



Application form for NICE data extraction and analysis for a scientific publication

Please complete this form fully and submit it to secretariaat@stichting-nice.nl

- 1.1 What is the project title? We suggest to use the provisional title of the proposed scientific publication.**

Characteristics and outcome of all Dutch COVID-19 patients admitted to the ICU; a comparison with viral pneumonia patients

- 1.2 Give at least five keywords which describe the project.**

COVID-19, viral pneumonia, ICU, critical ill, outcome, survival, mortality

- 2.1 Who is the researcher conducting the study? This person can be a junior researcher (e.g. PhD student). Will he/she act as contact person for this project with NICE? Is (s)he contact person for NICE in his/her ICU***

Name: Sylvia Brinkman

Academic title: Dr

Position and organization: senior researcher at the department medical informatics of Amsterdam UMC, University of Amsterdam

NICE contactperson for an ICU(yes/no) yes

Contactperson for this researchproject (yes/no) yes

Who is the project leader /supervisor? Will he/she act as contactperson for this project with NICE? Is (s)he contactperson for NICE in his/her ICU*

- 2.2**

Name: Nicolette de Keizer

Position and organization: registration manager of NICE

NICE contactperson for an ICU(yes/no) yes

Contactperson for this researchproject (yes/no) yes

Who else is involved in the project group? Please provide all information on all members and indicate if this person is NICE contact person. *

Name Fabian Termorshuizen

- 2.3** Position and organization: statistician at the department medical informatics of Amsterdam UMC, University of Amsterdam





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NICE contact person for an ICU (yes/no) yes

Name Dave Dongelmans

Position and organization: Intensivist at Amsterdam UMC

NICE contact person for an ICU (yes/no) yes

Name Sesmu Arbous

Position and organization: Intensivist at LUMC

NICE contact person for an ICU (yes/no) yes

Name Dylan de Lnage

Position and organization: Intensivist at UMCU

NICE contact person for an ICU (yes/no) yes

Which hospital(s), participating in NICE, is/are supporting this application?

Amsterdam UMC, locatie AMC, LUMC, UMCU

2.4 What are the responsibilities of the project team? Describe how this proposal fits into the project leader's and members' research lines and expertise. Please specify which member of the project team will be primarily responsible for writing the manuscript and/or supervising the writing process.

2.5

Conceptualization research question– Ideas; formulation or evolution of overarching research goals and aims: all involved members.

Methodology – Development or design of methodology; creation of models. Fabian, Sylvia, and Nicolette

Performing analyses: Fabian and Sylvia

Writing – original draft – Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation). Sylvia, Nicolette, and Fabian

Writing – review & editing – Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre- or post-publication stages. Dylan, Dave, and Sesmu

Is the project part of a larger project? If the answer is 'yes', please give details of how this project fits into the larger project. If this project is part of someone's PhD project, explicitly state that you are aware of the art 8 of 'Voorwaarden voor NICE extractieverzoeken'.

2.6





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This research question is not part of a larger project. However, since the start of the COVID-19 outbreak in the Netherlands the Dutch government urged all hospitals to register all suspected and confirmed COVID-19 patients admitted to the ICU in the COVID-DataBase. This data is linked with the regular NICE database. Multiple research questions will be addressed using these data, among which this research question

- 2.7 Given the duration and complexity of the projects, no projects will be awarded that are carried out by internship students or which are part of internships.** Please explicitly state that this project is not part of an internship.

This study is not part of an internship

- 3.1 What is the scientific background to the project?** Include references to appropriate recent literature and information on the additional value and implications of the project. It should consist of 500 to 1,000 words. This section and the section on the research question (3.2) should, together, be equivalent to the introduction section in a scientific publication.

Since the outbreak of COVID-19 in China and its European start in Italy, health professionals warned the world for the spread and severity of this disease. Their main concerns include the high need of hospital and ICU capacity and a high mortality rate. On the other hand, some politicians and even health professionals mention COVID-19 as an ordinary flu or pneumonia. Some studies indeed reported no or only a small elevated mortality risk among hospitalized COVID-19 patients, namely between 0% and 21% [REF] . However, there are also studies that mentioned mortality rates of 62 to 78 percent among COVID-19 patients admitted to the ICU [REF] which is much higher than other influenza like diseases in the ICU [REF]. These findings suggest that the mortality is only high among the approximately minority of the COVID-19 patients that are admitted to the ICU. It should be noted that patient characteristics and outcomes of the published studies are hard to compare because hospital and ICU admission policies differ between countries during these pandemic period. Furthermore the follow up period of the published studies have been different. Due to the urgent situation of the pandemic, some early studies reported outcome of COVID-19 patients ignoring the fact that a majority of patients were still in the ICU at the end of the study period. This might result in overestimation of mortality risks.

