Supplement 2

Supplemental Online Content

Brunvoll SH, Nygaard AB, Ellingjord-Dale M et al; Prevention of covid-19 and other acute respiratory infections with cod liver oil supplementation, a low-dose vitamin D supplement: quadruple blinded, randomised placebo controlled trial

The authors have provided this supplement to give readers additional information about the trial.

sTable 1. Analysed levels of the vitamin A, D and E in the cod liver oil and the placebo (corn oil).

	Vitamin A[a] (µg/ml)	**Vitamin D[b] (µg/ml)**	**Vitamin E[c] (mg/ml)**
Cod liver oil batches			
SN202484	59	2,4	0,6
SN202472	57	2,3	0,6
SN202462	60	2,4	0,6
SN202444	61	2,4	0,6
Placebo (corn oil) batches			
SN202432	3,9	0	0,732
SN202422	3,5	0	0,742
SN202412	3,3	0	0,771
SN202402	1,9	0	0,808

[a]The content of vitamin A (retinol OH) was determined in the unsaponifiable fraction by the use of HPLC and UV detection.
[b]The content of vitamin D (cholecalciferol) was determined by the use of HPLC and UV detection.
[c]The content of vitamin E was determined by the use of HPLC and UV detection.

sTable 2. Randomisation round, date, and the number of participants.

	Randomisation	
Round	Date	Number (%) of participants
1	19 November 2020	25 577 (73.6)
2	6 December 2020	5 396 (15.5)
3	23 February 2021	2 627 (7.6)
4	13 April 2021	1 141 (3.3)

sAppendix 1 The questions of the baseline and reporting questionnaires

Translation of the enrolment questionnaire, baseline questionnaire and reporting questionnaires

Translation of enrolment questionnaire

Check all the boxes which are relevant to you

I have had, or have, one of the following conditions or diseases: kidney failure or dialysis, hypercalcemia (elevated levels of calcium), severe liver disease (cirrhosis), sarcoidosis or other granulomatous diseases (Wegener)

I am intolerant to fish oil or corn oil

I have trouble swallowing cod liver oil or other oils

I am pregnant or planning to become pregnant within the next year

None of the above

Translation of relevant parts of the baseline questionnaires

General information about the participant

Sex

Male

Female

Other

Enter your age:

(Open number field)

What is your height in centimetres?

(Open number field)

What is your weight in kilos?

(Open number field)

Are you a smoker?

Yes

No, I have never smoked

Yes, I was a smoker before

Yes, I vape

Don’t know

Check off any illnesses or conditions you have.

You can tick one option per condition.

Chronic heart disease including congenital heart disease (not high blood pressure)

Yes

No

Don’t know

High blood pressure

Yes

No

Don’t know

Chronic lung disease (other than asthma)

Yes

No

Don’t know

Asthma

Yes

No

Don’t know

Diabetes

Yes

No

Don’t know

On immunosuppressive treatment

Yes

No

Don’t know

Cancer (being treated)

Yes

No

Don’t know

I would say my physical condition is:

Poor

Average

Good

What is the ethnical background of your parents?

Multiple answers are possible, if other please specify in the next question.

Europe

Africa

Asia

Other

If other ethnical background, please specify

(Open text field)

Sun exposure and vitamin D

What is your skin type?

Will easily turn red and rarely if ever tanned. I have light, sensitive skin and sometimes freckles.

Will almost always turn red and sometimes tanned.

Will be red sometimes, but always tanned after a while.

Will never be red, always tanned.

Naturally black/tanned skin.

How many hours have you spent in the sun during the months of July-October 2020?

The number of <u>hours</u> in the sun in total with the arms or other parts of the body uncovered by clothing.

0 hours

1-10 hours

11-30 hours

31-50 hours

Over 50 hours

Do you use cod liver oil?

Yes, all year

Yes, but only in the winter

No

How often do you take cod liver oil?

Every day

5-6 days a week

3-4 days a week

1-2 days a week

Less than 1 day a week

Do you take any supplements containing vitamin D?

Some examples are supplements containing only vitamin D, multi-vitamin supplements or a combined supplement with vitamin D and omega-3 fatty acids.

Cod liver oil is NOT to be included here.

Yes, all year

Yes, only in the winter

No

How often do you take supplements containing vitamin D?

Every day

5-6 days a week

3-4 days a week

1-2 days a week

Less than 1 day a week

How often do you eat fatty fish?

Fatty fish includes salmon, trout, halibut, mackerel, herring, and eel.

Never/rarely

1-3 times per month

1-2 times per week

3-4 times per week

5 times or more per week

How many slices of bread with fatty fish do you eat per week

Fatty fish includes salmon, trout, halibut, mackerel, herring, and eel.

Less than 1

1-3 slices

4-7 slices

8-14 slices

15 slices or more

Information about the participant's household and socioeconomic status

How many live in your household?

Number of people, including yourself (the ones you share a bathroom and/or kitchen with).

1 (I live alone)

2

3

4

5

6

More than 6

How many children (below the age of 18 years old) live in your household?

