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Changes in mental and sexual health among MSM using HIV pre-exposure prophylaxis during the SARS-CoV-2 pandemic: longitudinal analysis of the SwissPrEPared cohort study

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Summary

BACKGROUND: Changes in mental and sexual health among men having sex with men (MSM) due to the SARS-CoV-2 pandemic remain unclear.

METHODS: Design: Longitudinal analysis of an ongoing, multicentre, pre-exposure prophylaxis (PrEP) cohort (NCT03893188) in Switzerland. Participants: HIV-negative MSM aged ≥18 who completed at least one questionnaire before and one after the start of the SARS-CoV-2 pandemic. Outcomes: Primary: mental health, defined as anxiety and depression scores assessed by the Patient Health Questionnaire-4. Secondary: sexual behaviour, well-being, PrEP use and disruption of care. Outcomes were assessed over seven periods corresponding to different SARS-CoV-2 prevention measures in Switzerland. We performed pairwise comparisons between periods (Wilcoxon signed rank test).

RESULTS: Data from 1,043 participants were included. Whilst anxiety scores remained stable over time, depression scores worsened in the second wave and the second lockdown period compared to pre-pandemic scores. This was confirmed by pairwise comparisons (pre-SARS-CoV-2/second wave and pre-SARS-CoV-2/second lockdown: p <0.001). Downward trends in sexual activity,sexualized substance use, and a switch from daily to "event-driven" PrEP were found. Disruption of care affected 42.6% (790/1856) of daily PrEP users' follow-up visits.

CONCLUSION: In this longitudinal analysis of a PrEP cohort enrolling MSM, depression scores worsened in the second wave and the second lockdown compared to the pre-pandemic period.

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Introduction

To mitigate the viral transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), many governments introduced prevention measures based on social and behavioural restrictions (e.g. physical distancing, stay-at-home policies or quarantining) [1]. Although beneficial on many levels, these prevention measures have also been suggested to result in a widening of social, health and economic disparities between population groups [2], and to contribute to the development of mental health issues such as anxiety or depression [3–8].

The negative impact of SARS-CoV-2 prevention measures on mental health outcomes has been particularly pronounced in some minorities and evidence suggests that members of the lesbian, bisexual, gay and transgender (LGBT) community have been disproportionally affected by social and behavioural restrictions leading to isolation [3, 9–11]. These minorities were also found to be at higher risk of developing new mental health diseases [10, 12] or of experiencing a worsening of pre-existing mental health conditions [5, 7]. These aspects, along with higher prevalences of mental health problems (e.g. depression, anxiety and problematic substance use) [13, 14], greater economic insecurity, poorer job stability and less support from their families [15, 16], make members of the LGBT community more likely to experience negative consequences of the SARS-CoV-2 public health crisis [3, 10, 12].

The introduction of stringent prevention measures probably affected other health-related dimensions that are particularly relevant to the LGBT community. There is, for instance, conflicting evidence as to whether the SARS-CoV-2 pandemic resulted in a change in sexual behaviour: although some studies suggested a reduction in sexual activity among men having sex with men (MSM) during the first wave of the pandemic, other studies reported an increase in the number of sexual encounters [2, 8, 17, 18]. There is also uncertainty regarding the effect of the SARS-CoV-2 prevention measures on the quality of HIV prevention care, but evidence seems to indicate that access to and taking of pre-exposure prophylaxis (PrEP) were negatively affected [2, 12, 17, 19].

Longitudinal data are decisive in obtaining a reliable assessment of the impact of the SARS-CoV-2 pandemic on mental and sexual health outcomes. Therefore, we performed a longitudinal data analysis within a selected subgroup of the SwissPrEPared study, with the aim of investigating the effects of the SARS-CoV-2 prevention measures on mental and sexual health over a one-year period. More specifically, we were interested in describing how anxiety and depression, sexual behaviour, substance use, PrEP use and disruption of care varied over the different phases of the pandemic in MSM in Switzerland.

Materials and methods

We followed the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) statement for the reporting of observational studies [20]. The SwissPrEPared study was approved by all cantonal ethical committees (lead canton: Zurich, Switzerland – registration number: 2018-02015) and was registered with ClinicalTrials.gov (NCT03893188). Written informed consent was obtained from all participants included in this study.

Study design and setting

Data were obtained from the ongoing SwissPrEPared study, which is a large, multicentre, nationwide cohort study that aims to follow individuals interested in PrEP longitudinally over a three-year period. Recruiting centres are located in seven Swiss cities and consist of large tertiary referral hospitals, sexual health clinics and private clinical practices (e.g. general practitioners, infectious diseases specialists or dermatologists).

All study centres are part of the SwissPrEPared programme, which ensures standardization of PrEP counselling and STI (sexually transmitted infection) screening across the country. Programme participants have access to a secure, web-based, online platform where they complete standardized questionnaires on their personal electronic devices before their scheduled counselling. Counselling and STI screening occur at regular intervals, following the latest international recommendations: every three months for participants on daily PrEP and at least every six months (or less) for those taking PrEP intermittently (i.e. either daily for limited periods of time ["holiday PrEP"] or before and after sex ["event-driven" PrEP]) [21].

Study participants

The design and cohort profile of the SwissPrEPared study have been described elsewhere [22]. This ongoing cohort enrols HIV-negative individuals aged ≥18 years and presenting for PrEP counselling at participating centres. Potential study participants are informed of study enrolment in print and online magazines. No restrictions are applied to those with no indication for PrEP or those declining further PrEP use.

In this analysis, only MSM were included, i.e. either cis-MSM (assigned male at birth, self-identifying as male, having sex with men) or trans-MSM (assigned female at birth, self-identifying as male, having sex with men). Participants included in the analysis completed at least one questionnaire assessing mental health outcomes before the start of the SARS-CoV-2 pandemic in Switzerland (defined as February 28, 2020) and at least one thereafter.

Study outcomes

The primary outcome was defined as mental health outcomes, assessed using the Patient Health Questionnaire-4 (PHQ-4) [23]. This screening instrument consists of four questions based on a four-point Likert-type scale and evaluates the likelihood of depression (two questions) and anxiety (two questions) (see Appendix, table S1 for a comprehensive description of this instrument). Each question is rated from 0–3 (with higher values indicating a poorer outcome), thereby yielding a maximum score of 6 for each of the subscales. A score of 3 or greater on each subscale identifies potential cases of depression or anxiety and should prompt further evaluation and, in some cases, referral to specialized care.

The following endpoints were considered as secondary outcomes:

– Sexual behaviour, including number of sexual partners in the past three months, sex and condom use with casual partners, self-reported adaptation of sexual behaviour due to SARS-CoV-2 (four-item question), adaptation of dating behaviour due to SARS-CoV-2 (five-item question) and self-reported substance use (including use of chemsex substances, Ecstasy, cocaine and cannabis). Chemsex substances were defined as: γ-hydroxybutyric acid/γ-butyrolactone (GHB/GBL), ketamine, methamphetamine, mephedrone and stimulants other than mephedrone, as described previously [24].
– Well-being, defined as sexual happiness (10-item numeric ranking scale with lower values indicating poorer sexual well-being) [25] and financial coping (five-item Likert scale).
– PrEP use, defined as any change in pre-existing PrEP regimen (e.g. from daily to "event-driven" PrEP, discontinuation of PrEP) and PrEP adherence (self-reported frequency of missing a PrEP dose).

