Randomized Re-Opening of Training Facilities during the COVID-19 pandemic

The TRAiN study group

(Lise M. Helsingen[1]* MD, Magnus Løberg[1]* MD PhD, Erle Refsum[1] MD PhD, Dagrun Kyte Gjøstein[1] MA, Paulina Wieszczy[1] PhD, Ørjan Olsvik[2] PhD, Frederik E. Juul[1] MD, Ishita Barua[1] MD, Henriette C. Jodal[1] MD, Magnhild Herfindal[1] medical student, Yuichi Mori[1] MD PhD, Solveig Jore[3] DVM PhD, Fridtjof Lund-Johansen[4] MD PhD, Atle Fretheim[3] MD PhD, Michael Bretthauer[1]* MD PhD, Mette Kalager[1]* MD PhD, et al)

*these authors contributed equally

[1] Clinical Effectiveness Research Group, University of Oslo and Oslo University Hospital, Oslo, Norway

[2] Institute of Medical Biology, Norwegian Arctic University, Tromsø, Norway

[3] Norwegian Institute of Public Health, Oslo, Norway

[4] Department of Immunology, Oslo University Hospital, Oslo, Norway

Corresponding author:

Lise M Helsingen, MD

Clinical Effectiveness Research Group

University of Oslo

Postbox 1089 Blindern, 0317 Oslo, Norway

Email: l.m.helsingen@medisin.uio.no

Abstract

Background: Most countries closed training facilities during the COVID-19 pandemic. This may have negative consequences for people's health and wellbeing. We investigated SARS-CoV-2 virus transmission and COVID-19 disease attributable to training facilities.

Methods: We randomized members 18 to 64 years with no COVID-19 relevant comorbidities randomized Five training facilities in Oslo, Norway to access or no access to their training facility. Facilities were opened from May 22, 2020 for individuals randomized to training, applying increased social distancing (1 meter for floor exercise, 2 meters for high-intensity classes), enhanced hand and surface hygiene. Locker rooms were open, showers and saunas were closed. We measured SARS-CoV-2 PCR status by self-administered naso-, oropharyngeal and sputum sampling after two weeks and clinical disease by linkage to electronic patient records after three weeks.

Results: 3,764 individuals were randomized and included in analyses; 1,896 in the training and 1,868 in no-training arms. In the training arm, 81.8% trained at least once at the facilities, and 38.5% trained ≥six times. Out of 3,016 individuals who returned the SARS-CoV-2 PCR tests (80.5%), there was one positive test. The positive individual was randomized to training, but had not used the facility before testing day. Contact tracing revealed the workplace as transmission source. A total of 106 individuals (2.8%) had outpatient hospital visits, and six individuals were admitted to hospital during the three weeks after intervention start, with no differences between arms. There were no outpatient visits or hospital admissions due to COVID-19 in either group.

Conclusions: Provided good hygiene and social distancing measures, there was no increased COVID-19 spread at training facilities. NCT04406909

Introduction

Governments and health policy makers around the world have been taking preventive measures against COVID-19 exceeding previous pandemics (1). Social distancing such as increasing distance between individuals (minimum 1 or 2 meters) is of paramount importance to contain spread of COVID-19. Many countries have closed or restricted access to schools, stores, restaurants, and work places to achieve social distancing (2).

While increased social distancing between individuals may involve little disturbance for daily life, closures of schools, recreational activities and work places have potentially large consequences for education, health and wellbeing, and personal and societal economy. Thus, it is important to test social distancing measures properly, to gain knowledge about their negative consequences and their impact on preventing virus spread (3). Due to the uncertainty of contagiousness, immunity, morbidity and mortality of COVID-19, it is unclear how to resume activities without risking increased spread of COVID-19.

Training and exercise is important for health and wellbeing. In many countries, training facilities and gyms are an important part of training and exercise for individuals, and for population health. In Norway, by governmental emergency law, all training facilities and gyms have been closed since March 12, 2020 (4,5). Surveys have indicated that Norwegians have a more sedentary lifestyle and exercise less than before the restrictions (6). It is important to restrict unnecessary closure of training facilities to prevent societal downsides of the epidemic and negative effects on health and wellbeing.