0

1

2

3

4

5

More than 5 children

What is your highest completed level of education?

Primary school (up to 10 years "grunnskole", 7 years "folkeskole" or similar)

High school or vocational training

College or university, less than 4 years

College or university, 4 years or more

Other

What is your highest completed level of education?

Open text field

What is the estimated total income of your household, before taxes?

Less than 300 000 NOK

300 000 - 600 000 NOK

600 000 – 1 000 000 NOK

More than 1 million NOK

What is your current employment situation?

More than one answer is possible.

Employed

Stay at home

Unemployed

Retired (due to age)

On sick leave/social security benefits

Student

Temporarily laid off

Vaccination, covid-19 testing and respiratory tract infections

I have been tested for coronavirus in the throat and/or nose

Complete this question even if you have stated to have tested positive previously.

Yes, and at least one test was positive, and I have/ have had coronavirus

Yes, but the test(s) is/are negative

Yes, and I am waiting for the results

No, I have not been tested.

Are you, or have you been, hospitalised due to coronavirus?

Yes

No

How many days have you been admitted?

(Open number field)

Are/were you admitted to the intensive care ward?

Yes

No

I don’t know

Translation of the reporting questionnaires

(The reporting questionnaire was distributed up to six times during the trial in slightly different versions.)

Vaccination, covid-19 testing and respiratory tract infections

I have been tested for coronavirus in the throat and/or nose

Complete this question even if you have stated to have tested positive previously.

Yes, and at least one test was positive, and I have/ have had coronavirus

Yes, but the test(s) is/are negative

Yes, and I am waiting for the results

No, I have not been tested.

Are you, or have you been, hospitalised due to coronavirus?

Yes

No

How many days have you been admitted?

(Open number field)

Are/were you admitted to the intensive care ward?

Yes

No

I don't know

Check off all the symptoms you had in the period you got tested (in the nose and/or throat) for coronavirus.

State how long each symptom lasted.

This can be before or after the sampling of the nose and/or throat. Check the boxes for the symptoms you had/did not have in the period you were tested for coronavirus

Fever

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

High fever (measure to be higher than 39 °C)

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Heavy breathing (dyspnoea)

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Cough

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Fatigue

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Muscle aches

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Sore throat

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Impaired sense of smell/taste

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Stuffy or runny nose

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Headache

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Stomach pain/nausea/diarrhoea

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Memory issues

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Issues concentrating or thinking

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Other symptoms

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

No symptoms

I did not have this symptom

1-7 days

8-21 days

More than 21 days

I still have this symptom

Expand on what other symptoms you experienced when you had covid-19:

(Open text field)

Have you been vaccinated against covid-19?

Yes

No

If you answered yes, how many times have you received the covid-19 vaccine?

1

2

3, or more

Estimate the date of your last dose of vaccine

(Date field, DD.MM.YYYY)

How many times have you had light infections in the last 6 months?

For instance, a cold, the flu and urinary tract infections without hospitalisation. Covid-19 is NOT to be included here.

0

1-2

3-4

5-6

More than 6 times

How many of these were upper respiratory tract infections?

For instance, a cold, cough or sore throat without hospitalisation.

0

1-2

3-4

5-6

More than 6 times

How many times have someone in your household had an upper respiratory tract infection in the past 6 months?

For instance, a cold, cough or sore throat without hospitalisation. The total number of the household, including yourself.

0

1-5

6-10

11-15

More than 15 times

Compliance with the trial

Use of cod liver oil or placebo
Approximately how long have you taken cod liver oil/placebo?
Give an estimate. If you have had pauses, sum up the total time you have been taking the oil.
0-1 Months

2-3 Months

4-5 Months

6 Months

I have not taken the oil

I took the oil in a period, but have now quitted

Which date did you start taking the cod liver oil/placebo?

Date field

During the past two weeks, how many days have you taken cod liver oil/placebo?

Think of the past two weeks. If you have doubled the dose the day after you have forgotten a dose then count the dose as taken.

Every day

Forgotten 1 day

Forgotten 2 days

Forgotten 3 days

Forgotten 4-5 days

Forgotten 6-7 days

Forgotten 8-9 days

Forgotten 10 days or more

Which date did you stop taking the cod liver oil/placebo?

Date field

During the period you did take cod liver oil or placebo. How often did you take it?

Every day

5-6 days per week

3-4 days per week

1-2 days per week

I did not take it

Have you remembered to take cod liver oil or placebo on the weekends?

Yes, both Saturday and Sunday

Yes, but I forget sometimes

Yes, usually at least one day

No, usually I forget during the weekends

Do you take cod liver oil/placebo at the same time every day?

Yes, every day

Yes, mostly

No

How many bottles of cod liver oil/placebo have you received in total?

1

2

3

4

5

6

How much was left in your bottles at the end of the trial?

Sum up the volume left in all bottles that you have not taken.

1 deciliter (dl)

2-3 dl

4-5 dl

6-7 dl

8-9 dl

10-12 dl

13-15 dl

16 dl or more

If you have to guess, what do you think you received in the trial?