Finally, we were also interested in assessing whether the quality of HIV prevention care was affected by the SARS-CoV-2 prevention measures. Thus, we evaluated disruption of care, defined as the proportion of participants unable to attend their follow-up visits as scheduled (i.e. three months + two weeks between each recorded visit). Disruption of care was assessed in participants who started daily PrEP before January 1, 2020 and was not evaluated in those on intermittent PrEP (i.e. "holiday" or "event-driven" PrEP), since visit schedules for such individuals may differ between centres.

The outcomes were assessed over seven different periods corresponding to the varying prevention measures introduced (or lifted) by the Swiss Ministry of Health (Appendix, figure S1) [26]. These periods were defined as:

– pre-SARS-CoV-2 period (April 2019 [study inception] until February 28, 2020);
– pre-lockdown period (March 1 to March 15, 2020);
– first lockdown period (March 16 to April 26, 2020);
– first easing of measures (April 27 to June 14, 2020);
– inter-wave period (June 15 to October 28, 2020);
– second SARS-CoV-2 wave (October 29, 2020 to January 17, 2021);
– second lockdown period (January 18 to March 21, 2021).

Statistical methods

The aim of this study was primarily descriptive: the primary outcome, defined as mental health outcomes (i.e. PHQ-4 anxiety and depression subscales, ordinal variables), was assessed over time by comparing the participants' scores on each subscale (ranging from 0 to 6) between the different periods. We performed pairwise comparisons between periods using the Wilcoxon signed rank test with Bonferroni adjustment for multiple testing in the case of statistically significant results ($p < 0.05$). For the primary outcome (i.e. PHQ-4 depression or anxiety subscales), 21 comparisons were performed; thus, a level of £0.002 was considered significant. Alternative approaches (e.g. Friedman's ANOVA) were not applicable because the group sizes varied over time.

In the phase preceding March 1, 2020, for participants with multiple previous questionnaires, only the latest (i.e. the closest in time to March 1, 2020) was considered. The same approach was used for participants with more than one questionnaire during the other periods – only the last questionnaire completed during that period was considered – so as to maximize the potential effect of time on the outcome.

Secondary outcomes were assessed over all periods using the same approach as described above: for ordinal and continuous variables we performed pairwise comparison using the Wilcoxon signed rank test with adjustment for multiple comparisons; for binary/nominal variables we used the McNemar test. To quantify disruption of care, a descriptive analysis of the time lag between visits in daily PrEP users was performed.

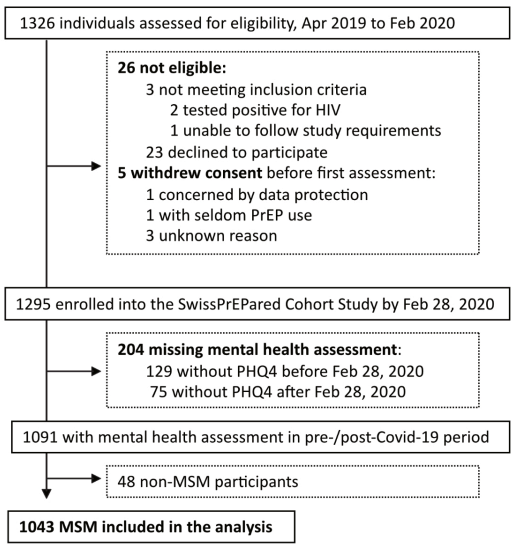
Additional exploratory analyses included dichotomization of the primary outcome (i.e. depression/anxiety screening: positive for scores ≥3 and negative for scores ≤2) and assessing the association of pre-existing anxiety or depression with poor mental health over time (using generalized estimating equation models that accounted for repeated measurements over time). For the latter, pre-existing anxiety or depression were defined as a score ≥3 on the relevant subscale at baseline, i.e. during the pre-SARS-CoV-2 period.

Categorical variables were expressed as proportions, continuous variables as median and interquartile range. A level of significance of 0.05 was used, unless multiple comparisons were performed. All statistical analyses were conducted in R, version 4.1.0. A detailed list of the libraries used in this work is provided in the Appendix.

Results

Data were collected from 14 participating centres between April 10, 2019 and March 22, 2021. Overall, 1,326 participants were assessed for eligibility (figure 1). Of these, 26 participants were found to be ineligible (two tested positive for HIV, one was unable to follow the study requirements

Figure 1: Flow diagram. MSM: men having sex with men; PHQ-4: Patient Health Questionnaire-4



and 23 declined study participation), whilst five withdrew their consent before the first visit (one concerned by data protection, one with infrequent PrEP use, three for unknown reasons). Thus, 1,295 participants were enrolled in the SwissPrEPared study by February 28, 2020. Of these, 252 were further excluded, either due to a lack of mental health data (129 with missing questionnaire before February 28, 2020 and 75 with missing questionnaire after this date), or because they did not identify as MSM (n = 48). Thus, data from 1,043 participants were eventually included in the analysis.

Baseline characteristics

Table 1 outlines participants' baseline characteristics (i.e. pre-SARS-CoV-2 period). Median age was 40 years (IQR: 33–47). All participants were MSM, predominantly identifying as cis-male (1040/1043, 99.7%). The majority were born in Switzerland (641/1043, 61.5%), while 497/1043 (47.7%) had a university degree.

On the PHQ-4 anxiety and depression subscales, most participants scored 0, 1 or 2 (figure 2, pre-SARS-CoV-2 period). When considered as a binary endpoint (score ≥ 3 on each subscale), 8% (83/1043) and 5.3% (55/1043) of the participants screened positive at baseline for anxiety and depression respectively.

