Test subject information for participation in medical-scientific research/study

The 'coronavirus' in children

Official title:
Clinical and immunological characteristics of COVID-19 in pediatric patients (COPP-IMM study)

Preface

Dear sir/madam,

We are asking your child to participate in medical-scientific research. You are receiving this invitation because your child is ill due to the coronavirus (COVID-19). Participation is on a voluntary basis. To participate, your permission is required.

Before you decide whether your child can participate in this research, your attending physician will provide you with an explanation and with this information brochure. Please take your time to read this information.

Do you have any questions? You can ask the researcher. You can also ask questions to an independent expert. At the end of this letter the name and contact information will be mentioned. You can also discuss it with your partner, friends or family. General information on participating in such research can be found on the website of the Dutch government: www.rijksoverheid.nl/mensenonderzoek

1. General information

This study has been initialized by the LUMC and is conducted by doctors and researchers in several hospitals in The Netherlands. About 60 children and/or youth are participating.
The Medical Ethical Committee, METC-LLD, has approved of this study and has deemed this study as causing hardly any strain on your child. General information on the supervision of research can be found on the following website:
https://www.kindenonderzoek.nl/voor- ouders/wetenschappelijk-onderzoek/.

2. Purpose of the study

The purpose of the study is to describe the illness that is caused by the coronavirus in children. We want to know more about how the disease effects children, what the course of the disease is, and what treatments are given to battle it. We aim to understand how the immune system in children respond to an infection with the coronavirus.

An illness can sometimes cause other complaints, besides the physical. For instance, emotional and social complaints caused by illness. We call these psycho-social symptoms. In this research we also want to investigate what psycho-social effects the disease causes in children.

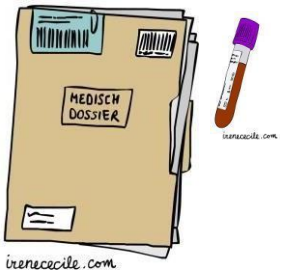
3. Background of the study

Since December 2019, a new virus has emerged, the coronavirus, or SARS-CoV-2. This virus causes the disease COVID-19. Due to the spread of this virus, there was a large worldwide outbreak. Adults and children can become ill. It appears that children become ill less frequent and not as severe as adults. We do not yet understand why this is. We also do not yet know why some children become ill and others do not. With this study we hope to gain a better understanding of it.

4. What does it mean to participate?

Will your child participate? Participation will last for the duration of your child's stay in hospital and consists of three parts:

1) Your child will undergo the regular examinations and treatment by the hospital's physicians. We want to use information from your child's patient file for our research, such as the symptoms your child suffered from, blood levels and the medication your child received.



Did your child reside in the Intensive Care Unit (ICU)? We will ask separate permission to retrieve the data from the check-up visits at the outpatient clinic. This would mean data about general health but also neuro-psychological tests. In other words: the functioning of your child's brain like intelligence and concentration.

During the time your child is/was admitted to hospital, blood may have been drawn. If there is any left over, we would like to utilize that as well. We will ask separate permission.

2) We also ask your permission to take one blood sample form your child for the benefit of this study. We will try to combine this with any drawing of blood already required. This way we try to avoid an extra blood draw. Only if this is not possible, for example if the required blood samples have already been collected, will you be consulted to plan another moment to take a blood sample.

3) Finally, we ask separate permission for sending you a questionnaire.

a. 12 weeks after the visit or admittance to the hospital we would like to send you and perhaps your child, a questionnaire. The questions are about how it went at home. And about how your child is doing (for example: happy/angry/quiet, sleep and contact with peers). This questionnaire is for all participants of the COPP study. Filling out this questionnaire will take you about 10-20 minutes.
b. Does your child qualify for the corona vaccine? Then we would like to send you an additional short questionnaire, once a year, for the duration of this study. This questionnaire is about corona vaccination. We ask whether your child has been vaccinated and if so, if your child has experienced any side effects of vaccination. Filling out this questionnaire will take you a maximum of 2 minutes.

We will ask separate permission for participation in follow-up research. Do you consent? Then

we may approach you to ask if your child would participate in follow- up research.