Many countries have introduced general rules for social distancing (1 meter distance, avoid body contact and greetings), and hygiene measures (hand wash and disinfection). These

measures have been widely accepted and followed. However, there is little scientific evidence available about the benefits and harms of closing training facilities for COVID-19 as a preventive measure of virus spread.

We hypothesised that the risk of SARS-CoV-2 transmission in training facilities with good hygiene and social distancing measures would be low, and thus safe to re-open to ensure health and wellbeing. This report describes the randomized testing of re-opening training facilities with close monitoring of COVID transmission and disease activity to understand the impact of training facilities closure for COVID-19.

Methods

All training facilities in Norway have been closed by governmental restriction during COVID-19 since March 12, 2020. For the purpose of the trial, five training facilities in Oslo, operated by three professional companies in Norway, opened their premises to participants randomized to training for the period of the trial. The training facilities were SATS Sjølyst and CC Vest (SATS Norway Inc., Oslo, Norway), STOLT Stovner and Rommen (STOLT Trening Inc, Oslo, Norway), and EVO Bryn (EVO Fitness Group Inc, Oslo, Norway). Facilities which did not participate in the project remained closed, and participants in the no-training control arm did not have access.

Eligible participants

All members of the five participating training facilities age 18 years or older who are not at increased risk for severe COVID-19 disease per criteria by the Norwegian Institute of Public Health, were eligible for participation. The criteria for high risk are at least one of the following: age 65 years or older; cardiovascular disease including hypertension; diabetes (https://www.fhi.no/nettpub/coronavirus/fakta/risikogrupper/, accessed May 15, 2020).

Eligible individuals were approached by email by their training facilities through member lists. Individuals signed up for the study through a secure website at the University of Oslo. Co-morbidities were assessed by self-assessment. A direct contact telephone line and email address to the study team was established for interested individuals in case of uncertainty of their medical status related to comorbidities, and other questions. All eligible individuals were informed about the nature of the trial, and provided consent before randomization.

Interventions

We randomized eligible individuals to either current practice which was no access (no-training arm), or to access (training arm) with mitigation measures as described by the "Norwegian guidelines for Hygiene and Social Distancing in Training Facilities during the COVID-19 Pandemic", available at https://t-i.no/wp-content/uploads/2020/04/Bransjestandard-for-sentre.pdf.

In brief, the following measures recommended in the guideline were implemented at all facilities during the trial period: Avoidance of handshake and other body contact; 1 meter distance between individuals at all times; 2 meter distance for high intensity activities such as spinning, workout classes; provision of disinfectants at all work stations; cleaning requirements of all equipment after each use by member; regular cleaning of facilities by personnel; and access control by entrance personnel to ensure distance measures and avoid overcrowding. Changing rooms were open, but showers and saunas remained closed. Staff was present during all opening hours. Lids on trash cans were removed. Individuals were advised to stay home if they had any COVID-19 related symptoms. No masks were required, but members were advised to avoid touching their eyes, nose and mouth.

Activities for the training arm included services the gyms provide ordinarily, including floor training facilities, group classes for spinning, exercise, yoga and other activities. Individuals in the no-training arm did not get access to any of the services inside the training facilities, along with all other members of training facilities in Norway during the trial period.

Intervention timeline

Individuals were approached between May 15 and May 24, 2020. Randomization of eligible individuals approved for participation took place successively between May 20 and May 25, 2020. The five training facilities opened their premises for individuals in the training group on May 22, 2020. Individuals randomized to the no-training arm were informed about their status as controls and did not have access to the facilities. Access control was ensured by the facilities.

Virus testing

All individuals in both groups were mailed a home-test kit including two swabs and a tube with virus transport medium for SARS-CoV-2 RNA. The tests were analysed with a commercially available real-time SARS-CoV-2 RT-PCR test (Cobas®, Roche Diagnostics Inc.) at the Department of medical microbiology, Oslo University Hospital. Participants were instructed to sample from the oropharynx, nose and saliva according to national guidelines (https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2020/saliva-sample-for-testing-sars-cov-2-infection-memo-2020.pdf) after median two weeks of training access in the training arm (June 8 or 9) and deliver the test to their training facility. Dedicated study personnel provided onsite collection of all tests, and helped sampling for those who did not want to self-sample, at all five facilities on June 8 and 9, 2020. The facilities remained open

for individuals in the training arm for an additional 7 days after testing, but remained closed for the no-training arm. We also offered SARS-CoV-2 RNA testing to all training facility employees who were in contact with individuals in the intervention arm.