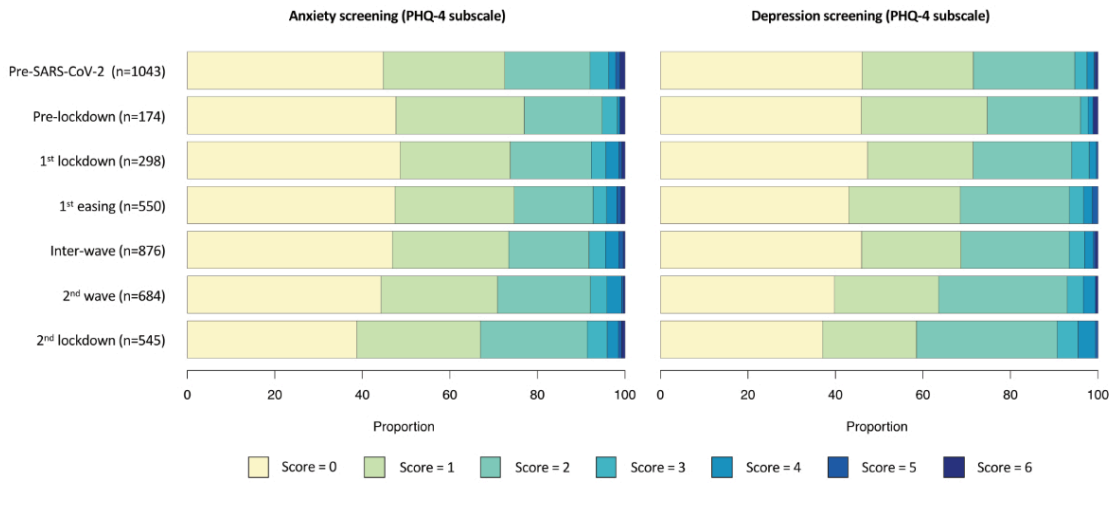
Baseline data on sexual behaviour, well-being and PrEP use are outlined in table 2 (pre-SARS-CoV-2 period). The median sexual partner count was 6 (IQR: 3–12), 91.7% (956/1043) of the participants reported having sex with casual partners and 9.6% (100/1043) reported consistent condom use. Concern about substance use was reported by 5.3% of participants, whilst 17.2% reported using chemsex substances, 16.8% reported using Ecstasy, 17.4% cocaine and 22.8% cannabis over the past three months. The median sexual happiness score was 7 (IQR: 6–8) and around

Table 1:
Participants with mental health data – baseline characteristics.

		Overall (n = 1043)
Age	Median [IQR]	40 [33–47]
Gender	Male	1043 (100%)
	– Cis-male	1040 (99.7%)
	– Trans-male	3 (0.3%)
Country of origin	Switzerland	641 (61.5%)
	Germany	105 (10.1%)
	France	35 (3.4%)
	Brazil	27 (2.6%)
	Italy	18 (1.7%)
	Others (each <18 participants)	217 (20.8%)
	– European countries	92 (42.4%)
	– Non-European countries	125 (57.6%)
Education	University	497 (47.7%)
	Higher education (excluding university)	242 (23.2%)
	Apprenticeship	193 (18.5%)
	High school/Baccalaureate	67 (6.4%)
	No or compulsory school	20 (1.9%)
	Other	24 (2.3%)

"Cis" refers to individuals for whom sex assigned at birth matches gender identity. "Trans" refers to a discrepancy between sex assigned at birth and the reported gender identity.

Figure 2: Anxiety and depression scores over the different SARS-CoV-2 periods in a sample of the SwissPrEPared cohort. Scores of 3 or greater identify potential cases of anxiety or depression. PHQ-4: Patient Health Questionnaire-4.



half the participants reported a comfortable financial situation (546/1043, 52.3%). Most participants were on PrEP at baseline (880/1043, 84.4%), with 64.3% (671/1043) using a daily regimen. Overall self-reported adherence (never missed a dose: 59.5%, 84.3% and 66.7% in daily, "event-driven" and "holiday" PrEP users respectively) was acceptable.

Primary outcome: anxiety and depression screening over time

Examination of the different periods indicated that most participants reported PHQ-4 anxiety scores of 0, 1 or 2 (figure 2 and Appendix, table S2) and that the proportion of participants with a positive anxiety screening was stable over time (figure 3 and Appendix, table S2). Pairwise comparisons of anxiety scores between the different periods revealed no significant differences (Appendix, table S4). Similar results were found for the comparisons of positive anxiety screenings (Appendix, table S4).

Compared to the pre-SARS-CoV-2 period, depression scores reported in the second wave and second lockdown period shifted towards both higher ratings on the ordinal scale and to more positive screenings (figures 2 and 3 and Appendix, table S2). Pairwise comparisons confirmed significant differences for these specific periods (ordinal scale, pre-SARS-CoV-2/second wave and pre-SARS-CoV-2/second lockdown: $p < 0.001$; positive screening, pre-SARS-CoV-2/second wave: $n = 684$, $p = 0.048$; positive screening, pre-SARS-CoV-2/second lockdown: $n = 545$, $p = 0.017$, Appendix, table S4).

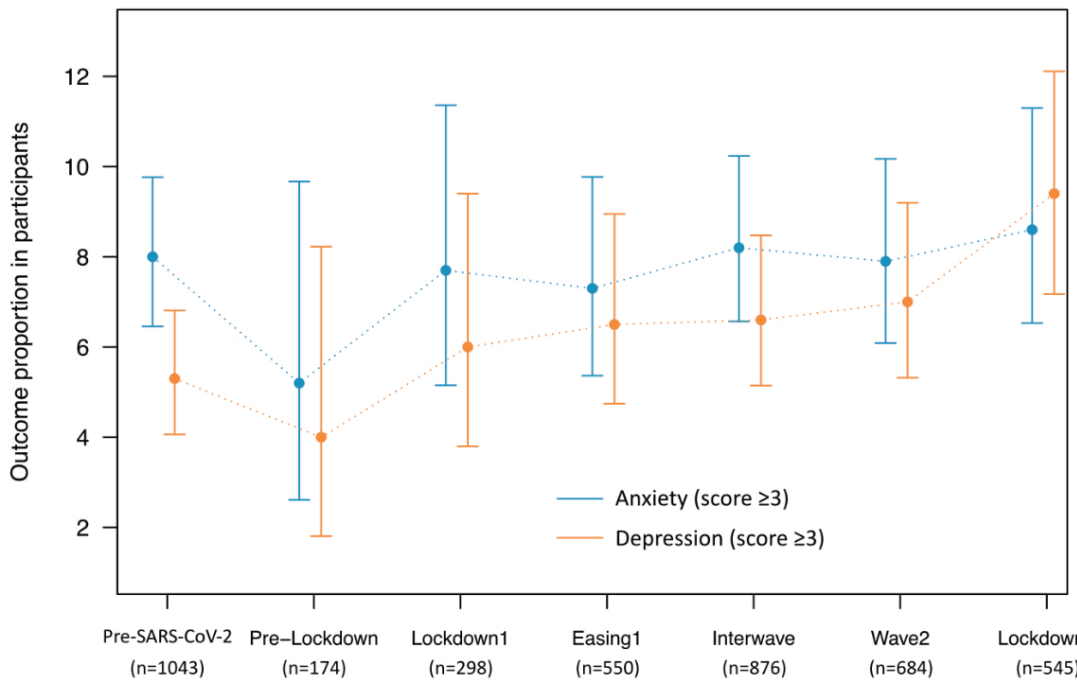
Secondary outcomes

For a comprehensive overview of all secondary outcomes, see Appendix, table S2**.**

Sexual behaviour over time

Both the median number of sexual partners and the occurrence of sex with casual partners followed a biphasic pattern over time, with an initial decrease during the first lockdown and first easing periods and a second decline during the second wave and second lockdown. Pairwise comparisons confirmed these changes in sexual behaviour over time ($p < 0.002$; Appendix, table S4). Compared to the pre-SARS-CoV-2 period, systematic condom use decreased over time, whilst the proportion of participants reporting no condom use increased. These differences between baseline and the following periods were confirmed by pairwise comparisons (Appendix, table S4). Data on the adaptation of sexual and dating behaviour were only available from the first easing period. From this time point, the proportion of participants reporting having no sexual contact steadily decreased. Similar results were found for those reporting having fewer online dates. Pairwise comparisons confirmed these differences between periods (Appendix, table S4). Finally, none of the endpoints related to substance use varied markedly over time, except for the use of chemsex substances (which declined during the first lockdown and easing) and the use of ecstasy (which declined over time compared to baseline). These findings were confirmed when performing pairwise comparisons (Appendix, table S4).