Cod liver oil

Placebo

I don't know

Side effects of the use of cod liver oil or placebo

Have you experienced side-effects when using the cod liver oil/placebo in the trial?

Yes

No

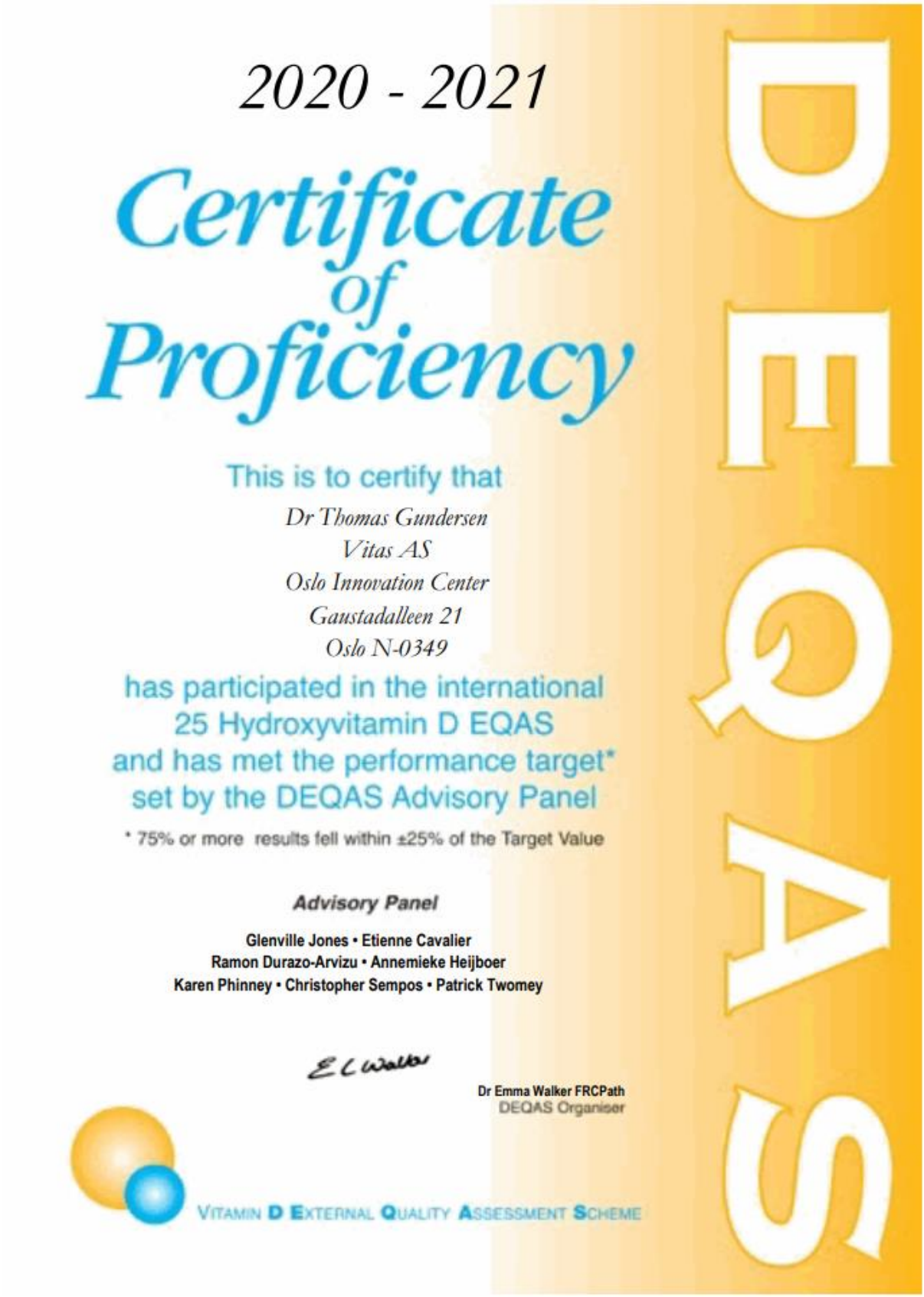
I have not yet begun taking cod liver oil/placebo

What sort of side-effects do you experience/did you experience?

Preferably use keywords

Open text field

sAppendix 2 Certificate of Proficiency, DEQAS



sTable 3. QC batches, 25(OH)D analyses of dried blood spots.

QC batch[a]	Type	Mean nmol/l	CV %
QC146	DBS	85.8	11.0
QC172	DBS	282.6	10.3
QC181	DBS	106.6	14.2

[a]Six QC samples for each sequence, three QC before and three QC after each sequence (96-well plates). In addition, the three QC before were reinjected in the middle of the sequence.

sTable 4. Ad-hoc subgroup analyses; Relative risk and CI[a] for the first and second co-primary endpoints (covid-19), according to randomised assignment to cod liver oil or placebo.

