in a calibrated Bio-Rad CFX 96 OPUS PCR Real-Time PCR instrument. The raw data was analyzed with the Bio-Rad CFX Maestro Software using a predefined threshold cut-off value of 100 RFU for all fluorophores. Recorded Ct values and end-RFU were calculated using Maestro version 5.2.8.222 and exported for further data analysis. A sample was considered positive based on the following criteria: Ct-values between 10-38 and end-RFU > 100 at Ct = 45. Samples that were neither positive for RNase-P (human internal control), nor virus, were excluded (n=23).

Due to cross reaction between the RT-qPCR assays for entero- and rhinovirus, samples positive for either or both were categorized as “rhino-/enterovirus” positive.

**Subtyping and Whole Genome Sequencing:** SARS-CoV-2 subtypes were determined by whole genome sequences generated by The Danish COVID-19 Genome Consortium (DCGC) from SARS-CoV-2 PCR-positive samples as described by Spiess & Gunalan et al.10.

**SARS-CoV-2 RNA concentration in wastewater:** data were sourced from a zip file that is published weekly on SSI's website: https://www.ssi.dk//sygdomme-beredskab-og-forskning/sygdomsovervaagning/c/covid-19---spildevandsovervaagning.

Statistical analyses

Data analysis was conducted using R version 4.4.011. Cohort demographics were compared to those of the general Danish population in October 2023, as reported by Statistics Denmark12.

Samples that tested positive for more than one virus were classified as "co-infection", regardless of the specific virus combination, and grouped separately from mono-infections.

Symptom comparisons across viruses used data from week 40, 2023, with symptom proportions reported unadjusted among all symptomatic individuals with the respective virus. Additionally, sex-adjusted and age-group-stratified risk ratios were calculated with log-binomial regression using the glm() function, with family set to binomial(link = ”logit”). To address the infrequent reporting of certain symptoms – especially for viruses detected less frequently and in stratified analyses – viruses detected fewer than 15 times were excluded from analyses to avoid convergence issues in the models. If convergence issues persisted, the individual symptoms were excluded.

Since VMD participants did not report about "sudden onset" of symptoms, a common part of the definition of influenza-like illness (ILI)13, an alternative definition was used in this study, referred to as aILI. This definition required at least one respiratory symptom (cough, sore throat, or shortness of breath) and at least one general symptom (fever, muscle-/joint pains, chills, headache, or excessive fatigue) for classification.

In analyses using the number of participants as the denominator, only data from the Digital Post cohort were included, as the actual size of the workplace cohort was uncertain. Additionally, in these analyses, the number of participants from the previous week was used, accounting for the estimated one-week delay in new Digital Post participants receiving their testing materials.

**Results**

**Description of cohort**

By the end of the study period, a total of 30,627 participants were enrolled in VMD with the majority (90%) being in the Digital Post cohort (Figure 1). Of the approximately 230,000 invitations sent via Digital Post, 27,480 participants enrolled in VMD corresponding to a participation rate of approximately 11.9%. 24,400 distinct households registered with a maximum household size of six participants. A stepwise increase in participants over time, coinciding with invitations rounds, was observed (Figure 1).

**Demographic representation**

VMD represented females more than males (table 1). The mean age was higher in the Digital Post cohort while it was lower in the workplace cohort compared to the general population. Children and young adults (ages 5-29) were mostly underrepresented, except for an overrepresentation of ages 20-29 in the workplace cohort. Ages 50-69, particularly in the Digital Post cohort, were overrepresented, while those 80+ were underrepresented. Among those who submitted samples, the mean age was slightly lower but still above the general population average (see supplementary material S5).

**Geographic representation**

Participant distribution across Denmark's five regions aligned with the general population. Within regions, participants were spread across municipalities (see supplementary material S6), with higher per capita participation in municipalities hosting workplaces from the workplace cohort.

**Sample collection**

The workplace cohort contributed 27% (n=3,401) of analyzed samples, averaging 0.88 samples per participant yearly with a 45% positivity rate, compared to the Digital Post cohort’s 0.34 samples and 56% positivity (Table 1). Workplace participants enrolled less than a day before their first sample, versus 47+ days for Digital Post. Median analysis time was shorter for the workplace cohort (4.02 vs. 5.14 days). Most samples were analyzed in week 49, 2023 (n=600), then later declined to 150-200 weekly. 6.88% of registered samples (n=934) were not received for analysis, with ages 20-29 most likely to have missing samples (see supplementary material S7).