5. What is expected of your child?

We really want the study to go well. That is why we are making the following agreements with you:

- If you consent to participate in the study, we can collect the encoded data about the illness of your child
- If you consent to an extra blood sample, we can draw extra blood vial(s) from your child.
- If you consent to the filling out of a questionnaire, you agree to fill out the questionnaire we send you.

If you wish to retreat from the study, you will contact the researcher about this.

6. Possible inconveniences

Your child will experience no inconveniences during the collecting of data. If the drawing of blood can be combined with the already required blood samples for the benefit of your child's treatment, there will be no extra inconvenience. It could happen that an extra blood draw is necessary for the blood sample. Because it could not be combined with other blood drawing. Do we need an extra blood draw? Then we make sure to reduce pain and fear as much as possible. For example, by using numbing cream, by supporting your child as much as possible and by providing tips for you, the parents/guardians, on how to support your child the best.
Filling out the questionnaires, which will be sent to your home, will take you or your child about 20-25 minutes, depending on your child's experiences.

7. Possible advantages and disadvantages

Consider the advantages and disadvantages carefully before you decide whether your child can participate in this study.

Your child will not benefit from participating in this research. Participation of your child can contribute to more knowledge about the disease COVID-19 and the treatment against it.

Possible disadvantages for participating in this study? It might be necessary to draw extra blood which can cause your child fear or pain. Besides that, it will cost you or your child about 20 to 25 minutes to fill out the questionnaires.

If you do not wish to participate or want to stop the participation in the study.

You yourself decide whether your child participates or not. Participation is voluntary.
If you or your child decide not to participate, this will have no adverse consequences.
The treatment of your child will continue as normal.

You can always stop the participation of your child, also during the study. You do not need to give a reason why your child quits the study. You are required to inform the researcher right away.
The data collected up to that point will be used in the study.

8. End of the study

Participation of your child in the study will stop when:

- Your child is discharged from the hospital and the data from questionnaires and potential follow- up research have been collected.
- You or your child wish to stop participating in the study. You can do so at any moment. Inform the researcher right away. You do not have to give an explanation.
- The researcher thinks it is better for you to quit.
- When your child resists participation to the study. We will act conform the "behavioural code resistance in minors". We will discuss with you as the parent/guardian how this resistance manifests itself in your child.
- One of the following institutes decides that the study needs to stop:
    - the LUMC,
    - the government, or
    - the medical- ethical committee who assesses the study

The study is completed if enough data has been collected about the coronavirus and its effects on children. The study is also finished if not enough test subjects participate in the study (for example because there are too few new coronavirus infections in the Netherlands). After processing all the data, the researcher will inform you about the most significant findings of the study. This will happen about a year after your child's participation.

9. Use and retaining of your data and your body material

For the benefit of this study, personal data and body material (blood) are collected from your child and are used and stored. It concerns personal data like gender, region, date of birth and information about the health of your child. All the data and the body material of your child are necessary to be able to answer the questions that are asked in this study and to be able to publish the results. We ask for your permission to use the personal data and the body material of your child.

Confidentiality of your personal data and body material

To protect the privacy of your child the personal data and body material will be coded. The name and other information that would directly identify your child are removed. Only with the key to the code can the information be traced back to your child. The key to the code is safely stored at the local research facility (LUMC). In reports and publications regarding the study, the information cannot be traced back to your child.

Access to your personal data for verification

A few people receive access to the personal data of your child at the research facility (LUMC). Also to the data which has not been coded. This is necessary for the purpose of verifying that the study has been conducted properly and is reliable. These following people can access the research results of your child for the purpose of verification of the study:

- An inspector who works for the LUMC
- National controlling authorities, for example the Dept. of Health Inspection & Youth. (Inspectie Gezondheidszorg en Jeugd -IGJ)

They keep the personal data of your child confidential. We ask your permission for this.

Retention period personal data and body material.

The personal data of your child needs to be kept at the research location (LUMC) for 15 years.
The body material from your child is not destroyed after use. We save it and keep it at the LUMC. It

is kept for 15 years in order to, as the study advances, be able to make new determinations with it that pertain to this study. As soon as it is no longer needed, we will destroy the body material.