Co-primary endpoint, covid-19	**Overall (*n* = 34 601)**	**Cod liver oil group (*n* = 17 278)**	**Placebo group (*n* = 17 323)**	**Relative Risk (CI[a])**	***p*[b]**
	number (%) of participants with event				
First: SARS-CoV-2 positive test result					
Sex					0.98
Women	292 (1.31)	150 (1.34)	142 (1.27)	1.06 (0.82, 1.36)	
Men	163 (1.33)	77 (1.26)	86 (1.40)	0.90 (0.64, 1.26)	
Age[c, d]					<0.001*
<45 years	266 (1.59)	135 (1.62)	131 (1.56)	1.04 (0.80, 1.35)	
≥45 years	189 (1.06)	92 (1.03)	97 (1.09)	0.95 (0.69, 1.29)	
Body mass index[d]					1.00
≤25 kg/m^2	224 (1.32)	111 (1.30)	113 (1.34)	0.97 (0.73, 1.30)	
>25 kg/m^2	231 (1.31)	116 (1.33)	115 (1.30)	1.02 (0.77, 1.36)	
Sun exposure Jul–Oct 20[d]					0.97
≤30 hours	184 (1.33)	100 (1.44)	84 (1.23)	1.17 (0.85, 1.62)	
>30 hours	271 (1.30)	127 (1.23)	144 (1.38)	0.89 (0.69, 1.16)	
Vitamin D supplement use[e]					0.97
No	351 (1.31)	181 (1.34)	170 (1.27)	1.06 (0.84, 1.33)	
Yes	104 (1.34)	46 (1.21)	58 (1.48)	0.82 (0.53, 1.25)	
Fatty fish consumer[f]					0.51
No	180 (1.42)	96 (1.50)	84 (1.33)	1.13 (0.82, 1.57)	
Yes	270 (1.27)	130 (1.23)	140 (1.31)	0.94 (0.72, 1.22)	
Vaccinated study period[c,g]					<0.001**
No	362 (1.63)	178 (1.61)	184 (1.64)	0.98 (0.78, 1.23)	
Yes	93 (0.75)	49 (0.79)	44 (0.72)	1.09 (0.70, 1.71)	
Strict compliance[h]					0.30
No	164 (1.45)	72 (1.35)	92 (1.55)	0.87 (0.62, 1.22)	
Yes	291 (1.25)	155 (1.30)	136 (1.20)	1.09 (0.84, 1.40)	
Second: Serious covid-19[i]					
Sex					0.26
Women	150 (0.67)	90 (0.81)	60 (0.54)	1.50 (1.01, 2.23)	
Men	72 (0.59)	31 (0.51)	41 (0.67)	0.76 (0.43, 1.33)	
Age[j,k]					0.04
<45 years	123 (0.73)	71 (0.85)	52 (0.62)	1.38 (0.90, 2.12)	
≥45 years	99 (0.55)	50 (0.56)	49 (0.55)	1.02 (0.63, 1.63)	
Body mass index[j,k]					0.07
≤25 kg/m^2	95 (0.56)	57 (0.67)	38 (0.45)	1.49 (0.91, 2.44)	
>25 kg/m^2	127 (0.72)	64 (0.73)	63 (0.71)	1.03 (0.68, 1.56)	
Sun exposure Jul–Oct 20[k]					0.27
≤30 hours	95 (0.69)	54 (0.78)	41 (0.60)	1.30 (0.80, 2.12)	
>30 hours	127 (0.61)	67 (0.65)	60 (0.57)	1.13 (0.74, 1.72)	
Vitamin D supplement use[e]					0.19
No	165 (0.61)	91 (0.68)	74 (0.55)	1.22 (0.85, 1.77)	
Yes	57 (0.74)	30 (0.79)	27 (0.69)	1.14 (0.61, 2.14)	

sTable 4. Ad-hoc subgroup analyses; Relative risk and CI[a] for the first and second co-primary endpoints (covid-19), according to randomised assignment to cod liver oil or placebo.

Co-primary endpoint, covid-19 ***continued***	**Overall (*n* = 34 601)**	**Cod liver oil group (*n* = 17 278)**	**Placebo group (*n* = 17 323)**	**Relative Risk (CI[a])**	***p*[b]**
	number (%) of participants with event				
Second: Serious covid-19[h]					
Fatty fish consumer[f,j]					0.04
No	98 (0.77)	58 (0.91)	40 (0.63)	1.44 (0.89, 2.34)	
Yes	123 (0.58)	63 (0.59)	60 (0.56)	1.06 (0.69, 1.62)	
Vaccinated study period[g,j]					<0.001[†]
No	179 (0.80)	93 (0.84)	86 (0.77)	1.10 (0.77, 1.56)	
Yes	43 (0.35)	28 (0.45)	15 (0.25)	1.83 (0.86, 3.89)	
Strict compliance (yes)[h]	154 (0.66)	79 (0.66)	75 (0.66)	1.00 (0.69, 1.47)	0.55

Data were missing for 1.7–5.4% of the participants.

[a]First co-primary and second co-primary endpoints (covid-19) 97.0% and 98.2% confidence interval (CI), respectively

[b]The logistic procedure test of the global hypothesis Wald test, significance criterion α=0.03 and 0.018 for the first and second co-primary endpoints, respectively.