**Percentage positive, and incidence rates**

A total of 12,642 samples were analyzed, with 6,708 testing positive (table 1). From week 24, 2023, VMD’s median weekly positivity rate was 52.5%. Positivity peaked at 70% in week 50, 2023, with nearly 50% of samples positive for SARS-CoV-2. Another peak of 66% occurred in week 35, 2024, based on fewer samples. Influenzavirus A rose before week 50, 2023, peaked in early 2024, and declined after week 4, 2024. RSV showed a similar seasonal pattern but with fewer positive samples. Rhino-/enterovirus was consistently prevalent, peaking at 43% in week 39, 2024, while endemic coronaviruses peaked at 10% in week 4, 2024. Three endemic coronaviruses circulated at low levels in winter and spring, disappeared in summer, and resurged slightly in fall 2024. The fourth, NL63, was the least detected coronavirus, with almost no cases during the SARS-CoV-2 wave in 2023, and a seasonal pattern that instead appeared to be shifted towards spring and summer. Parainfluenzavirus type 3 and human metapneumovirus were present at low levels until mid-summer. Few samples were positive for influenzavirus B, parainfluenzavirus 1, 2, 4, and adenovirus. Co-infections were rare (n = 263), with seven samples testing positive for three viruses. The most common co-infection involved SARS-CoV-2 and rhino-/enterovirus (n = 62), followed by adenovirus and rhino-/enterovirus (n = 15).

**Symptoms**

VMD participants reported a median of 7 symptoms, with influenzavirus A having the highest median (9 symptoms, see supplementary material S9). Runny nose, sneezing, sore throat and cough were frequently reported in all virus-groups (figure 3). Over 75% of influenzavirus A-positive symptomatic participants reported fever and cough, respectively.

Influenzavirus A had the highest prevalence of most symptoms (figure 4) and, after adjusting for sex, was linked to the highest risk of fever, headache, fatigue, cough, altered taste, nausea, lack of appetite, muscle/joint pain, chest pain, and chills. hMPV was associated with the highest risk of shortness of breath, followed by influenzavirus A. SARS-CoV-2 posed a lower fever risk than influenzavirus A but higher than most other viruses, with a similar trend for muscle/joint pain, headache, fatigue, chills, lack of appetite, and nausea. Endemic coronaviruses were associated with the highest risk of sneezing, runny nose, and red/itchy eyes (see supplementary material S10 for sex-adjusted RRs, and S11-13 for sex-adjusted and age-group stratified RRs).

**Participant behavior**

The evaluation questionnaire received 5,019 responses, with 1,307 (27%) reporting having had symptoms potentially related to a respiratory infection during their enrolment. Of these, 774 submitted a sample, meaning at least 41% did not.

Seventeen participants reported to have sought medical advice following a VMD test, though 14 (82.3%) reported that they would have done so regardless of the test. Conversely, 45 (8.3%) chose not to contact their doctor but would have if not for the VMD result. Furthermore, 114 (21%) reported staying home from work or school due to their test result, while 135 (25%) refrained from social activities. Notably, 82 (16,6 %) reported attending work or school after receiving their test result, despite initially planning to stay home.

Among 2,480 respondents, 59% preferred VMD in a future pandemic, 14% preferred testing centers, 21% had no preference, and 6% selected “Do not know”.

**Symptoms over time and symptom dynamics**

While the number of samples and symptomatic individuals over time changed during the study period, the proportion of them reporting fever, aILI, and cough respectively, remained relatively stable (figure 4).

The most frequently reported symptom at the time of sampling was runny/congested nose followed by sore throat and coughing. Median difference in symptoms at sampling and after 7-28 days was -2 [-4;0] (figure 4).

**SARS-CoV-2 variants and wastewater surveillance**

SARS-CoV-2 was the most commonly detected virus in VMD (see Figure 2 and supplementary material S8). The peak in weekly SARS-CoV-2 incidence rate coincided with the highest proportion of the variants BA.2.86\* and JN.1\* among sequences of SARS-CoV-2. Trends in SARS-CoV-2 detection were consistent between VMD and wastewater surveillance (figure 5).

Symptoms were reported at similar levels regardless of SARS-CoV-2 variant identified in samples (figure 6).

**Discussion**

VMD provided information about viral respiratory infections in a geographically diverse cohort not seeking healthcare, offering a snapshot of the Danish population.

**Demography**

The Digital Post cohort included more children under 15 and adults over 50, while the workplace cohort attracted younger adults, reflecting employment patterns and the inclusion of educational institutions14. The youngest children, teenagers aged 15-19, and adults over 70 were underrepresented. Both cohorts had a slight gender imbalance, with fewer male participants.