Transmission and contact tracing of individuals positive for SARS-CoV-2 RNA were performed by trained personal of the Norwegian Institute of Public Health according to the Norwegian law for communicable disease, and included interviews with the affected individuals and their contacts, guidance for isolation measures, and referral to health care services if needed.

A commercially available rapid self-sampling kit, for dried blood spots for testing for SARS-CoV-2 antibodies, will be mailed to all participants between 3 and 4 weeks after study start, and will be mailed back in a prepaid envelope. The antibody testing will be performed at Oslo University Hospital.

Clinical endpoint assessment

On June 15, 2020 (three weeks after study start), we retrieved all admissions and outpatient contacts for all somatic diagnoses (ICD-10 coding); ICU admissions, ventilator treatment, and death for all individuals in both arms from the trial area hospital databases for electronic patient records. Norway has a public, single-payer hospital system with full coverage of data for all individuals. Thus, our data are 100% complete. For individuals with diagnoses which may relate to COVID-19, we contacted physicians at the respective hospitals for details to investigate if the contact was related to COVID-19.

Study endpoints

The primary study endpoint was the proportion of SARS-CoV-2 positive individuals in the two study arms after 14 days. Co-primary endpoint was hospital admission in the two arms after 21 days. Future long-term secondary project endpoints will include the proportion of individuals with SARS-CoV-2 antibodies in the two study arms after 30 days; comparison of ICU admission and ventilator treatment; and death of COVID-19 after three months.

Population Data on COVID-19

From publicly available sources by the Norwegian Institute of Public Health (www.fhi.no) and the Norwegian Directorate of Health (www.helsedirektoratet.no), we retrieved data on number and rates of SARS-CoV-2 positive individuals, hospital admissions, intensive care treatment and death due to COVID-19 in the trial area during the study period.

Sample size and statistics

We assumed non-inferiority of training versus no-training with regard to SARS-CoV-2 transmission and hospital admission. Based on the most recent update of COVID-19 before the start of the trial from the Norwegian Institute of Public Health (May 11, 2020), we assumed that 1% of individuals in in each group would test positive for SARS-CoV-2 at the end of the intervention. We defined the smallest meaningful difference for SARS-CoV-2 transmission to be 1% between the two arms. Thus, the non-inferiority margin would be 1% for the training arm as compare to the no-training arm. For a power of 90% with an alpha of 0.05, we planned to include at least 1,696 individuals in each arm. See the trial protocol for further power calculations for transmission rates and hospital admission.

Participants were followed for the primary and secondary endpoints as described above. The primary analytic approach of the trial follows the intention-to-treat (ITT) principle. We

compared the differences in event rates for the trial endpoints between the arms by chi-square test. Due to small numbers, we did not perform significance testing for all diagnosis sub-groups (table 2). Analyses were performed using Stata Statistical Software release 16 (StataCorp LLC, College Station, TX.)

The study was approved by the Regional Ethical Committee of South-East Norway and the data protection officers at participating sites. All individuals provided written informed consent before enrolment. An Independent Data Safety and Monitoring Committee (DSMB) was established to ensure adequate handling of all data and trial participants.

Results

The trial area was the city of Oslo with surrounding municipalities with a total population of 821,000. One week before the start of the trial, the facilities approached members between 18 and 64 years living in the trial area by email and asked for interest in participating in the trial.

In total, 3,938 individuals signed up for the trial online and provided written consent. Before randomization and intervention start, the study team found 174 individuals ineligible (10 were not members at the participating facilities; 55 were outside the eligible age range; 9 fulfilled one or more exclusion comorbidities; seven were employees at the participating facilities; and 73 withdrew consent. Thus, 3,764 individuals were randomized and included in the analyses; 1,896 in the training arm and 1868 in the no-training arm (figure 1). Table 1 displays participant characteristics and shows that the arms were well-balanced. There were 1,929 female and 1,835 male participants, the majority was between 20 and 50 years old.