[c]Further details are found in sTable 7 and sFigure 1

[d]These results are supported using logistic regression with Age, Body mass index and Sun exposure observed individual values. Treatment type 3 effect p-value are all >0.91 and explanatory effect type 3 p-values are <0.001, 0.40, and 0.53, respectively.

[e]Taking vitamin D supplements (including cod liver oil) ≥5 days/week was an exclusion criterion, but those with a lower frequency of usage were included.

[f]Consuming fatty fish ≥1–2 days/week and/or ≥1–3 slices of bread with fatty fish/week.

[g]Reported having ≥1 SARS-CoV-2 vaccines during the intervention period.

[h]Strict compliance (n=11 959 cod liver oil group, n=11 412 placebo group): reported cod liver oil/placebo consumed >0.5 L or consuming cod liver oil/placebo >2-3 months

[i]SARS-CoV-2 positive test and self-reported dyspnoea (n=222) and/or hospitalisation (n=17, 8 in the cod liver oil group and 9 in the placebo group) or death (n=0).

[j]Further details are found in sTable 8 and sFigure 2.

[k]These results are supported using logistic regression with Age, Body mass index and Sun exposure observed individual values. Treatment type 3 effect p-value are 0.17, 0.16, and 0.16 and explanatory effect type 3 p-values are <0.001, 0.06, and 0.30, respectively.

[*]The type 3 analysis of effects resulted in p-value for the Age factor (<45 years versus ≥45 years) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.99.

[**]The type 3 analysis of effects resulted in p-value for the Vaccinated study period factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.97.

[†]The type 3 analysis of effects resulted in p-value for the Vaccinated study period factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.16.

sTable 5. Ad-hoc subgroup analyses; Relative Risk and 99.9% CI for the third and fourth co-primary endpoints (acute respiratory infections), according to randomised assignment to cod liver oil or placebo.

Co-primary endpoint, acute respiratory infections	**Overall (*n* = 34 601)**	**Cod liver oil group (*n* = 17 278)**	**Placebo group (*n* = 17 323)**	**Relative Risk (99.9% CI)**	***p*[a]**
	number (%) of participants with event				
Third: SARS-CoV-2 negative test result					
Sex					<0.001*
Women	11 564 (51.75)	5 769 (51.69)	5 795 (51.81)	1.00 (0.96, 1.04)	
Men	5 547 (45.27)	2 777 (45.40)	2 770 (45.14)	1.01 (0.94, 1.07)	
Age[b]					<0.001**
<45 years	9 938 (59.32)	4 960 (59.47)	4 978 (59.18)	1.01 (0.96, 1.05)	
≥45 years	7 173 (40.19)	3 586 (40.12)	3 587 (40.25)	1.00 (0.94, 1.06)	
Body mass index[b]					<0.001†
≤25 kg/m^2	8 742 (51.46)	4 414 (51.76)	4 328 (51.16)	1.01 (0.96, 1.06)	
>25 kg/m^2	8 369 (47.51)	4 132 (47.22)	4 237 (47.81)	0.99 (0.94, 1.04)	
Sun exposure Jul–Oct 20[b]					0.19
≤30 hours	6 743 (48.85)	3 403 (48.98)	3 340 (48.72)	1.01 (0.95, 1.06)	
>30 hours	10 368 (49.85)	5 143 (49.79)	5 225 (49.91)	1.00 (0.95, 1.04)	
Vitamin D supplement use[c]					0.17
No	13 214 (49.18)	6 603 (49.03)	6 611 (49.33)	0.99 (0.95, 1.04)	
Yes	3 897 (50.39)	1 943 (50.97)	1 954 (49.82)	1.02 (0.95, 1.10)	
Fatty fish consumer[d]					<0.001††
No	6 547 (51.49)	3 298 (51.68)	3 249 (51.30)	1.01 (0.95, 1.07)	
Yes	10 259 (48.20)	5 103 (48.14)	5 156 (48.26)	1.00 (0.95, 1.05)	
Vaccinated study period[e]					<0.001‡
No	11 561 (51.91)	5 703 (51.63)	5 858 (52.18)	0.99 (0.95, 1.03)	
Yes	5 550 (45.01)	2 843 (45.61)	2 707 (44.40)	1.03 (0.96, 1.10)	
Strict compliance[f]					<0.001‡‡
No	5 995 (53.07)	2 828 (52.85)	3 167 (53.27)	0.99 (0.94, 1.05)	
Yes	11 116 (47.70)	5 718 (47.94)	5 398 (47.44)	1.01 (0.97, 1.06)	
Fourth: Acute respiratory infections					
Sex					<0.001‡
Women	5 269 (23.58)	2 677 (23.99)	2 592 (23.17)	1.04 (0.96, 1.12)	
Men	2 529 (20.64)	1 287 (21.04)	1 242 (20.24)	1.04 (0.93, 1.17)	
Age[g]					<0.001‡‡
<45 years	4 409 (26.32)	2 253 (27.01)	2 156 (25.63)	1.05 (0.97, 1.15)	
≥45 years	3 389 (18.99)	1 711 (19.14)	1 678 (18.83)	1.02 (0.92, 1.13)	
Body mass index[g]					0.06
≤25 kg/m^2	3770 (22.19)	1954 (22.92)	1816 (21.47)	1.07 (0.97, 1.17)	
>25 kg/m^2	4028 (22.87)	2010 (22.97)	2018 (22.77)	1.01 (0.92, 1.11)	
Sun exposure Jul–Oct 20[g]					0.18
≤30 hours	3 126 (22.65)	1 610 (23.17)	1 516 (22.12)	1.05 (0.94, 1.16)	
>30 hours	4 672 (22.46)	2 354 (22.79)	2 318 (22.14)	1.03 (0.95, 1.12)	
Vitamin D supplement use[c]					0.002
No	5 958 (22.18)	3 026 (22.47)	2 932 (21.88)	1.03 (0.95, 1.11)	
Yes	1 840 (23.79)	938 (24.61)	902 (23.00)	1.07 (0.94, 1.22)	