Retaining and use of personal data and body material for other research

The personal data of your child and the body material might be significant for other scientific research related to the coronavirus and its effect on children. Do you agree with the use of it after this study? In that case the body material of your child will be retained for 15 years at the LUMC. Do you not agree? Then your child can still participate in the current study. You can express your preference on the consent form.

Revoke permission

You can revoke your permission at any time. The personal data of your child will not be used from that moment on. This counts for this study and also for the retaining of data and its use in future research. The collected data up to the moment of the revoking of permission, will still be used in the study. The body material from your child will be disposed of upon the revoking of your permission. If the body material has already been utilised for measurements, this data will be used.

More information on your rights concerning the processing of personal data

You can find general information on your rights concerning the processing of personal data of you and your child on the following website: https://autoriteitpersoonsgegevens.nl/.

For questions regarding your rights, or a complaint about the processing of your personal data, you can contact the entity responsible for processing your personal data. In this case that is the LUMC. Do you have any questions or complaints about the processing of your personal data? Contact the research facility (LUMC). You can also contact the Data Protection Officer of the LUMC or the Authority Personal Data. In **appendix A** you can find all the contact information and the website of the LUMC.

Where can you find more information regarding this study?

Information regarding this study can be found at www.covidkids.nl. There is no personal data of your child on this website. On this website you can find a summary of the results of this study (in the dashboard).

10. No compensation for participating

There is no compensation for participating in this study.

11. Insurance for test subjects

Your child does not run any additional risks by participating in this study. Therefor there is no need for the researcher to provide an extra insurance.

12. Do you have any questions?

For questions, you can contact the researcher. For independent advice on participation in this study, you can contact the independent physician Dr Meijer. She knows a lot about the study but is not involved in it.

Do you have any complaints about this study? You can discuss this with the researcher or your

attending physician. Do you prefer not to? Then you can address the Complaints Officer of the LUMC. You can find all the information in **Appendix A**: contact information.

13. Signing the consent form.

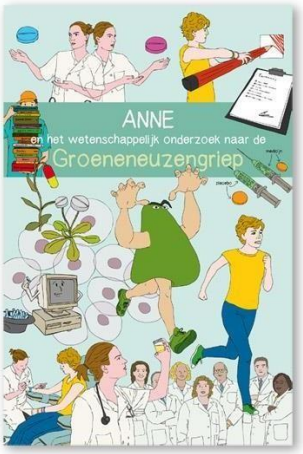
After ample consideration time, you will be asked about your decision on participation of your child in the study. Children older than 16 can decide for themselves whether they want to participate. Children in the age of 12 to 15 years old, will decide together with the parents/guardians. For children underthe age of 12, the parents or guardians will decide on behalf of the child.

Do you give permission? Then we ask you to fill out the accompanying consent form. With the permission you declare that you understood the information. You also consent to the participation of your child in the study. Both you and the researcher will receive a signed copy of this consent form.

Thank you for your attention.

Do you wish to learn more?

Do you wish to learn more about research in children in general? You can check www.kindenonderzoek.nl
On this website you can also find a comic for children called ‘Anne en de Groeneneuzengriep’ (Anna and the GreenNoseFlue”), dealing with research. For this study, the preface and chapters 1, 2, 3, 6a, 9, 10, 11 and 12 are relevant.



Do you wish to learn more about the coronavirus and this study? You can check www.covidkids.nl

Appendices to this information

A. Contact information
B. Consent form parents /guardians
C. Information form under 12
D. Information form 12 to 15 years old

Appendix A: contact information

Contact information LUMC

Principal investigator:
Dr E.P. Buddingh
Leiden University Medical Centre, Willem-Alexander Children's hospital
e.p.buddingh@lumc.nl / copp@lumc.nl
Phone number: 071-5262824
www.covidkids.nl

Independent physician:
Drs. C. Meijer
Leiden University Medical Centre, Willem-Alexander Children's hospital
c.r.meijer-boekel@lumc.nl
Phone number: 071-5262824

Complaints:
For complaints, please contact the Complaints Officer of the LUMC through e-mail: patientservicebureau@lumc.nl
You can also call patiëntenservicebureau (071-5262989; during office hours).

