Long COVID symptoms in SARS-CoV-2-positive children aged 0–14 years and matched controls in Denmark (LongCOVIDKidsDK): a national, cross-sectional study

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COVID-19 in Denmark

• First confirmed case of SARS-CoV-2 in late February 2020.
• First lockdown of daycare facilities and schools etc. in March 2020.
• From May 2020 open public testing was available to all including citizens without symptoms of SARS-CoV-2.
• LongCOVIDKidsDK survey in July 2021 where most restrictions were lifted.
Objective

To investigate:
- the prevalence of long-lasting symptoms
- the duration and intensity of symptoms
- quality of life, psychological and social outcomes in children aged 0–14 years who had been infected with SARS-CoV-2 compared to controls with no history of SARS-CoV-2 infection.
Methods

• Nationwide cross-sectional study including all children with a confirmed SARS-CoV-2-positive PCR test (cases) and matched controls.
• A survey was sent to mothers (proxy reporting) of all Danish children aged 0–14 years.
• Questionnaire included 23 most common long COVID symptoms and Pediatric Quality of Life Inventory (PedsQL).
Definition of long COVID

We used the WHO clinical case definition of post-COVID-19 condition in adults as:

• **persistent or fluctuating symptoms with an influence on daily functioning following SARS-CoV-2 infection for at least 2 months that cannot be explained by an alternative diagnosis.**

WHO. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021.
Results – Response rate

185,364 children invited to participate in survey via proxy reporting

- 38,132 in the case group
- 147,212 in the control group

1,127 excluded because of suspected SARS-CoV-2 infection

- 10,997 responded
  - 1,449 aged 0–3 years
  - 6,032 aged 4–11 years
  - 3,516 aged 12–14 years

- 33,016 responded
  - 3,855 aged 0–3 years
  - 18,372 aged 4–11 years
  - 10,789 aged 12–14 years
Results - At least one symptom lasting more than two months (cases vs. controls)

0-3 years
40.0% vs. 27.2%; OR 1.78 [95% CI 1.55–2.04], p<0.0001

4-11 years
38.1% vs. 33.7%; OR 1.23 [95% CI 1.15–1.31], p<0.0001

12-14 years
46.0% vs. 41.3%; OR 1.21 [95% CI 1.11–1.32], p<0.0001
Results – Odds of reporting symptoms in cases vs. controls

0-3 years

| Symptoms                          | OR [95%CI]   | p value |
|-----------------------------------|--------------|---------|
| Stomach aches                     | 2.48 [1.63,3.77] | <.0001  |
| Fatigue                           | 3.50 [2.21,5.55] | <.0001  |
| Pain in muscles/joints            | 1.84 [0.54,6.30] | 0.33    |
| Rashes                            | 1.57 [1.11,2.22] | 0.010   |
| Mood swings                       | 1.63 [1.22,2.19] | 0.0011  |
| Nausea                            | 8.30 [1.61,42.91] | 0.011   |
| Fever                             | 5.89 [2.95,11.77] | <.0001  |
| Loss of appetite                  | 3.72 [2.44,5.67] | <.0001  |
| Trouble breathing                 | 4.40 [2.13,9.11] | <.0001  |
| Dark circles under the eyes       | 6.15 [2.60,14.55] | <.0001  |
| Palpitations                      | 3.94 [1.81,8.56] | 0.0005  |
| Cold hands/feet                   | 4.85 [3.27,8.64] | <.0001  |
| Cough                             | 3.25 [0.84,11.24] | 0.063   |
| Chapped lips                      |               |         |
| Discoloured fingers/toes          |               |         |
| Extreme paleness                 |               |         |

Higher in controls ←     → Higher in cases
Results – Odds of reporting symptoms in cases vs. controls

4-11 years

Symptoms
- Stomach aches
- Chest pain
- Headache
- Fatigue
- Pain in muscles/joints
- Sore throat
- Dizziness
- Rashes
- Mood swings
- Nausea
- Fever
- Loss of appetite
- Trouble breathing
- Dark circles under the eyes
- Palpitations
- Trouble remembering and concentrating
- Cold hands/feet
- Cough
- Chapped lips
- Dizziness when standing
- Light sensitivity
- Discoloured fingers/toes
- Extreme paleness

OR [95%CI]  p value
0.95 [0.78, 1.17]  0.67
2.66 [1.16, 6.00]  0.018
1.66 [1.34, 2.05] <0.0001
1.80 [1.51, 2.14] <0.0001
1.38 [1.05, 1.81]  0.021
4.56 [2.65, 7.85] <0.0001
4.07 [1.82, 9.10]  0.0006
0.64 [0.51, 0.80] <0.0001
0.72 [0.65, 0.80] <0.0001
1.32 [0.93, 1.93]  0.13
3.21 [1.24, 8.34]  0.016
1.44 [1.15, 1.81]  0.0018
2.61 [1.65, 4.14] <0.0001
1.53 [1.19, 1.97]  0.0009
2.31 [1.13, 4.73]  0.022
0.86 [0.73, 1.02]  0.081
1.23 [0.82, 1.83]  0.31
1.85 [1.34, 2.59]  0.0001
1.17 [0.87, 1.58]  0.30
2.05 [0.82, 5.16]  0.13
1.18 [0.85, 1.64]  0.31
0.61 [0.07, 5.11]  0.65
1.17 [0.68, 2.01]  0.58