Figure 3: Proportion of participants (with 95% CIs) who screened positive for anxiety or depression over the different SARS-CoV-2 prevention periods. A positive screening was defined as a score of 3 or greater on the relevant Patient Health Questionnaire-4 (PHQ-4) subscale. The McNemar test was used to compare outcome proportions between periods (two-sided test).



Well-being over time

Sexual happiness remained stable over time, with pairwise comparisons showing differences between only a few periods (Appendix, tables S3 and S4). Robust follow-up data on financial coping were only available from the second wave period. There were no marked differences between periods (Appendix, table S4).

PrEP use over time

The proportion of participants reporting taking PrEP on the day of the study visit showed a universal upward trend over time, except during the first lockdown period. This trend was confirmed by the pairwise analysis (Appendix, table S4). There were only minor fluctuations in PrEP regimens over time, except during the first easing period, when a reduction in daily PrEP and an increase in "holiday" and "event-driven" PrEP was reported. Pairwise comparisons of the pre-SARS-CoV-2 period and the first easing period confirmed these findings (Appendix, table S4). Self-reported adherence remained stable over time, with overall good adherence across all PrEP regimens, and showed no significant differences between periods (Appendix, tables S3 and S4).

Disruption of care

Figure 4 illustrates the lengths of time between follow-up visits occurring during the SARS-CoV-2 pandemic in daily PrEP users who started PrEP before Jan 1, 2020 (n = 534 PrEP users). The median time between visits was 13.3 weeks (IQR 11.3–17.8). Disruption of care, namely visits with a time interval >14 weeks, affected 42.6% of the visits (790/1856 visits).

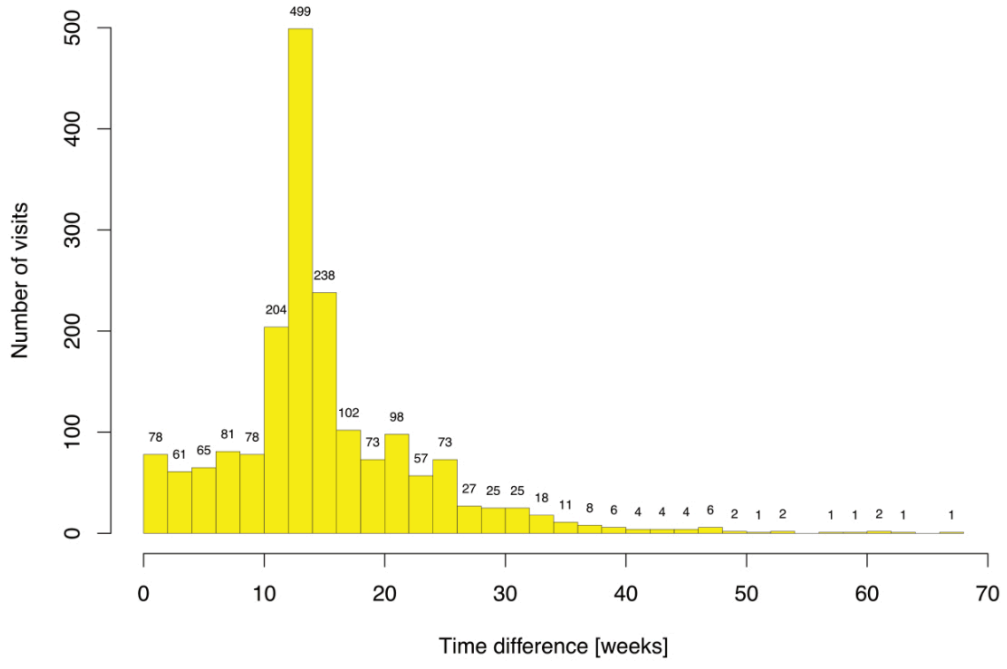
Association of pre-existing anxiety or depression with poor mental health over time

The effects of pre-existing (i.e. baseline) anxiety or depression on the likelihood of screening positive for anxiety or depression was assessed over six different periods (i.e. from the pre-lockdown period to the end of the second lockdown). Participants with pre-existing anxiety or depression were more likely to screen positive for anxiety over time (pre-existing anxiety: OR 5.6, 95%CI 3.6–8.9, p <0.001; pre-existing depression: OR 2.8, 95%CI 1.6–4.8, p <0.001). Similar results were found when screening positive for depression was considered as the outcome (pre-existing anxiety: OR 2.7, 95%CI 1.6–4.6, p <0.001; pre-existing depression: OR 5.9, 95%CI 3.3 to 10.6, p <0.001).

Discussion

In this longitudinal analysis including 1,043 MSM from a large, ongoing, prospective, nationwide HIV PrEP study, we examined the effect of SARS-CoV-2 prevention measures on mental and sexual health over a one-year period. Whilst anxiety scores remained stable over time, we found that depression screenings, assessed both on the PHQ-4 ordinal scale and as a binary outcome (positive/negative screening), worsened in the second wave and second lockdown period when compared to the pre-pandemic phase. Further analyses revealed changes in sexual behaviour and substance use over the different periods (e.g. downward trends in the number of sexual partners and the occurrence of sex with casual partners and a decline in chemsex and

Figure 4: Histogram showing the lengths of time (in weeks) between follow-up visits occurring during the SARS-CoV-2 pandemic in daily PrEP users who started PrEP before Jan 1, 2020 (n = 534 PrEP users). The median time between visits was 13.3 weeks (IQR 11.3–17.8). Disruption of care, namely visits with a time interval >14 weeks, affected 42.6% of the visits occurring during the SARS-CoV-2 pandemic (790/1856 visits).



Ecstasy use), as well as changes in the way participants used PrEP (i.e. switching from daily PrEP to "holiday" or "event-driven" PrEP). Finally, we were able to show that the SARS-CoV-2 pandemic resulted in the disruption of important care, with more than 40% of scheduled visits occurring later than initially planned.

Using a longitudinal design, our analysis suggests negative effects of the SARS-CoV-2 pandemic on mental health. This is consistent with results from previously published, smaller, cross-sectional studies [2, 3, 8, 10, 16] and from a few cohort studies including other populations [27, 28]. In contrast to other reports, however, only a small fraction of our cohort (i.e. less than 10%) screened positive for anxiety or depression. A possible explanation for these findings may be that our cohort included mostly middle-aged, well-educated MSM originating from Switzerland, who reported a comfortable initial financial situation that was maintained over the course of the pandemic. These characteristics are in marked contrast with factors suggested to result in poorer mental health outcomes (such as younger age, an immigration background, belonging to an ethnic minority and financial insecurity) [2, 10, 16] and should prompt the development of recruitment strategies targeted at younger, less educated individuals [22]. Another reason for these results might be the use of coping mechanisms, such as the use of dating apps or social media to maintain social contacts or obtain emotional support [7]. Finally, the fact that the individuals included in our analysis were part of a prevention programme with regular follow-up visits may also have played a beneficial role, as evidence suggests that retention in care yields better mental and sexual health outcomes [29].