Privacy:
Data Protection Officer of the LUMC: If you have questions about the protection of your privacy you can contact the Data Protection Officer of the LUMC via privacy@lumc.nl

For more information on your rights:
Contact info LUMC
Albinusdreef 2
2333 ZA Leiden
Central phone number: (071) 526 91 11
For more information on your rights see the website of the LUMC:
https://www.lumc.nl/12367/Deelnemers-wetenschappelijk-onderzoek/

Appendix B: Consent form parents or guardians

The 'coronavirus' in children

Official title:
Clinical and immunological characteristics of COVID-19 in pediatric patients (COPP-IMM study)

I was asked to give permission for participation of the following person/my child to this medical scientific research:

Name participant (child): Date of birth:_____/___/ ___

- I have read the information letter for the test subject/parents or guardians. I was also able to ask questions. My questions were answered satisfactory. I had enough time to decide whether I want my child to participate.
- I understand that participation is voluntary. I also know that I can decide for my child not to participate, at any moment. I am not required to give a reason for that.
- I understand that consent for participation in the study will be cancelled if my child resists participation (conform the "behavioural code resistance in minors").
- I understand that for the purpose of verifying the study, a few people may receive access to all the personal data of my child. These people are mentioned in this information letter. I give my consent to allow access for these people.
- I give permission to retain the research data of my child for up to 15 years after the end of this study

Please tick the boxes which apply:

I give permission to use data from the electronic patient file of my child for the benefit of this study. *(In case of a negative answer your child won't be able to take part in this study)*	☐ Yes ☐ No
If applicable, I give permission for the use and storage of left-over body material	☐ Yes ☐ No
I give permission for an extra drawing of blood from my child for the benefit of this study	☐ Yes ☐ No
I give permission to retain body material of my child after this study for up to 15 years to use for follow-up study into COVID-19 as is stated in the information letter.	☐ Yes ☐ No
I give permission to retrieve information from the outpatient clinic after my child was admitted to the ICU, including the results of the neuro-psychological tests.	☐ Yes ☐ No ☐ N/A

I give permission to send me, and perhaps my child, the questionnaires that have been explained in this information sheet. The general questionnaire will be sent about 12 weeks after admittance /visit to the hospital. The short questionnaire about corona vaccination will be sent once a year, for the duration of this study.	☐ Yes ☐ No
I give permission to retain the personal data of my child for 15 years and to use it for future research concerning COVID-19	☐ Yes ☐ No
I give permission to approach my child again after this study for a follow- up study.	☐ Yes ☐ No

- My e-mail address is: _____

Name parent/guardian**:
Signature: Date:____/___/ ___
Name parent/guardian**:
Signature: Date:____/___/ ___

I hereby declare to have fully informed the person(s) mentioned above, about the study concerned.

If, during the course of the study, information emerges that might impact the consent of the parent or guardian, I will inform him or her timely.

Name researcher (or their representative):
Signature: Date:____/___/ ___

Additional information was given by:
Name:
Function:
Signature: Date:____/___/ ___

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* Strike out what does not apply.
** If the child is younger than 16 years of age, either the parent with parental authority or the legal guardian will sign this form. Children between the ages of 12 and 15 years old who can make their own decisions (mentally competent), will also need to sign a form.

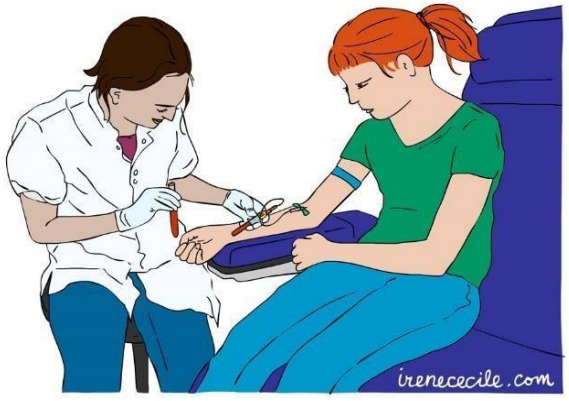
Appendix C: Information on medical research for children under 12

What is it about?

We want to ask you to participate in a study into the coronavirus. We really want to know why you got sick with the coronavirus.
You can decide for yourself if you want to participate or not.

What will happen?