Higher in controls ← → Higher in cases
Results – Odds of reporting symptoms in cases vs. controls

12-14 years

| Symptoms                              | OR [95% CI] | p value |
|---------------------------------------|-------------|---------|
| Stomach aches                         | 0.91 [0.68, 1.22] | 0.54 |
| Chest pain                            | 3.53 [2.00, 6.24]  | <.0001 |
| Headache                              | 1.55 [1.27, 1.96]  | <.0001 |
| Fatigue                               | 1.39 [1.21, 1.60]  | <.0001 |
| Pain in muscles/joints                | 1.47 [1.13, 1.90]  | 0.0036 |
| Sore throat                           | 5.32 [2.99, 9.46]  | <.0001 |
| Dizziness                             | 2.32 [1.63, 3.31]  | <.0001 |
| Rash                                  | 1.03 [0.81, 1.33]  | 0.79   |
| Mood swings                           | 0.75 [0.65, 0.88]  | 0.0002 |
| Nausea                                | 1.25 [0.86, 1.82]  | 0.24   |
| Fever                                 | 2.96 [0.40, 11.10] | 0.10   |
| Loss of appetite                      | 1.12 [0.96, 1.29]  | 0.11   |
| Trouble breathing                     | 2.94 [1.91, 4.53]  | <.0001 |
| Dark circles under the eyes           | 1.24 [0.93, 1.65]  | 0.15   |
| Palpitations                          | 1.66 [0.95, 2.90]  | 0.073  |
| Trouble remembering and concentrating | 0.91 [0.76, 1.08]  | 0.29   |
| Cold hands/feet                       | 1.12 [0.87, 1.44]  | 0.40   |
| Cough                                 | 2.99 [1.38, 6.45]  | 0.0018 |
| Chapped lips                          | 1.26 [0.94, 1.70]  | 0.12   |
| Dizziness when standing               | 2.10 [1.48, 2.97]  | <.0001 |
| Light sensitivity                     | 0.74 [0.49, 1.11]  | 0.34   |
| Discoloured fingers/toes              | 1.51 [0.47, 4.81]  | 0.45   |
| Extreme paleness                      | 0.82 [0.48, 1.38]  | 0.45   |
Results – Duration of symptoms in cases

0-3 years Stomach aches

|                     | At least 2 months | At least 3 months | At least 6 months | At least 9 months |
|---------------------|-------------------|-------------------|-------------------|-------------------|
|                     | Cases             | Cases             | Cases             | Cases             |
| Total n             | 1,194             | 1,194             | 899               | 167               |
| Stomach aches, n (%)|                   |                   |                   |                   |
| Almost never and Sometimes | 77 (6·4) | 62 (5·2) | 35 (3·9) | 7 (3·0) |
| Often and Almost always | 40 (3·3) | 34 (2·8) | 15 (1·7) | 0 |

4-11 years Headache

|                     | At least 2 months | At least 3 months | At least 6 months | At least 9 months |
|---------------------|-------------------|-------------------|-------------------|-------------------|
|                     | Cases             | Cases             | Cases             | Cases             |
| Total n             | 5,023             | 5,023             | 3614              | 628               |
| Headache, n (%)     |                   |                   |                   |                   |
| Almost never and Sometimes | 486 (9·6) | 439 (8·7) | 281 (7·8) | 37 (5·9) |
| Often and Almost always | 126 (2·5) | 115 (2·3) | 79 (2·2) | 14 (2·2) |

12-14 years Trouble breathing

|                     | At least 2 months | At least 3 months | At least 6 months | At least 9 months |
|---------------------|-------------------|-------------------|-------------------|-------------------|
|                     | Cases             | Cases             | Cases             | Cases             |
| Total n             | 2,857             | 2,857             | 2,367             | 494               |
| Trouble breathing, n (%)|                   |                   |                   |                   |
| Almost never and Sometimes | 108 (3·6) | 91 (3·2) | 69 (2·9) | 11 (2·2) |
| Often and Almost always | 37 (1·3) | 35 (1·2) | 21 (0·9) | 5 (1·0) |
Results – Emotional and social functioning

PedsQL Emotional functioning:
4-11 years: median score 80.0 [IQR 65.0–95.0]) in cases vs. 75.0 [60.0–85.0] in controls, p<0.0001
12-14 years: 90.0 [70.0–100.0] vs. 85·0 [65·0–95·0], p<0·0001

PedsQL Social functioning:
12-14 years: 100.0 [90.0–100.0] vs. 95.0 [80.0–100.0], p<0.0001
Results – Psychological outcomes

Worried about what will happen to me

Others don’t want to be friends

Teased

Trouble being with peers

Trouble sleeping

Sad

Scared
Perspectives

• Our results show more long-lasting symptoms among children with previous SARS-CoV-2 infection and adds new knowledge about the youngest children – pointing at long COVID.

• The study also finds many symptoms among controls with worse social and emotional status - pointing at “pandemic symptoms”.

• We also looked into adolescents (15-19) years and found the similar differences between groups, however more symptoms among girls.

• Represents the parents’/children’s own perception of symptoms.

• Important basis for understanding this new condition long COVID as well as “pandemic symptoms”.

• Next: Symptom clusters – variants – vaccine effects – prevention and treatment of long COVID.
Thank you for your attention

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