The data analysis on sexual behaviour suggested a downward, biphasic trend in the number of sexual partners and in the occurrence of sex with casual partners, which reflected, to some extent, the introduction and lifting of the SARS-CoV-2 prevention measures over time. Similarly, the decline observed in Ecstasy and chemsex substances use might also be attributed to the different phases of the SARS-CoV-2 pandemic, when social life in Switzerland was restricted (Appendix, figure S1). These findings are in line with other studies reporting an adaptation of sexual behaviour over the course of the time periods with different pandemic-related prevention measures [8, 10, 12, 17, 18, 30, 31]. In our study, however, ratings on sexual happiness remained stable over time. Because one would expect that a restricted social and sexual life would lead to lower sexual happiness ratings, the stability in happiness ratings might reflect a certain degree of social desirability bias in the answers related to the number of partners and/or sex with casual partners. This suggests that the individuals included in our study may not have fully adhered to physical distancing recommendations. These findings are consistent with studies reporting a lack of adaptation in sexual behaviour over the course of the pandemic (“quarantine-fatigue”) [18, 32], as well as with other reports where individuals at considerable risk of HIV were found to maintain a certain degree of exposure to risky situations [8, 31, 33].

Our study revealed that SARS-CoV-2 restrictions resulted in disruption of care, which is consistent with other studies reporting interruptions in access to PrEP/ HIV care during the pandemic [2, 17, 31, 34, 35]. The potential magnitude of these issues is of concern, as only modest SARS-CoV-2-related disruptions to HIV testing may result in substantial short-term increases in new HIV infections [36]. Interestingly, disruption of care occurred in our study despite the fact that, similar to other PrEP programmes [33, 37], two large SwissPrEPared centres offered telehealth services and home self-testing during lockdown phases. Thus, although telehealth seems to represent a good alternative in times of limited access to PrEP services [35, 37, 38], it may not fully substitute in-person visits, especially when STI or HIV screenings are needed [35]. These findings emphasize the need to maintain access to in-person health care in order to minimize collateral damage due to the SARS-CoV-2 pandemic or any other public health emergency.

This study provides longitudinal data on mental and sexual health outcomes over the different phases of the SARS-CoV-2 pandemic, including pre-pandemic data. In contrast to previously published studies [2, 3, 8, 10, 16], we used validated instruments with good psychometric properties for outcome assessment [39] and applied them to a large sample from an ongoing, prospective PrEP cohort, which enabled us to make robust inferences on mental and sexual health trajectories over time.

Our analysis has some limitations, however. Firstly, our cohort was a mostly middle-aged, well-educated and financially comfortable MSM population, and we cannot exclude that a certain degree of selection bias occurred. However, our findings remain applicable to several PrEP cohorts from other high-income countries which share a similar profile to ours [40–43]. Secondly, because the framing of some questions (e.g. number of sexual partners) referred to a rather wide time span (i.e. previous three months), the effect of shorter time periods, such as the pre-lockdown or first lockdown periods, on the study outcomes may have been underestimated: because of recall bias and the rather long time elapsed between visits, we cannot exclude that when participants completed their questionnaire at the beginning of a new prevention measures phase, their outcome assessment referred to the previous period rather than the period under consideration. Thus, in the case of multiple questionnaires completed in the same period, we selected the assessment nearest to the end of the period to maximize the effect of the period being considered on the participant’s responses. Thirdly, when assessing the effects of the different periods on mental and sexual health outcomes, we did not use more complex methodological approaches, such as interrupted time series [44] or unsupervised machine learning [45], since the main aim of this study was primarily descriptive and performing additional analyses was unlikely to change the main findings of this paper.

In this longitudinal analysis focusing on a subset of participants from a large, ongoing, prospective PrEP cohort study, there was a worsening of depression screening scores assessed with the PHQ-4 questionnaire over the different phases of the SARS-CoV-2 pandemic. Additional analyses identified changes in sexual behaviour, in substance use, in the way participants used PrEP and in their access to HIV prevention care over time. Follow-up data from the ongoing SwissPrEPared study (NCT03893188) will help evaluate the long-term effects of the SARS-

CoV-2 prevention measures on mental and sexual health outcomes in MSM and other sexual minorities.

Availability of data and material

The small, highly representative and individual-level datasets analyzed during the current study and used to generate table S1 and figures S1 to S4 and the Appendix are not publicly available due to the sensitive nature of the data they contain. Source data are thus not provided with this paper. Investigators with a request for selected data should send a proposal to the SwissPrEPared e-mail address (info[at]swissprepared.ch). The provision of data will be considered by the Scientific Board of the SwissPrEPared cohort study and the relevant study team. Data provision is subject to Swiss legal and ethical regulations and will be detailed in a material and data transfer agreement.

Authors' contributions

BLW, FH, RDK and BH participated in study conception and design, data interpretation and critical revision of the manuscript. BLW and FH drafted the first manuscript. FH and RDK performed the statistical analyses. AJS, MRe, MRa, EB, EBEA, DLB, AC, MC, VC, CD, SL, JN, MS, BS, PB and JN participated in data acquisition and critical revision of the manuscript. DH, RB, NL, AL, BBQ and JSF participated in study conception and design and critical revision of the manuscript. All authors listed on the title page have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission.

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Potential competing interests

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Appendix

Table S1 Patient Health Questionnaire-4 (PHQ-4) items

Over the last two weeks, how often have you been bothered by any of the following:	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
Little interest or pleasure in doing things	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Feeling nervous, anxious, or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3

Kroenke K, Spitzer RL, Williams JB, Loewe B. An ultra-brief screening scale for anxiety and depression: the PHQ–4. Psychosomatics. 2009;50(6):613–21

Table S2 Anxiety and depression scores in all SARS-CoV-2 periods.