We are going to collect information from your patient file. We are also going to draw blood from you 1 (extra) time.



And lastly, we will ask you and your parents/guardians to fill out a questionnaire.
This will take you 20-25 minutes.

When and how long?

- We will draw blood from you 1 (extra) time when you are in the hospital. We will schedule an appointment with you for that. Drawing blood only takes a very short time: it will be done in only one minute!
- The questionnaires that you and your parents/guardians will fill out, will take 25 minutes or less.
- Other than that, there is nothing you need to do!

What are the advantages and disadvantages?

- There are **no advantages** for you. Participating helps the researchers to better understand the Coronavirus. It will help to cure other children sooner in the future.
- Drawing blood can **hurt a little bit**
- If you do **not participate** in the study, there are no disadvantages. You will be treated like you would have been anyway.

Important to know:

- You don't **have to** participate.
- You can always **quit without giving an explanation.**
- You can always **ask questions**.

If you have questions

You can talk about your questions with your parents/guardians. You and/or your parents/guardians can ask them to theresearcher Emmeline Buddingh. You can e-mail the researcher at: copp@lumc.nl

Write your questions here:

Appendix D: Information Form 12- to 15-year-olds

The 'coronavirus' in children

Dear…….

Are you taking part in a medical study? Here you can read more about the study and your rights. Read this carefully because then you understand what you can decide on. It is fine to take your time to think about it before you decide.

Your parents/guardians will also receive information about this study. You can discuss it with your parents/guardians. They will make a decision togetherwith you.

Questions and contact

Do you have any questions? Talk about it with your parents/guardians. Or ask them to the researcher. You can write your questions down below.

You can also e-mail the researcher, Dr E.P. Buddingh, at copp@lumc.nl.

Do you want to talk about the study with a Doctor who is not involved in the study? You can e-mail Dr Meijer: c.r.meijer-boekel@lumc.nl.

Write your questions here:

Tip: take a picture of your questions so you have them when you talk to the doctor/researcher

About the study

This study deals with the Coronavirus in children and is conducted by the LUMC, but also in other hospitals in The Netherlands. Around 60 children and/or youth are participating. The study has been verified by a special team, the Medical Ethical Committee of the LUMC (METC-LDD). They have approved this study and have determined that this study causes hardly any discomfort.

Why this study?

This study is done to research the new illness caused by the 'coronavirus'. This new virus makes adults, as well as children, sick. We don't know exactly how the illness works yet. That's why we want to see how it affects you. For example, we want to know how long you are sick, what medication you get and how you got well. We also want to know how the illness effected your daily life.

How does participation work?

You don't have to do anything extra to participate in the study. If you agree to participate, we will draw blood from you one extra time and we will send you a questionnaire.

Participation in the study consists of three parts:

1. The doctors will note all information about your illness in the computer. This is your digital 'patient file'. We want to use the information in your patient file for our study.

   Were you admitted to the Intensive Care Unit (ICU)? Then we will ask separate permission to gain access to the information from the routine outpatient clinic visit after this ICU stay. That means the results from tests that doctors do to see how you are doing after having been admitted to the ICU. For example, your general health, ability to concentrate and an intelligence test.

   During your stay in hospital, maybe a blood sample has already been taken from you. Is there any left over from that? Then we would like to use that as well.

2. Besides that, we would like to draw some extra blood from you. We ask your permission to do this. We will try to do this at the same time it was already necessary to draw blood. Otherwise, we will ask you at a different time if we can draw blood an extra time. We will support you with this and we will make sure it won't bother you too much.

3. About 12 weeks after your visit or admittance to the hospital, we will send you and your parents/guardians a questionnaire. This is about whether you still have complaints after you got home and how you are doing in general (for example: mood, sleep and contact with friends). The filling out of the questionnaire will take about 10 - 20 minutes. Filling out this questionnaire will take you about 10-20 minutes. Do you qualify for the corona vaccine? Then we would like to send you an additional short questionnaire, once a year, for the duration of this study. This questionnaire is about corona vaccination. We ask you if you have been vaccinated and if so, if you have experienced any side effects of vaccination. Filling out this questionnaire will take you a maximum of 2 minutes.

About the treatment

It doesn't matter whether you participate in the study or not, you will receive the normal treatment.