**Logistical setup and testing behavior**

VMD faced few logistical issues, though the Digital Post cohort had to wait for test kits to be delivered by mail. This lack of immediacy and flexibility likely contributed to the cohort’s relatively low participation rate of 11.9%. In contrast, the UK COVID-19 Infection Survey achieved a 51% registration rate in England in its early phases15. Reduced public interest in testing following the COVID-19 pandemic and the absence of incentives may also have played a role in the lower participation rate.

The workplace cohort submitted more samples per participant and had lower positivity rate which may reflect a lower threshold for testing in this cohort, facilitated by easy access to test kits. Their short registration-to-sample intervals also indicates that they waited to sign-up until they experienced symptoms, making the cohort size larger than the number of registered participants.

Over 40% of participants did not swab themselves every time they experienced symptoms. Among those who did, most reported aILI symptoms, with the proportions of aILI, fever, and coughing remaining relatively constant over time. This suggests that participants often waited until symptoms had reached a certain threshold before performing a swab.

**Frequency of respiratory viruses**

VMD identified widespread community transmission of SARS-CoV-2 in late 2023, including one of the first BA.2.86 sequences in Denmark16, illustrating that VMD possesses the ability to provide early warning.

Rhino-/enterovirus became the second most common virus identified in VMD samples and was consistently present with no clear seasonality, consistent with prior findings17.

**Comparison to other similar system**

In Denmark, the sentinel surveillance system also documented a peak of SARS-CoV-2 positivity rate in weeks 49 and 50 of 20238, but at a lower level than VMD. The summer 2024 SARS-CoV-2 wave was also more pronounced in the VMD system than in the sentinel surveillance. Additionally, endemic coronaviruses were more common in VMD, while influenzavirus and RSV were more common in sentinel surveillance. The viruses that commonly cause symptoms in the general population therefore appear to differ from those that prompt individuals to visit a doctor, though differing demographics and testing thresholds also likely plays in.

The Dutch Infectieradar18 system, similar to VMD, also observed a SARS-CoV-2 peak in late 2023, albeit smaller in magnitude than VMD. Both systems observed a summer resurgence, with VMD again showing higher positivity rates. Influenzavirus A peaked in both systems in week 4, 2024. Rhinovirus was dominant in Infectieradar, with no clear seasonality, as seen in VMD.

**Comparing symptoms across time, viruses and variants**

SARS-CoV-2 symptoms were intermediate between influenzavirus A virus and the other respiratory viruses, similar to previous discriptions19,20. Sequencing of SARS-CoV-2 allowed for further evaluation of symptoms associated with circulating variants, which was of importance for the initial risk assessment at the emergence of the JN.1 variant21. Current results from VMD suggest that the variants identified in VMD, including the newer KP and XEC variants, give rise to comparable symptoms.

The follow-up symptom questionnaire demonstrated a general decline in symptoms over time, but provided limited novel insights, highlighting the challenges in capturing the dynamic nature of symptoms associated with respiratory infectious diseases22.

**Health seeking behavior**

Few participants contacted their doctor after VMD test results, though some refrained from doing so after receiving their result. Some participants may just have wanted their doctor to perform a test on them, which they instead did themselves through VMD. However, this also raises concerns that participation in home-test programs like VMD, where no clinician is involved in interpretation of symptoms and analysis results, might lead some participants to neglect symptoms requiring medical evaluation23.

Some participants returned to work/school after a test results despite having symptoms, likely interpreting results as a “green light” to resume activities24. The reasons behind these behavioral changes warrant further investigation.

**Limitations**

Selection bias in VMD is a concern, as more health-conscious individual, those with higher health-literacy25, or those with symptoms are disproportionately inclined to participate. Underrepresentation of young children and older adults, along with digital platform challenges for older populations, limits generalizability of VMD and its results – and comparability to systems like the sentinel surveillance system.

VMD predominantly captured infections that had reached a particular level of symptom severity, instead of the full spectrum of respiratory infections. Also, low participation and adherence to sampling in VMD may have been impacted by factors like testing thresholds and logistical issues, particularly in the Digital Post cohort. These could increase in future health crises due to heightened public interest in understanding the cause of symptoms, reduced turnaround times for test results, and more accessible sample drop-off points at workplaces, pharmacies, grocery stores or similar locations.

**Strengths**

VMD provided unique surveillance of respiratory viruses in individuals with community-acquired infections who had not sought medical care. This allowed for insights into symptoms associated with different viruses in healthy individuals. VMD’s identifiable samples enabled integration with demographic data such as age, sex, vaccination status, and previous infections. The system allows for characterization of self-testing behavior within different groups, e.g., it can be explored whether vaccinated individuals rely more or less on self-tests than unvaccinated individuals.