In many countries shortage of ICU capacity was a fact or a realistic fear and ICU triage protocols needed to be updated. Ideally those protocols are not only expert-based but evidence-based and data driven. To better understand COVID-19 as a new disease and provide input for triage we need information on patient characteristics and outcomes of as many COVID-19 patients from different ICU settings. Since the first confirmed case in the Netherlands on 15 February 2020 the National Intensive Care Evaluation (NICE) registry collected data on all COVID-19 cases admitted to Dutch ICUs. This enables the opportunity to analyze all COVID-19 patients from one healthcare system, which according to our knowledge is not been done before.



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References

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3. Lei Z, Cao H, Jie Y, Huang Z, Guo X, Chen J, et al. A cross-sectional comparison of epidemiological and clinical features of patients with coronavirus disease (COVID-19) in Wuhan and outside Wuhan, China. *Travel medicine and infectious disease*. 2020:101664.
4. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *Jama*. 2020;323(20):2052-9.
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6. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *Jama*. 2020;323(16):1612-4.
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8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2020;395(10229):1054-62.
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11. van Asten L, Luna Pinzon A, de Lange DW, de Jonge E, Dijkstra F, Marbus S, et al. Estimating severity of influenza epidemics from severe acute respiratory infections (SARI) in intensive care units. *Critical care (London, England)*. 2018;22(1):351.
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18. (SIR) SI. COVID-19 in Swedish intensive care 2020 [Available from: <https://www.icuregswe.org/en/data--results/covid-19-in-swedish-intensive-care/>.

3.2 What is the research question? This section is equivalent to the last paragraph in the introduction section in a scientific publication and should include the aims and objectives of the project.

The aim of this study is to describe the clinical characteristics and outcome of COVID-19 patients admitted to Dutch ICUs. In order to put those in perspective, we compare these with a historical ICU population admitted due to community-acquired viral pneumonia.

4.1 Which data are required? Please provide a complete, but concise description including inclusion and exclusion criteria and time period. Use the NICE datadictionary on



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<https://stichting-nice.nl/dd/#start> to describe the required data. A minimum amount of variables will be used to ensure data protection and privacy. Describe how variables will be categorized, if appropriate. Non-standard definitions should be supported by references to the literature. This section should, together with the sections on outcomes and statistical methods, be equivalent to the methods section in a scientific publication. Contact Stichting NICE for questions regarding available variables and definitions.

The national COVID-DB linked to the more comprehensive clinical data of ICU patients in the NICE-DB will be used. In this study the linked data of the patients with confirmed COVID-19 admitted to the ICU between February 15th 2020 and June 1st 2020 will be used. The patient characteristics (age, gender, BMI, mechanical ventilation, length of stay, comorbidities, APACHE IV APS) and outcome of the linked COVID-19 patients at the ICU will be compared with patients admitted to the ICU with a diagnosis of community-acquired viral pneumonia between January 1st 2016 and January 1st 2020. To select those patients from NICE-DB, APACHE IV reason for ICU admission “viral pneumonia” will be used in combination with a maximum length of stay in the hospital of 3 calendar days prior to ICU admission.

- 4.2 What are the outcomes used in the project?** Please define the primary outcome and any secondary outcomes clearly and fully, including references to the literature where necessary.

We will focus on the in-hospital mortality

- 4.3 What statistical methods will be used in the project?** Please be as precise as possible. Contact Stichting NICE regarding advise on available statistical methods. For complex questions it is recommended to plan a meeting to discuss methodology.

The crude in-hospital mortality among COVID-19 ICU patients and viral pneumonia patients will be compared by using a Kaplan-Meier survival graph and a Cox proportional hazards model. To correct for important clinical differences between the two cohorts that may confound the association between the cohort and observed in-hospital mortality, the Cox regression model will be expanded with adjustment for: age, gender, BMI, comorbidities (immunological insufficiency, chronic renal failure, chronic respirator insufficiency, chronic cardiovascular insufficiency, cirrhosis, and malignancy) present before hospitalization, and the acute physiology score (APS) of the APACHE-IV prognostic model to describe the severity of physiological disturbance in the first twenty-four hours of ICU admission. The hazard ratio (HR) for in-hospital mortality among COVID-19 patients compared to the viral pneumonia patients and associated 95%-confidence will be calculated

- 4.4 Which tables or figures do you want to include in your scientific publication?** Please provide empty tables and ‘fake’ figures (or copies from other sources), with as much information on the data you require.