Inconveniences

Do you give permission for the drawing of extra blood? We will try to do it at the same time that we already draw blood from you. Otherwise, we will have to draw blood for one extra time. We will support you in this and will make sure it won't bother you too much.

Important to know:

The information we collect is “coded’. This means that your personal data is saved under a number and we won’t know which number it is yours.

Advantages and disadvantages :

1. An advantage of participating in this study is that you help to find out more about the new ‘coronavirus’
2. A disadvantage of participating in this study is that you may have to have blood drawn one extra time.

Do you have to participate?

No, it is **your choice** whether to participate or not. If you don’t want to participate then you don’t have to. Even if your parents/guardians would prefer you to participate. Do you want to participate? Then sign the consent form. You can **always quit** at a later stage if you wish to. Tell the researcher you wish to stop your participation. You don’t have to explain why.

Revoking permission

If you wish to stop your participation in the study, you inform the researcher. This is called: revoking your permission. The information that was already collected will still be used for the study.

Your personal data

For the study we need three things from you:

Personal data = information on who you are, for example your date of birth or where you live.	
Medical information = (also a sort of personal data) information about your health, for example if you are sick and if you use any medication.	
Your blood = to research how the immune system in children with the Coronavirus reacts.	

These **three things are necessary for the study**. You and your parents/guardians give permission so we can use these things. Do you want to know more about what we do with your information? You can ask your parents/guardians, there is more explanation in their information letter. You can also ask the researcher.

Your decision

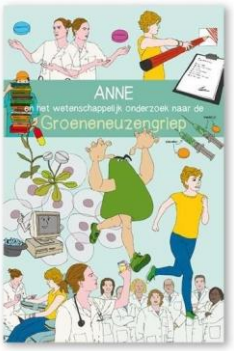
The form

Do you agree to participate? Then you sign the consent form. We also need a signature from your parents/guardian.

You can also decide if it is okay that we approach you for follow-up research. In the case of follow-up research, we might approach you with information about participation in this study. You can decide at that moment whether or not you want to participate in this follow-up study.

Wish to learn more?

Do you want to learn more about medical research or about your rights? Check www.kindenonderzoek.nl
On this website you will also find the comic called 'Anne en de Groeneneuzengriep' (Anna and the GreenNoseFlue") about research.For this study, the preface and chapters 1, 2, 3, 6a, 9, 10, 11 and 12 are relevant.



Do you wish to learn more about the coronavirus and this study? You can check www.covidkids.nl

Consent form children aged 12 to 15

- I **understood** the information. I was also able to ask questions. My **questions have been answered**.
- I had **enough time to decide** if I want to participate in this study.
- I know I am **not obligated** to participate.
- I understand that **I can quit at any time** if I don't want to participate any longer.

Please tick the boxes that apply:

I give permission to use data from my electronic patient file for the benefit of this study. *(If you chose "No" you won't be able to participate in this study)*	☐ Yes ☐ No
I was admitted to the Intensive Care Unit (ICU) and I give permission to retrieve information from the outpatient clinic, including the results of neuro-psychological research like intelligence testing.	☐ Yes ☐ No ☐ I did not stay at the ICU
If applicable, I give permission for the use and storage of left-over body material	☐ Yes ☐ No
I give permission for an extra drawing of blood for this study	☐ Yes ☐ No
I give permission to send me the questionnaires that have been explained in this information sheet. The general questionnaire will be sent about 12 weeks after my visit/admittance to the hospital. A short questionnaire about corona vaccination will be sent once a year, for the duration of this study.	☐ Yes ☐ No
I give permission to approach me later for follow-up research.	☐ Yes ☐ No

I agree to participate in this study.

Name participant:

Signature: Date:_____/___/ ___

<u>This part is for the researcher:</u>

I hereby declare to have fully informed this test subject, about the study concerned.
If, during the course of the study, information emerges that might impact the consent of the test subject, I will inform him or her timely.

Name researcher (or their representative):

Signature: Date:_____/___/ ___

<*if applicable*> Additional information was given by:

Name:
Function:
Signature: Date:_____/___/ ___

The test subject will be given a complete information letter, together with a signed version of the consent form.