	Pre-Covid-19 (N=1043)	Pre-lockdown (N=174)	1st lockdown (N=298)	1st easing (N=550)	Inter-wave (N=876)	2nd wave (N=684)	2nd lockdown (N=545)
Anxiety screening (PHQ-4, anxiety subscale)							
Score = 0	467 (44.8%)	83 (47.7%)	145 (48.7%)	261 (47.5%)	410 (46.8%)	303 (44.3%)	211 (38.7%)
Score = 1	290 (27.8%)	51 (29.3%)	75 (25.2%)	150 (27.3%)	233 (26.6%)	182 (26.6%)	154 (28.3%)
Score = 2	203 (19.5%)	31 (17.8%)	55 (18.5%)	99 (18.0%)	161 (18.4%)	145 (21.2%)	133 (24.4%)
Score = 3	44 (4.2%)	6 (3.4%)	10 (3.4%)	17 (3.1%)	33 (3.8%)	26 (3.8%)	25 (4.6%)
Score = 4	17 (1.6%)	1 (0.6%)	9 (3.0%)	13 (2.4%)	27 (3.1%)	23 (3.4%)	14 (2.6%)
Score = 5	10 (1.0%)	0 (0%)	2 (0.7%)	5 (0.9%)	9 (1.0%)	3 (0.4%)	4 (0.7%)
Score = 6	12 (1.2%)	2 (1.1%)	2 (0.7%)	5 (0.9%)	3 (0.3%)	2 (0.3%)	4 (0.7%)
Anxiety screening, positive							
Score ≥3	83 (8.0%)	9 (5.2%)	23 (7.7%)	40 (7.3%)	72 (8.2%)	54 (7.9%)	47 (8.6%)
Depression screening (PHQ-4, depression subscale)							
Score = 0	481 (46.1%)	80 (46.0%)	141 (47.3%)	237 (43.1%)	403 (46.0%)	272 (39.8%)	202 (37.1%)
Score = 1	265 (25.4%)	50 (28.7%)	72 (24.2%)	140 (25.5%)	199 (22.7%)	163 (23.8%)	117 (21.5%)
Score = 2	242 (23.2%)	37 (21.3%)	67 (22.5%)	137 (24.9%)	216 (24.7%)	201 (29.4%)	175 (32.1%)
Score = 3	29 (2.8%)	3 (1.7%)	12 (4.0%)	18 (3.3%)	31 (3.5%)	25 (3.7%)	26 (4.8%)
Score = 4	17 (1.6%)	2 (1.1%)	5 (1.7%)	11 (2.0%)	18 (2.1%)	19 (2.8%)	22 (4.0%)
Score = 5	3 (0.3%)	0 (0%)	1 (0.3%)	7 (1.3%)	4 (0.5%)	0 (0%)	3 (0.6%)
Score = 6	6 (0.6%)	2 (1.1%)	0 (0%)	0 (0%)	5 (0.6%)	4 (0.6%)	0 (0%)
Depression screening, positive							
Score ≥3	55 (5.3%)	7 (4.0%)	18 (6.0%)	36 (6.5%)	58 (6.6%)	48 (7.0%)	51 (9.4%)

Scores of 3 (or greater) identify potential cases of anxiety or depression. PHQ-4: Patient Health Questionnaire-4.

Table S3 Secondary outcomes in all SARS-CoV-2 phases.

	Pre-SARS-CoV-2	Pre-lockdown	1st lockdown	1st easing	Inter-wave	2nd wave	2nd lockdown
	(N=1043)	(N=174)	(N=298)	(N=550)	(N=876)	(N=684)	(N=545)
Number of sexual partners in previous 3 months							
Median [IQR]	6 [3 – 12]	6 [3 – 12]	5 [3 – 10]	4 [2 – 8]	6 [3 – 10]	5 [3 – 10]	5 [3 – 10]
Sex with casual partners							
Yes	956 (91.7%)	151 (86.8%)	256 (85.9%)	432 (78.5%)	765 (87.3%)	588 (86.0%)	445 (81.7%)
Condom use with casual partners							
Never	362 (34.7%)	76 (43.7%)	142 (47.7%)	317 (57.6%)	429 (49.0%)	357 (52.2%)	309 (56.7%)
Sometimes	427 (40.9%)	73 (42.0%)	98 (32.9%)	169 (30.7%)	321 (36.6%)	229 (33.5%)	172 (31.6%)
Mostly	154 (14.8%)	19 (10.9%)	33 (11.1%)	32 (5.8%)	78 (8.9%)	59 (8.6%)	44 (8.1%)
Always	100 (9.6%)	6 (3.4%)	25 (8.4%)	32 (5.8%)	48 (5.5%)	39 (5.7%)	20 (3.7%)
Adaptation of sexual behavior due to SARS-CoV-2							
No sexual contact	NA	NA	0 (0%)	119 (21.6%)	50 (5.7%)	20 (2.9%)	15 (2.8%)
Reduced sexual contacts			1 (0.3%)	412 (74.9%)	683 (78.0%)	543 (79.4%)	430 (78.9%)
No behaviour change			0 (0%)	12 (2.2%)	135 (15.4%)	115 (16.8%)	89 (16.3%)
Increase in sexual contacts			0 (0%)	7 (1.3%)	8 (0.9%)	6 (0.9%)	11 (2.0%)
Missing	1043 (100%)	174 (100%)	297 (99.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adaptation of dating behavior due to SARS-CoV-2 (use of dating apps)							
Deleted dating app	NA	NA	0 (0%)	15 (2.7%)	14 (1.6%)	5 (0.7%)	4 (0.7%)
Less online dates			1 (0.3%)	315 (57.3%)	359 (41.0%)	275 (40.2%)	200 (36.7%)

Use dating app as usual			0 (0%)	55 (10.0%)	176 (20.1%)	128 (18.7%)	108 (19.8%)
More online dates			0 (0%)	10 (1.8%)	7 (0.8%)	9 (1.3%)	8 (1.5%)
Others			0 (0%)	6 (1.1%)	1 (0.1%)	1 (0.1%)	0 (0%)
Missing	1043 (100%)	174 (100%)	297 (99.7%)	149 (27.1%)	319 (36.4%)	266 (38.9%)	225 (41.3%)
Concern about drug use							
Yes	55 (5.3%)	9 (5.2%)	12 (4.0%)	21 (3.8%)	38 (4.3%)	30 (4.4%)	25 (4.6%)
Chemsex substances intake (past 3 months)							
Yes	179 (17.2%)	29 (16.7%)	39 (13.1%)	75 (13.6%)	147 (16.8%)	111 (16.2%)	92 (16.9%)
Ecstasy intake (past 3 months)							
Yes	175 (16.8%)	25 (14.4%)	24 (8.1%)	52 (9.5%)	102 (11.6%)	59 (8.6%)	48 (8.8%)
Cocaine intake (past 3 months)							
Yes	182 (17.4%)	27 (15.5%)	37 (12.4%)	79 (14.4%)	139 (15.9%)	104 (15.2%)	85 (15.6%)
Cannabis intake (past 3 months)							
Yes	238 (22.8%)	34 (19.5%)	52 (17.4%)	138 (25.1%)	217 (24.8%)	164 (24.0%)	118 (21.7%)
Sexual happiness (10-item numeric scale)							
Median [IQR]	7 [6 – 8]	8 [6 – 8]	7 [5 – 8]	7 [5 – 8]	8 [6 – 8]	7 [5 – 8]	7 [5 – 8]
Financial coping							
Very comfortable	206 (19.8%)	NA	NA	NA	10 (1.1%)	165 (24.1%)	117 (21.5%)
Comfortable	546 (52.3%)				35 (4.0%)	339 (49.6%)	282 (51.7%)
Neither comfortable nor difficult	220 (21.1%)				15 (1.7%)	132 (19.3%)	105 (19.3%)
Difficult	50 (4.8%)				4 (0.5%)	34 (5.0%)	31 (5.7%)
Very difficult	21 (2.0%)				1 (0.1%)	14 (2.0%)	10 (1.8%)
Missing	0 (0%)	174 (100%)	298 (100%)	550 (100%)	811 (92.6%)	0 (0%)	0 (0%)