sTable 5. Ad-hoc subgroup analyses; Relative Risk and 99.9% CI for the third and fourth co-primary endpoints (acute respiratory infections), according to randomised assignment to cod liver oil or placebo.

Co-primary endpoint, acute respiratory infections ***continued***	**Overall (*n* = 34 601)**	**Cod liver oil group (*n* = 17 278)**	**Placebo group (*n* = 17 323)**	**Relative Risk (99.9% CI)**	***p*[a]**
		number (%) of participants with event			
Fourth: Acute respiratory infections					
Fatty fish consumer[d]					<0.001[§]
No	3 075 (24.19)	1 539 (24.12)	1 536 (24.25)	0.99 (0.90, 1.10)	
Yes	4 689 (22.03)	2 405 (22.69)	2 284 (21.38)	1.06 (0.97, 1.16)	
Vaccinated study period[e]					<0.001[§§]
No	4 880 (21.91)	2 454 (22.22)	2 426 (21.61)	1.03 (0.95, 1.12)	
Yes	2 918 (23.67)	1 510 (24.23)	1 408 (23.09)	1.05 (0.94, 1.17)	
Strict compliance (yes)[f]	6 824 (29.28)	3 531 (29.61)	3 293 (28.94)	1.02 (0.96, 1.09)	0.79

Data were missing for 1.7–5.4% of the participants.

[a]The logistic procedure test of the global hypothesis Wald test, significance criterion α=0.001.

[b]These results are supported by using logistic regression with Age, Body mass index and Sun exposure observed individual values. Treatment type 3 effect p-values are all >0.53, and explanatory effect type 3 p-values are <0.001, <0.001 and 0.37, respectively.

[c]Taking vitamin D supplements (including cod liver oil) ≥5 days/week was an exclusion criterion, but those with lower frequency of usage were included.

[d]Consuming fatty fish ≥1–2 days/week and/or ≥1–3 slices of bread with fatty fish/week.

[e]Reported having ≥1 SARS-CoV-2 vaccines during the intervention period.

[f]Strict compliance (n=11 959 cod liver oil group, n=11 412 placebo group): reported cod liver oil/placebo consumed >0.5 L or consuming cod liver oil/placebo >2-3 months

[g]These results are supported by using logistic regression with Age, Body mass index and Sun exposure observed individual values. Treatment type 3 effect p-values are all between 0.07 and 0.09, and explanatory effect type 3 p-values are <0.001, 0.04 and 0.66, respectively.

[*]The type 3 analysis of effects resulted in p-value for the Sex factor (Women versus Men) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.98.

[**]The type 3 analysis of effects resulted in p-value for the Age factor (<45 years versus ≥45 years) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.89.

[†]The type 3 analysis of effects resulted in p-value for the Body mass index factor (<25 kg/m^2 versus ≥25 kg/m^2) of <0.001, p-value for the treatment (cod liver oil/placebo) 1.00.

[††]The type 3 analysis of effects resulted in p-value for the Fatty fish consumer factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.90.

[‡]The type 3 analysis of effects resulted in p-value for the Vaccinated study period factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.88.

[‡‡]The type 3 analysis of effects resulted in p-value for the Strict compliance factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.71.

[‡]The type 3 analysis of effects resulted in p-value for the Sex factor (Women versus Men) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.07.

[‡‡]The type 3 analysis of effects resulted in p-value for the Age factor (<45 years versus ≥45 years) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.06.

[§]The type 3 analysis of effects resulted in p-value for the Fatty fish consumer factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.09.

[§§]The type 3 analysis of effects resulted in p-value for the Vaccinated study period factor (No versus Yes) of <0.001, p-value for the treatment (cod liver oil/placebo) 0.08.

sTable 6. Ad-hoc subgroup analyses; the third and fourth co-primary endpoints (acute respiratory infections), according to skin type and assignment to cod liver oil or placebo.