COVID-19 in Oslo during the trial

During the trial period, 4,408 individuals in Oslo were tested for SARS-CoV-2 outside the trial. The number of new PCR-confirmed COVID-19 cases was 207; 85 in the first week and 122 in the second week of the trial. The rate of positive tests of all tests taken in Oslo outside the trial increased from 1.1% in the first week to 3.6% in the second week of the trial (rates per 100,000: 3.5 in first week, 11.7 in second week). The daily number of patients who were in hospital in Oslo due to COVID-19 decreased gradually during the trial period, from 35 patients on May 22 to 21 patients on June 8, 2020.

Training activity

Among individuals randomized to training, a large majority (81.8%) trained at least once at the facility, and 38.5% trained six times or more (table 1).

COVID-19 transmission

After the two-week trial period, 88.7% of the individuals randomized to training and 71.4% of those randomized to no-training performed the SARS-CoV-2 PCR test, for a total of 3,016 tests. There was one positive test; in an individual randomized to the training arm (table 2). Investigations including interviews and environment checks for the case revealed that the individual did not use the training facility during the trial period until the day of the SARS-CoV-2 sampling. The individual had been present at the workplace where two other individuals had tested positive for SARS-CoV-2 shortly before the participant tested positive in the trial. Thus, transmission was most likely unrelated to the trial intervention, and there was no transmission during trial intervention related to the case.

Clinical disease

During the trial period, a total of 106 outpatient contacts for somatic disease were registered for 106 (2.8%) trial participants in the hospitals serving the trial area (table 2). There were six hospital admissions of trial participants; 4 in the training arm and 2 in the no-training arm. Five of the registered hospital contacts or admissions were unrelated to any COVID-19 associated condition or symptom. One patient was admitted with pulmonary embolism. We contacted the attending physician who after chart review ruled out that the condition was related to COVID-19. Thus, no trial participants in any of the two arms had hospital admissions or outpatient visits for COVID-19 (figure 1, table 2).

Employees

Out of 91 employees who worked at the training facilities during the trial period and agreed to provide data, 83 (91.2%) were tested for SARS-CoV-2. None were positive.

Discussion

Our trial showed no virus transmission or increase in COVID-19 disease related to opening of trainings facilities providing good hygiene and social distancing routines. The difference in SARS-CoV-2 test positivity between the training and no-training arms was 0.05% (one versus zero cases), well below the predefined non-inferiority margin of 1%.

By emergency law, all training facilities were closed in Norway during the pandemic. The closure was reasoned by the assumption that training activity at the facilities would increase the risk of virus transmission between members of the facilities and thus COVID-19 disease among members, staff and the community. However, basic hand hygiene and social distancing measures by securing 1 to 2 meters distance between individuals are well-proven

and important virus transmission protection measures. They are inexpensive, easy to apply, and do not require large resources.

During the COVID-19 pandemic, countries introduced closure of important societal activities because it was assumed that the simple measures would not be enough to contain virus transmission. However, if virus containment, including contact tracing and quarantine, hand hygiene and personal social distancing measures are sufficient to prevent virus spread, closures could be avoided and thus harms reduced. Our trial sought to test if closure of training facilities is needed, or if open facilities can provide enough hygiene and social distancing to prevent virus spread.

If hygiene and distancing measures could be achieved, we assumed it would be safe to open training facilities. For the purpose of the trial, the research group and the Norwegian training facility association (Virke Training) established national mitigation guidelines for hygiene and social distancing for training facilities in Norway in collaboration with the Norwegian Institute of Public Health. The guidelines were used in the trial and enforced by employees at the facilities at all times. The results of our trial shows that with these easy and simple-to-adhere mitigations, training facilities are safe and may be allowed to re-open.