VMD can operate alongside the healthcare system, avoiding strain on resources and preventing unnecessary exposure in testing centers. The two cohorts allowed us to assess how sampling pickup/drop-off methods affected participation rates and behavior. Also, the system's flexibility, demonstrated by its ability to adapt to include additional pathogens in the RT-PCR panel and to continuously include more participants, is also a strength. Finally, VMD can be seen as a citizen science initiative which benefits from its large RT-PCR panel, enabling many participants to identify the specific respiratory virus responsible for their symptoms.

**Conclusions**

VMD demonstrated feasibility of a community-based surveillance system, providing continuous insights into respiratory virus trends and symptomatology in the general population. Samples were collected directly from workplaces and sent in by post, from a cohort large enough to provide detailed epidemiological insights and early warning signals. With VMD, it can be explored if SARS-CoV-2 waves continue in similar magnitude as observed thus far within the general population, and how prior infections and vaccinations influence symptomatology, e.g., it can be explored whether SARS-CoV-2 symptoms evolve to resemble those of other endemic coronaviruses with time or if they remain similar to those caused by influenzavirus A. VMD’s scalable platform offers a proactive tool that prepares us for the next pandemic, minimizing our reliance on healthcare system resources.

**Ethics**

This article has been prepared on the basis of a study carried out as part of a task imposed on Statens Serum Institut according to national legislation. Therefore, no approval requirements from the ethics committees is obliged.

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**Conflict of interest**

None.

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**Figures and tables**

Figure 1: Overview of participation in Virus Monitoring in Denmark. A) CONSORT diagram of participant recruitment. B) Cumulated number of participants per week (line) and number of samples analyzed per week (bars). The vertical red lines indicate the calendar weeks where Digital Post invitations were sent out. Data from week 24, 2023 to week 46, 2024.

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| --- | --- | --- | --- | --- |
| Table 1: Demographic and participation characteristics of participants in Virus Monitoring in Denmark, total cohort and stratified by workplace cohort or Digital Post cohort. Data from week 24, 2023 to week 46, 2024. The cohort demography is compared to the population of Denmark in October 2023. | | | | |
|  | Total | Workplace cohort | Digital Post cohort | Population, Denmark, October 2023 |
| **Registered individuals** | 30627 | 3147 | 27480 | 5959464 |
| **Sex = M, n (%)** | 13182 (43.0) | 1447 (46.0) | 11735 (42.7) | 2962468 (49.7) |
| **Age, mean (SD)** | 46.67 (19.99) | 36.02 (16.00) | 47.89 (20.04) | 41.83 (23.81) |
| **Age groups n (%)** |  |  |  |  |
| 0-4 | - | - | - | 307653 (5.16) |
| 5-9 | 1346 (4.4) | 130 (4.1) | 1216 (4.4) | 310040 (5.2) |
| 10-14 | 2451 (8.0) | 211 (6.7) | 2240 (8.2) | 322958 (5.42) |
| 15-19 | 875 (2.9) | 131 (4.2) | 744 (2.7) | 350828 (5.89) |
| 20-29 | 2188 (7.1) | 774 (24.6) | 1414 (5.1) | 786628 (13.2) |
| 30-39 | 3063 (10.0) | 611 (19.4) | 2452 (8.9) | 757520 (12.71) |
| 40-49 | 4108 (13.4) | 533 (16.9) | 3575 (13.0) | 719668 (12.08) |
| 50-59 | 6873 (22.4) | 500 (15.9) | 6373 (23.2) | 809737 (13.59) |
| 60-69 | 6679 (21.8) | 235 (7.5) | 6444 (23.4) | 692092 (11.61) |
| 70-79 | 2935 (9.6) | 19 (0.6) | 2916 (10.6) | 585415 (9.82) |
| >80 | 109 (0.4) | 3 (0.1) | 106 (0.4) | 316925 (5.32) |
| **Region n (%)** |  |  |  |  |
| Capital of Denmark | 10405 (34.1) | 1352 (43.4) | 9053 (33.1) | 1910395 (32.06) |
| Central Denmark | 6482 (21.3) | 412 (13.2) | 6070 (22.2) | 1364853 (22.9) |
| Northern Denmark | 3015 (9.9) | 541 (17.4) | 2474 (9.0) | 593898 (9.97) |
| Zealand | 4387 (14.4) | 332 (10.7) | 4055 (14.8) | 851815 (14.29) |
| Southern Denmark | 6207 (20.4) | 479 (15.4) | 5728 (20.9) | 1238503 (20.78) |
| **Samples analyzed** | 12642 | 3401 | 9241 |  |
| **Positive Samples** | 6708 | 1520 | 5188 |  |
| **Samples pr. individual n (%)** |  |  |  |  |
| 0 | 21949 (71.7) | 1152 (36.6) | 20797 (75.70) |  |
| 1 | 6555 (21.4) | 1550 (49.3) | 5005 (18.2) |  |
| 2 | 1445 (4.72) | 271 (8.61) | 1174 (4.27) |  |
| 3 | 436 (1.42) | 87 (2.76) | 349 (1.27) |  |
| More than 4 | 242 (0.79) | 87 (2.76) | 155 (0.56) |  |
| **Samples pr. registered participant pr.  year,**  **mean (SD)** | 0.40  (0.87) | 0.88  (1.49) | 0.34  (0.74) |  |
| **Days from enrolment to first sample registration,**  **median [IQR]** | 34.40  [0.95;69.6] | 0.68  [0.50;0.85] | 47.86  [26.73;82.75] |  |
| **Days from sample taken to analysis result,**  **median [IQR]** | 5.00  [3.29;6.43] | 4.02  [2.14;5.87] | 5.14  [3.92;6.82] |  |
| **Total samples pr. year of participation in VMD for each age group** |  |  |  |  |
| 0-4 | - | - | - |  |
| 5-9 | 0.25 | 0.67 | 0.18 |  |
| 10-14 | 0.24 | 0.96 | 0.20 |  |
| 15-19 | 0.39 | 1.01 | 0.30 |  |
| 20-29 | 0.65 | 1.37 | 0.48 |  |
| 30-39 | 0.66 | 1.43 | 0.50 |  |
| 40-49 | 0.59 | 1.26 | 0.47 |  |
| 50-59 | 0.43 | 1.18 | 0.37 |  |
| 60-69 | 0.37 | 1.49 | 0.34 |  |
| 70-79 | 0.23 | 0.97 | 0.22 |  |
| >80 | 0.10 | 0.67 | 0.04 |  |
| **Households** | 24400 | 2410 | 21990 |  |
| **Region n (%)** |  |  |  |  |
| Capital of Denmark | 8277 (33.9) | 1004 (41.7) | 7273 (33.1) |  |
| Central Denmark | 5167 (21.2) | 313 (13.0) | 4854 (22.1) |  |
| The North Denmark | 2459 (10.1) | 477 (19.8) | 1982 (9.0) |  |
| Zealand | 3507 (14.4) | 248 (10.3) | 3259 (14.8) |  |
| Southern Denmark | 4990 (20.5) | 368 (15.3) | 4622 (21.0) |  |