Co-primary endpoint, acute respiratory infections	**Cod liver oil group (*n* = 17 278)**		**Placebo group (*n* = 17 323)**		***p*[a]**
	number (%) of participants with event				
Third: SARS-CoV-2 negative test result	No	Yes	No	Yes	
Skin type					<0.001*
Easily burnt, rarely tan	648 (7.80)	701 (8.56)	613 (7.37)	685 (8.41)	
Easily burnt, sometimes tan	918 (11.04)	1 003 (12.25)	881 (10.59)	1 004 (12.33)	
Sometimes burnt, always tan	5 699 (68.56)	5 563 (67.96)	5 694 (68.46)	5 494 (67.49)	
Never burnt, always tan	879 (10.57)	754 (9.21)	945 (11.36)	781 (9.59)	
Naturally tan	169 (2.03)	165 (2.02)	184 (2.21)	177 (2.17)	
Fourth: Acute respiratory infections	No	Yes	No	Yes	
Skin type					<0.001**
Easily burnt, rarely tan	987 (7.82)	362 (9.34)	982 (7.73)	316 (8.43)	
Easily burnt, sometimes tan	1 417 (11.23)	504 (13.00)	1 385 (10.90)	500 (13.34)	
Sometimes burnt, always tan	8 633 (68.39)	2 629 (67.83)	8 651 (68.07)	2 537 (67.67)	
Never burnt, always tan	1 300 (10.30)	333 (8.59)	1 382 (10.87)	344 (9.18)	
Naturally tan	286 (2.27)	48 (1.24)	309 (2.43)	52 (1.39)	

[a]The logistic procedure test of the global hypothesis Wald test, significance criterion α=0.001.

*The joint tests analysis of effects resulted in p-value for the Skin type factor <0.001, the p-value for the treatment (cod liver oil/placebo) 0.47.

**The joint tests analysis of effects resulted in p-value for the Skin type factor <0.001, the p-value for the treatment (cod liver oil/placebo) 0.31.

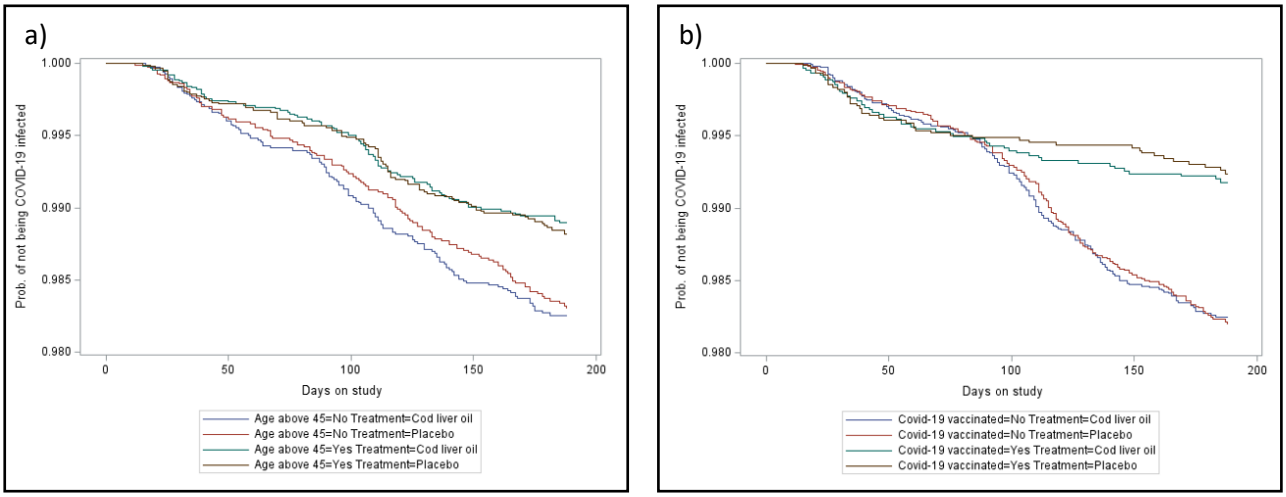
sTable 7. Logistic regression with explanatory variables, positive SARS-CoV-2 test result

Summary of Stepwise Selection								
Step	Effect Entered	Effect Removed	DF	Number In	Score Chi-Square	Wald Chi-Square	Pr > ChiSq	Variable Label
1	Cov19_VaccineYN		1	1	48.2679		<0.001	Covid-19 vaccinated (No versus Yes)
2	gen_age_above45		1	2	5.8448		0.02	Age (<45 years versus ≥45 years)