The primary concern with COVID-19 is clinical disease, measured as hospital admission, need for ventilator support, and death. As a surrogate, positivity for SARS-CoV-2 RNA is often used. However, high SARS-CoV-2 RNA test positivity in individuals or groups of individuals is not necessarily a surrogate for seriousness of COVID-19 disease in a population, because SARS-CoV-2 infected individuals who do not themselves become seriously ill or who do not transmit the disease to others who become seriously ill, may

contribute to achieve immunity in the population and thus contain the disease. Therefore, we measured both SARS-CoV-2 positivity and incidence of COVID-19 disease to understand the relationship of the surrogate outcome with the clinically significant disease outcomes. As our results show, there was no increase in COVID-related disease due to the opening of training facilities.

Our trial was limited by the low number of events in both arms. Only one individual tested positive for SARS-CoV-2, and there was no clinical COVID-19 disease during the trial. As shown, there was indeed COVID-19 activity in Oslo during the study period, with both new cases and patients outside of the trial admitted to hospital. Our results may thus reflect the low risk of transmission and clinical COVID-19 disease in healthy individuals without COVID-19 risk factors, who were those who participated in the trial. We believe our trial population is representative of many users of training facilities and the results may thus be applied to other regions and countries (7). However, it is unclear if our findings also apply to areas with higher COVID-19 incidence rates.

Our sample size was based on estimates from prevalence testing in the community for COVID-19 activity. Most individuals in community testing had clinical signs or symptoms suspicious for COVID-19. Thus, in accordance with recent evidence from population sampling in Iceland (7), we assumed considerably higher SARS-CoV-2 rates in our sampling of individuals with no symptoms. This was not confirmed, as our observed rate in the trial was similar to those in the community.

Compliance with SARS-CoV-2 testing was slightly higher in the training arm (89%) than in the no-training arm (71%). However, both compliance rates are high and we consider them

satisfactory to provide valid results. Disease endpoints in the trial were gathered through complete hospital registries and thus are not prone to self-reporting bias. We did not have any missing data for clinical disease. Finally, the number of individuals who withdrew consent after randomization to the no-training group was small, and there were no participants who withdrew after intervention start.

It is important to perform randomized implementation and de-implementation of societal measures with large potential harms and burden for individuals and the population at large. Our study showed that it is feasible to apply rigorous randomized testing of public health measures during an ongoing disease outbreak. We have demonstrated that such testing is doable, and demonstrated that it is safe to re-open training facilities in Norway. The Norwegian government indeed allowed re-opening of all facilities as of June 15, 2020, provided the hygiene and social distancing measures applied in the trial can be followed. We are currently planning new randomized testing towards normal activity at Norwegian training facilities, according to the principles of rapid-cycle randomized implementation for health care services (8,9).

Acknowledgments

In addition to the authors mentioned above, the TRAiN study group comprised the following individuals: Anita Aalby, Madeleine Berli, Siv Furholm, Anne-Lise Horvli (all University of Oslo, Oslo, Norway); Line Norum (STOLT Training, Oslo, Norway); Halvor Lauvstad, Judit Somogyi (both EVO Training, Oslo, Norway); Alexander Myers, Tonje Poulsson, Wenche Evertsen (all SATS Training, Oslo, Norway); Hilde Sandvoll and Kjersti Oppen (both Virke Training, Oslo, Norway). The DSMB consisted of Katja Fall MD, PhD, Örebro University, Sweden, and Dag Berild MD, PHD, Oslo University Hospital. We thank the Department of

Medical Microbiology at Oslo University Hospital for virus testing, the hospitals in the Oslo region for their support with the clinical data, and all staff at the participating training facilities for their engagement and enthusiasm to establish this trial on very short notice.