Taking PrEP at visit							
	880 (84.4%)	154 (88.5%)	233 (78.2%)	509 (92.5%)	832 (95.0%)	651 (95.2%)	518 (95.0%)
PrEP regimen							
Daily, constant	671 (64.3%)	120 (69.0%)	198 (66.4%)	303 (55.1%)	585 (66.8%)	456 (66.7%)	352 (64.6%)
Holiday PrEP	87 (8.3%)	14 (8.0%)	15 (5.0%)	98 (17.8%)	117 (13.4%)	87 (12.7%)	82 (15.0%)
"Event-driven"	115 (11.0%)	17 (9.8%)	17 (5.7%)	88 (16.0%)	118 (13.5%)	98 (14.3%)	75 (13.8%)
Other regimen	6 (0.6%)	2 (1.1%)	3 (1.0%)	20 (3.6%)	10 (1.1%)	9 (1.3%)	8 (1.5%)
Missing	164 (15.7%)	21 (12.1%)	65 (21.8%)	41 (7.5%)	46 (5.3%)	34 (5.0%)	28 (5.1%)
PrEP adherence (i.e. frequency of missed medication)							
In daily PrEP users	*(N=671)*	*(N=120)*	*(N=198)*	*(N=303)*	*(N=585)*	*(N=456)*	*(N=352)*
Never	399 (59.5%)	77 (64.2%)	112 (56.6%)	174 (57.4%)	318 (54.4%)	267 (58.6%)	204 (58.0%)
Once a month	207 (30.8%)	39 (32.5%)	67 (33.8%)	105 (34.7%)	216 (36.9%)	154 (33.8%)	111 (31.5%)
Once every second week	56 (8.3%)	4 (3.3%)	14 (7.1%)	19 (6.3%)	41 (7.0%)	26 (5.7%)	27 (7.7%)
Once a week	6 (0.9%)	0 (0%)	2 (1.0%)	1 (0.3%)	7 (1.2%)	9 (2.0%)	7 (2.0%)
More than once a week	2 (0.3%)	0 (0%)	3 (1.5%)	4 (1.3%)	3 (0.5%)	0 (0%)	3 (0.9%)
Missing	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
In "event-driven" PrEP users	*(N=115)*	*(N=17)*	*(N=17)*	*(N=88)*	*(N=118)*	*(N=98)*	*(N=75)*
Never	97 (84.3%)	11 (64.7%)	12 (70.6%)	69 (78.4%)	89 (75.4%)	81 (82.7%)	63 (84.0%)
Once or twice	17 (14.8%)	5 (29.4%)	5 (29.4%)	18 (20.5%)	24 (20.3%)	16 (16.3%)	9 (12.0%)
Three to five times	1 (0.9%)	1 (5.9%)	0 (0%)	0 (0%)	3 (2.5%)	1 (1.0%)	2 (2.7%)

Six to 10 times	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)	2 (1.7%)	0 (0%)	1 (1.3%)
More than 10 times	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
In holiday PrEP users	*(N=87)*	*(N=14)*	*(N=15)*	*(N=98)*	*(N=117)*	*(N=87)*	*(N=82)*
Never	58 (66.7%)	9 (64.3%)	9 (60.0%)	69 (70.4%)	66 (56.4%)	51 (58.6%)	49 (59.8%)
Once or twice	25 (28.7%)	5 (35.7%)	6 (40.0%)	22 (22.4%)	40 (34.2%)	31 (35.6%)	26 (31.7%)
Three to five times	1 (1.1%)	0 (0%)	0 (0%)	3 (3.1%)	6 (5.1%)	1 (1.1%)	6 (7.3%)
Six to 10 times	0 (0%)	0 (0%)	0 (0%)	1 (1.0%)	1 (0.9%)	2 (2.3%)	1 (1.2%)
More than 10 times	3 (3.4%)	0 (0%)	0 (0%)	2 (2.0%)	3 (2.6%)	1 (1.1%)	0 (0%)
Missing	0 (0%)	0 (0%)	0 (0%)	1 (1.0%)	1 (0.9%)	1 (1.1%)	0 (0%)

Table S4 P-values for pairwise comparison between periods.

Outcome: anxiety screening (PHQ-4, anxiety subscale, scores ranging from 0 to 6), using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.951	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.259	5	1.000	Sample (n)	p-value	**First easing**						
First easing	550	0.916	101	0.803	30	0.755	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.926	141	0.304	262	0.738	462	0.877	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.226	117	0.611	190	0.569	396	0.167	620	0.243	Sample (n)	p-value	**2nd lock-down**
2nd lockdown	545	0.127	89	0.333	152	0.729	316	0.025	492	0.147	378	0.695	
Outcome: depression screening (PHQ-4, anxiety subscale, scores ranging from 0 to 6), using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.69	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.933	5	1.000	Sample (n)	p-value	**First easing**						
First easing	550	0.179	101	0.834	30	0.634	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.210	141	0.884	262	0.632	462	0.643	Sample (n)	p-value	**2nd wave**		
2nd wave	684	<0.001	117	0.372	190	0.172	396	0.256	620	0.005	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	0.146	152	0.094	316	0.154	492	0.005	378	0.509	
Outcome: Number of sexual partners in previous 3 months, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.661	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.004	5	0.361	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	<0.001	30	0.229	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.072	141	0.129	262	0.034	462	<0.001	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.010	117	0.135	190	0.339	396	<0.001	620	0.008	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	0.033	152	0.435	316	0.219	492	0.003	378	0.041	
Outcome: Sex with casual partners, using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.112	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.009	5	0.480	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	0.124	30	0.387	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.001	141	0.451	262	0.755	462	0.002	Sample (n)	p-value	**2nd wave**		
2nd wave	684	<0.001	117	0.473	190	0.728	396	0.211	620	0.047	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	0.081	152	0.188	316	0.353	492	<0.001	378	0.032	