sTable 8. Logistic regression with explanatory variables, serious covid-19

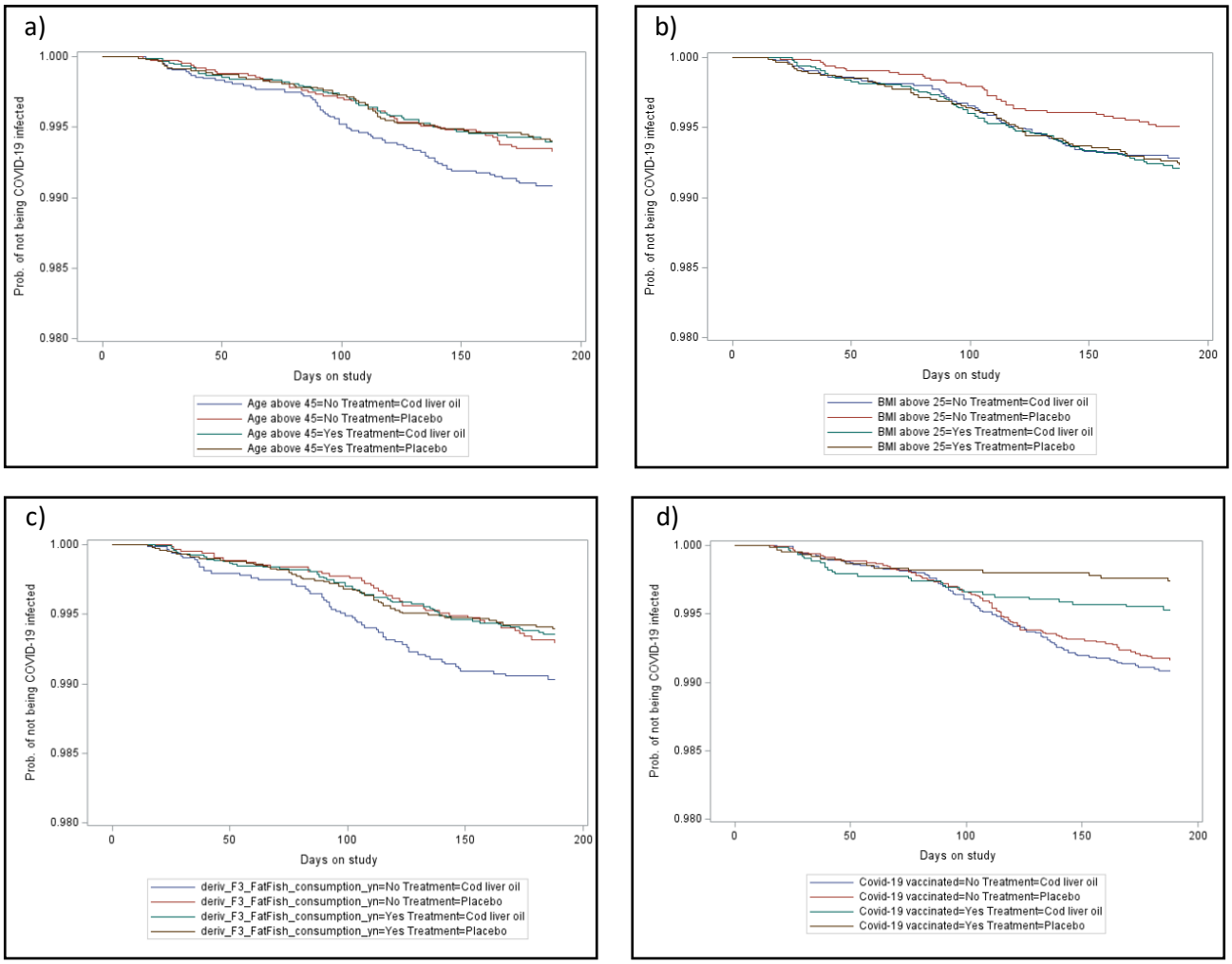
Summary of Stepwise Selection								
Step	Effect Entered	Effect Removed	DF	Number In	Score Chi-Square	Wald Chi-Square	Pr > ChiSq	Variable Label
1	Cov19_VaccineYN		1	1	26.4426		<0.001	Covid-19 vaccinated (No versus Yes)
2	BMI_Above25		1	2	4.4747		0.03	Body mass index (≤25 kg/m^2 versus >25 kg/m^2)
3	deriv_F3_FatFish_con		1	3	3.1783		0.07	Fatty fish consumer (No versus Yes)
4	gen_CLOC_compliance_		1	4	2.1361		0.14	Strict compliance (Yes)
5	Treatment		1	5	1.5609		0.21	Cod liver oil versus Placebo
6	deriv_F3_VitaminD_us		1	6	1.2593		0.26	Vitamin D supplement use (No versus Yes)

sFigure 1 Positive SARS-CoV-2 test result over the intervention period



The Kaplan-Meier curve demonstrates the probability of a SARS-CoV-2 positive test result stratified by a) Age (<45 years versus ≥45), and b) Vaccinated study period (No versus Yes) for the cod liver oil and the placebo groups over the intervention period ($p<0.05$).

sFigure 2 Serious Covid-19 over the intervention period



The Kaplan-Meier curve demonstrates the probability of serious covid-19 stratified by a) Age (<45 years versus ≥45), b) Body mass index (BMI, ≤25 kg/m^2 versus >25 kg/m^2), c) Fatty fish consumer (No versus Yes), and d) Vaccinated study period (No versus Yes) for the cod liver oil and the placebo groups over the intervention period ($p<0.05$).