Author Contributions

Conception and design: M. Bretthauer, M. Kalager, M. Løberg, L. Helsingen

Analysis and interpretation of the data: all authors

First draft of the article: M. Bretthauer

Critical revision of the article for important intellectual content: all authors

Final approval of the article: all authors

Collection and assembly of data: all authors

REFERENCES

1. WHO Director-General. 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 (accessed march 13, 2020)
2. Flaxman S, Mishra S, Gandy A, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature 2020. https://doi.org/10.1038/s41586-020-2405-7
3. Ioannidis JPA. A fiasco in the making? As the coronavirus pandemic takes hold, we are making decisions without reliable data. STAT. March 17, 2020. https://www.statnews.com/2020/03/17/a-fiasco-in-the-making-as-the-coronavirus-pandemic-takes-hold-we-are-making-decisions-without-reliable-data/?fbclid=IwAR3Ss4Qb8MM3EN_BxPFCetD2uF4usls_IP5AV1Iy9E0d54IpfryZMyIgB9g (accessed June 21, 2020)

4. https://lovdata.no/dokument/SF/forskrift/2020-03-27-470#KAPITTEL_3 (accessed June 21. 2020)
5. https://lovdata.no/dokument/LTI/forskrift/2020-04-16-803
6. Helsingen LM, Refsum E, Kyte Gjostein D, et al. Trust, threats, and consequences of the COVID-19 pandemic in Norway and Sweden: A comparative survey. doi: https://doi.org/10.1101/2020.05.16.20089953
7. Gudbjartsson DF, Helgason A, Jonsson H, et al. Spread of SARS-CoV-2 in the Icelandic Population. N Engl J Med 2020, April 14, 2020. DOI: 10.1056/NEJMoa2006100
8. Horwitz LI, Kuznetsova M, Jones SA. Creating a Learning Health System through Rapid-Cycle, Randomized Testing. N Engl J Med 2019;381:1175-81.
9. Kalager M, Bretthauer M. Improving cancer screening programs. Science 2020;367:143-44

Table 1: Characteristics of the trial participants in the training and no-training arms, and of the employees working at the training facilities during the trial. All data in numbers (%).

	Total	Training arm	No-Training arm
Trial participants	N (%)	N (%)	N (%)
Individuals	3764	1896 (50.4)	1868 (49.6)
Sex			
Women	1929	974 (50.5)	955 (49.5)
Men	1835	922 (50.2)	913 (49.8)
Age at enrolment			
18-20 years	91	46 (50.5)	45 (49.5)
21-30 years	1278	643 (50.3)	635 (49.7)
31-40 years	1113	564 (50.7)	549 (49.3)
41-50 years	709	366 (51.6)	343 (48.4)
51-60 years	478	236 (49.4)	242 (50.5)
61-65 years	95	41 (43.2)	54 (66.8)
Training activity [1]			
0 times		345 (18.2)	1868 (100)
1-2 times		314 (16.6)	0
3-5 times		435 (22.9)	0
6-10 times		464 (24.5)	0
More than 10 times		221 (11.7)	0
Employees			
Individuals	81		
Sex			
Women	56		
Men	25		
Age at enrolment			
18-20 years	3		
21-30 years	19		
31-40 years	24		
41-50 years	20		
51-60 years	14		
61-65 years	0		

[1] Times trained at training facility during study period (data were available from four of the five facilities)

Table 2: COVID-19 virus testing and clinical disease in the training and no-training arms. All data in numbers (%).

	Total (3764 individuals)	**Training arm** (1896 individuals)	**No-training arm** (1868 individuals)	**P-value**
SARS-CoV-2 tests	3016 (80.1)	1682 (88.7)	1334 (71.4)	
Positive SARS-CoV-2 tests	1	1[1] (0.05)	0	0.37
COVID-19 hospital admissions	0	0	0	
Non-COVID-19 related hospital admissions	6 (0.16)	4 (0.22)	2 (0.11)	0.59
Cardiovascular	1	1	0	
Gastroenterology	1	0	1	
Surgery[2]	3	3	0	
Gynecology	1	0	1	
COVID-19 outpatient contacts	0	0	0	
Non-COVID-19 outpatient contacts	106 (2.8)	48 (2.5)	58 (3.1)	0.03
Surgery[2]	46	20	26	
Gynecology	15	8	7	
Endocrinology/nephrology	12	6	6	
Cardiovascular	4	3	1	
Pulmonology	3	2	1	
Gastroenterology	6	0	6	
Dermatology	3	2	1	
Oncology	9	3	6	
Neurology	8	4	4	

[1]Infection not related to training activity

[2] Surgery includes orthopedics and Ear-Nose-Throat

Figure 1: Study flowchart and graphical abstract