Outcome: Condom use with casual partners, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.181	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.002	5	0.586	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	0.040	30	0.817	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	<0.001	141	0.069	262	0.668	462	0.034	Sample (n)	p-value	**2nd wave**		
2nd wave	684	<0.001	117	0.137	190	0.500	396	0.938	620	0.018	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	0.037	152	0.242	316	0.360	492	0.035	378	0.444	
Outcome: Adaptation of sexual behavior due to Covid-19, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	No data	No data	Sample (n)	p-value	**1st lockdown**								
1st lockdown	No data	No data	No data	No data	Sample (n)	p-value	**First easing**						
First easing	No data	No data	No data	No data	30	NA	Sample (n)	p-value	**Inter-wave**				
Inter-wave	No data	No data	No data	No data	262	NA	462	<0.001	Sample (n)	p-value	**2nd wave**		
2nd wave	No data	No data	No data	No data	190	NA	396	<0.001	620	0.057	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	No data	No data	No data	No data	152	NA	316	<0.001	492	0.663	378	0.196	
Outcome: Adaptation of dating behavior due to Covid-19 (use of dating apps), using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	No data	No data	Sample (n)	p-value	**1st lockdown**								
1st lockdown	No data	No data	No data	No data	Sample (n)	p-value	**First easing**						
First easing	No data	No data	No data	No data	30	NA	Sample (n)	p-value	**Inter-wave**				
Inter-wave	No data	No data	No data	No data	262	1.0	462	<0.001	Sample (n)	p-value	**2nd wave**		
2nd wave	No data	No data	No data	No data	190	NA	396	0.004	620	0.967	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	No data	No data	No data	No data	152	NA	316	<0.001	492	0.691	378	0.194	
Outcome: Concern about drug use, using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.724	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.302	5	NA	Sample (n)	p-value	**First easing**						
First easing	550	0.327	101	1.000	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.281	141	1.000	262	0.606	462	0.646	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.268	117	0.221	190	1.000	396	0.823	620	0.607	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.486	89	1.000	152	0.074	316	1.000	492	1.000	378	1.000	

Outcome: chemsex substances intake (past 3 months), using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.267	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	1.000	5	NA	Sample (n)	p-value	**First easing**						
First easing	550	0.002	101	0.502	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.675	141	0.453	262	0.814	462	0.050	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.229	117	1.000	190	0.789	396	0.050	620	0.391	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.289	89	0.547	152	1.000	316	0.072	492	0.067	378	1.000	
Outcome: Ecstasy intake (past 3 months), using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.628	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	<0.001	5	1.000	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	0.039	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	<0.001	141	0.332	262	1.000	462	0.020	Sample (n)	p-value	**2nd wave**		
2nd wave	684	<0.001	117	0.114	190	0.814	396	0.486	620	0.008	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	0.043	152	0.547	316	1.000	492	0.029	378	0.458	
Outcome: Cocaine intake (past 3 months), using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.773	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.089	5	NA	Sample (n)	p-value	**First easing**						
First easing	550	0.055	101	0.683	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.461	141	1.000	262	0.110	462	1.000	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.048	117	1.000	190	0.146	396	1.000	620	0.419	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.124	89	1.000	152	0.302	316	1.000	492	0.391	378	1.000	
Outcome: Cannabis intake (past 3 months), using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.646	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.265	5	NA	Sample (n)	p-value	**First easing**						
First easing	550	0.457	101	0.332	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.024	141	1.000	262	0.095	462	0.583	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.450	117	0.789	190	0.080	396	0.880	620	0.525	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.810	89	1.000	152	0.066	316	0.082	492	0.028	378	1.000	

Outcome: Sexual happiness (10-item numeric scale), using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.392	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.046	5	1.000	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	0.027	30	0.273	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	0.502	141	0.053	262	0.019	462	<0.001	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.005	117	0.346	190	0.592	396	0.110	620	0.006	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.008	89	0.489	152	0.533	316	0.316	492	0.011	378	0.680	
Outcome: Financial coping, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	No data	No data	Sample (n)	p-value	**1st lockdown**								
1st lockdown	No data	No data	No data	No data	Sample (n)	p-value	**First easing**						
First easing	No data	No data	No data	No data	No data	No data	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	1.0	No data	No data	No data	No data	No data	No data	Sample (n)	p-value	**2nd wave**		
2nd wave	684	0.469	No data	No data	No data	No data	No data	No data	620	1.000	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.562	No data	No data	No data	No data	No data	No data	492	0.149	378	0.687	
Outcome: Taking PrEP at visit, using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	0.185	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	0.090	5	0.480	Sample (n)	p-value	**First easing**						
First easing	550	0.003	101	1.000	30	1.000	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	<0.001	141	0.190	262	<0.001	462	0.337	Sample (n)	p-value	**2nd wave**		
2nd wave	684	<0.001	117	0.450	190	<0.001	396	0.165	620	0.296	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	<0.001	89	1.000	152	<0.001	316	0.831	492	0.486	378	0.327	
Outcome: PrEP regimen, using McNemar test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	174	NA	Sample (n)	p-value	**1st lockdown**								
1st lockdown	298	NA	5	NA	Sample (n)	p-value	**First easing**						
First easing	550	<0.001	101	NA	30	NA	Sample (n)	p-value	**Inter-wave**				
Inter-wave	876	NA	141	NA	262	NA	462	0.004	Sample (n)	p-value	**2nd wave**		
2nd wave	684	NA	117	NA	190	NA	396	0.170	620	NA	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	545	0.008	89	NA	152	NA	316	0.347	492	0.440	378	NA	

Outcome: PrEP adherence (i.e. frequency of missed medication) in daily PrEP users, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	98	0.336	Sample (n)	p-value	**1st lockdown**								
1st lockdown	163	0.622	3	1.000	Sample (n)	p-value	**First easing**						
First easing	260	0.376	54	0.120	17	0.251	Sample (n)	p-value	**Inter-wave**				
Inter-wave	491	0.180	87	0.109	170	0.789	244	0.552	Sample (n)	p-value	**2nd wave**		
2nd wave	389	0.453	78	0.065	123	0.153	203	0.785	401	0.644	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	299	0.224	52	0.092	91	0.710	164	0.666	307	0.309	237	0.436	
Outcome: PrEP adherence (i.e. frequency of missed medication) in "event-based" PrEP users, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	6	1.0	Sample (n)	p-value	**1st lockdown**								
1st lockdown	5	0.773	0	NA	Sample (n)	p-value	**First easing**						
First easing	19	0.345	1	NA	1	NA	Sample (n)	p-value	**Inter-wave**				
Inter-wave	22	0.967	4	1.000	5	1.000	24	1.000	Sample (n)	p-value	**2nd wave**		
2nd wave	24	0.618	5	0.149	3	1.000	20	0.276	30	0.286	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	14	0.608	3	0.346	5	1.000	20	0.356	29	0.686	18	0.454	
Outcome: PrEP adherence (i.e. frequency of missed medication) in "holiday PrEP" users, using Wilcoxon Signed Rank test													
	Pre-SARS-CoV-2												
Pre-SARS-CoV-2	Sample (n)	p-value	**Pre-lockdown**										
Pre-lockdown	11	0.346	Sample (n)	p-value	**1st lockdown**								
1st lockdown	10	0.424	0	NA	Sample (n)	p-value	**First easing**						
First easing	42	0.167	7	1.000	2	NA	Sample (n)	p-value	**Inter-wave**				
Inter-wave	50	0.644	9	0.346	5	0.773	40	0.660	Sample (n)	p-value	**2nd wave**		
2nd wave	40	0.565	10	0.586	7	0.149	38	0.484	49	0.644	Sample (n)	p-value	**2nd lockdown**
2nd lockdown	26	0.407	5	0.174	3	1.0	24	1.000	35	0.608	32	0.644	
Cells highlighted in green indicate a statistically significant result (p<0.002); PHQ-4: Patient Health Questionnaire-4													

Supplementary Fig. 1. Timeline of main measures implemented to mitigate the SARS-CoV-2 transmission in Switzerland until March 22, 2021