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A Kaplan Meier curve and the following tables:

Patient characteristics of COVID-19 and viral pneumonia patients

	COVID-19 N (%)	Viral pneumonia N (%)	P value
Number of patients			
Age: <40			
Age: 40-45			
Age: 45-50			
Age: 50-55			
Age: 55-60			
Age: 60-65			
Age: 65-70			
Age: 70-75			
Age: 75-80			
Age: 80-85			
Age: >85			
Age: Unknown			
Gender: Male			
BMI: <18.5			
BMI: 18.5 - 25			
BMI: 25 - 30			
BMI: 30 - 35			
BMI: 35 - 40			
BMI: >40			
BMI: Unknown			
Immunological insufficiency			
Chronic renal failure			
Chronic respiratory insufficiency or COPD			
Chronic cardiovascular insufficiency			
Cirrhosis			
Malignancy			
APS: <34			
APS: 34-43			
APS: 43-52			
APS: 52-64			
APS: >64			



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Outcomes of COVID-19 and viral pneumonia patients

	COVID-19	Viral pneumonia	P value
Number of patients			
In-hospital mortality N (%)			
Length of stay hospital Mean(SD)			
Mechanical ventilation at ICU admission N (%)			
Mechanical ventilation in 1 st 24 hours of ICU admission N (%)			

	HR (95%-CI)	P value
COVID-19 vs virale pneumonia		
Age 40-45 vs <40		
Age 45-50 vs <40		
Age 50-55 vs <40		
Age 55-60 vs <40		
Age 60-65 vs <40		
Age 65-70 vs <40		
Age 70-75 vs <40		
Age 75-80 vs <40		
Age 80-85 vs <40		
Age >85 vs <40		
Gender Female vs Male		
BMI <18.5 vs 18.5-25		
BMI 25-30 vs 18.5-25		
BMI 30-35 vs 18.5-25		
BMI 35-40 vs 18.5-25		
BMI ≥40 vs 18.5-25		
BMI Missing vs 18.5-25		
Immunological insufficiency		
Chronic renal failure		
Chronic respiratory insufficiency		
Chronic cardiovascular insufficiency or COPD		
Cirrhosis		
Malignancy		
APS 34-43 vs <34		



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	HR (95%-CI)	P value
APS 43-52 vs <34		
APS 52-64 vs <34		
APS >64 vs <34		

5.1 Are additional permissions from ICUs or patients required for this project? If the answer is 'yes', give details of the permissions required, including the person responsible for obtaining them and the expected timescale.

No

5.2 Are any additional (non-NICE) data required to carry out this project? If the answer is 'yes', give details of the data required, including the person responsible for obtaining the data and the expected timescale.

No

6. Do you consider carrying out the analyzes yourself at the department of Medical Information at the AMC with the supervision of the NICE researchers? If yes, can you prove by means of diplomas / certificates that you are qualified to carry out the analyzes? Are you a PhD candidate who wants to include more than two publications in your PhD theses based on NICE data then you are obliged to perform the analyses at the dept. Medical Informatics (KIK) under supervision of senior researcher of this department. Provide information which days during which time period you will visit the department.

The member requesting these analyses is a member of the NICE researchers, so this is not applicable

7. How will this project be funded? *Preferably, the costs for the analyses are included in the fundraising. If the application is not part of a funded project, an alternative can be considered in consultation with the KIK.*

Not applicable

8. Please include an estimate of the time needed for data extraction, analysis and interpretation and state your means of funding for this part of the project.

We would like to perform the analyses and writing process within a period of a month since information and insight in the COVID-19 patients is very important at this moment

9. Do you wish to work with a particular member of the board of directors of NICE? If the answer is 'yes', please name this person.

No



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10. Dutch language summary. Please describe your research in approximately 100 words in Dutch. This summary will be published on the NICE website.

Er zijn tegenstrijdige uitspraken gedaan over COVID-19, sommige noemen hoge sterftcijfers en andere verwijzen naar COVID-19 als een gewone griep of virale longontsteking. COVID-19 deelt inderdaad symptomen met virale longontsteking, maar het is onbekend in hoeverre COVID-19-patiënten vergelijkbare kenmerken en resultaten hebben als reguliere patiënten met virale longontsteking die op de IC zijn opgenomen. Deze studie beschrijft verschillen in kenmerken en uitkomsten tussen de patiënten met COVID-19 en virale longontsteking die zijn opgenomen op Nederlandse IC's. Klinische gegevens van het National Intensive Care Evaluation (NICE) -register van alle Nederlandse bevestigde COVID-19-patiënten opgenomen tussen 15 februari 2020 en 1 juni 2020 en van virale pneumonie-patiënten opgenomen tussen 1 januari 2016 en 1 januari 2020 worden gebruikt. Patiëntkenmerken en resultaten tussen de twee groepen werden vergeleken. De ongecorrigeerde en voor patiënten kenmerken gecorrigeerde ziekenhuismortaliteit onder patiënten met COVID-19 en virale longontsteking werd vergeleken door de hazard ratio's en de bijbehorende 95% -betrouwbaarheidsintervallen te berekenen met behulp van Cox-modellen.

11. What are the intended journals? Please provide three options.

Lancet, BMJ, Jama or ICM

By submitting this form, I agree to be bound by the “Voorwaarden verbonden aan een data-extractieverzoek bij NICE” attached to this document.

Name: Sylvia Brinkman

Date: 3-5-2020

Signature: SB

**: These data are stored for administrative and communication purposes and are subject to the Privacy Policy as described on the website of the NICE Foundation.*