Figure 2: Weekly distribution of viruses in Virus Monitoring in Denmark during the study period. Left panel: Percentage of positive samples. Right panel: Incidence pr. 100.000 with logarithm scale based on the Digital Post cohort. Data from week 24, 2023 to week 46, 2024. The dotted line represents the expansion of the RT-PCR panel, and the dashed line represents the week from which samples were reanalyzed with the extended RT-PCR panel.



Figure 3: A: prevalence of symptoms in participants infected with each virus, data from week 40, 2023, to week 46, 2024. Only responses from participants who have reported at least one symptom are included. Error bars represents 95% confidence interval. B: distribution of the number of symptoms reported per positive sample, stratified by virus and ordered by median symptom count, from highest to lowest. n indicates the number of symptomatic individuals per virus.



Figure 4: Top panel: prevalence of symptoms over time. Only symptomatic individuals who perform a sample from week 40, 2023, to week 46, 2024. Bottom panel: number of each symptom reported among individuals with a positive test at time of sampling (Baseline), symptoms that were only reported at the time of sampling but were not present after 7-28 days (Gone at Follow-up) and those that were only reported at 7-28 days after the sample, but not at the time of sampling (New at Follow-up). Includes only individuals who answered both symptom questionnaires.



Figure 5: Top panel shows the weekly incidence rate of SARS-CoV-2 in VMD (red line, left y-axis) and the weekly concentration of SARS-CoV-2 RNA in wastewater surveillance (blue line, right y-axis), with the peak of both curves in the same level, both on logarithmic scales. Bottom panel shows SARS-CoV-2 variant composition in VMD samples during the study period. Data from week 40, 2023 to week 46, 2024.



Figure 6: Prevalence of individual symptoms in participants infected with different SARS-CoV-2 subvariants. Only responses from participants who have reported at least one symptom are included. Error bars represents 95% confidence. Data from week 24, 2023 to week 46, 2024.

