

Online Supplemental Material

Diabetes and overweight/obesity are independent, non-additive, risk factors for the in-hospital severity of COVID-19: An international, multi-center retrospective meta-analysis.

Author List

Main writing group

Danielle K. Longmore, Jessica E. Miller, Siroon Bekkering, Christoph Saner, Edin Mifsud, Yanshan Zhu, Richard Saffery, Alistair Nichol, Graham Colditz, Kirsty R. Short, David P. Burgner.

International BMI-COVID Consortium

F [Anfasa](#), TL [Benfield](#), MJT [Blaauw](#), LJM [Boonman-de Winter](#), AL [Brucato](#), EA [Buanes](#), E [Burhan](#), E [Calabro](#), A [Ceschi](#), RL [Chinhoyi](#), HFEW [Cuijpers](#), A [Dofferhoff](#), X [Fang](#), L [Favre](#), P [Ferrari](#), T [Fomina](#), JA [Fulcher](#), A [Giacomelli](#), D [Goodman-Meza](#), P [Goyal](#), AL [Groenendijk](#), J [Hoogerwerf](#), SB [Israelsen](#), M [Karolyi](#), APM [Kerckhoffs](#), DM [Kirkegaard-Klitbo](#), S [Koesnoe](#), C [Luo](#), D C [Lye](#), NAB [Ntusi](#), SWX [Ong](#), L [Oreni](#), H [Pangestu](#), M [Papadimitriou-Olivgeris](#), S [Paramita](#), E [Pawelka](#), L [Persani](#), CW [Pitoyo](#), M [Plataki](#), Prasenohadi, IB [Prasetya](#), X [Qu](#), M [Rajan](#), JB [Ringel](#), M [Safford](#), T [Santoso](#), D [Soranna](#), T [Sprong](#), CRT [Stoll](#), AD [Susanto](#), AF [Syam](#), C [Torlasco](#), M [van Apeldoorn](#), JS [van de Maat](#), K [Veerman](#), A [Verbon](#), X [Wen](#), M [Westerman](#), E-J [Wils](#), Y [Xia](#), BE [Young](#).

Supplemental Material

Diabetes and overweight/obesity are independent, non-additive, risk factors for the in-hospital severity of COVID-19: An international, multi-center retrospective meta-analysis. 1

Author List1

Main writing group 1

International BMI-COVID Consortium..... 1

List of Investigators.....4

Main writing group 4

International BMI-COVID Consortium..... 4

Statistical Analysis Plan (SAP).....6

Table S1 - Types of hospitals for contributing sites and dates of data collection 10

Table S2 – National obesity prevalence by site country¹11

1. OECD, (2017), Obesity Update 2017, Paris www.oecd.org/health/obesity-update.htm 11

2. Ministry of Health Singapore, Obesity trend and Programmes, 6 Jan 2020, Singapore, <https://www.moh.gov.sg/news-highlights/details/obesity-trend-and-programmes#:~:text=Written%20Answer,has%20remained%20stable%20since%202013> 11

Table S3 – Characteristics of the study population, by study site 11

Table S4 - Characteristics of study population by study sites, detailed 16

Figure S1 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with diabetes. Models adjusted for: BMI categories (≥ 12 -<18, ≥ 18 -<25, ≥ 25 -<30, ≥ 30), age (<65, ≥ 65), sex (male/female), pre-existing cardiovascular disease (yes/no), hypertension (yes/no), pre-existing respiratory condition (yes/no),. Reference is patients without diabetes. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model. 28

Figure S2. Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality male compared to female (panel A) and patients ≥ 65 years of age compared to <65 years of age (panel B). Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among males (panel A) and patients ≥ 65 years of age (panel B)30

Figure S3 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with pre-existing cardiovascular disease. Models adjusted for: BMI categories (≥ 12 -<18, ≥ 18 -<25, ≥ 25 -<30, ≥ 30), age (<65, ≥ 65), sex (male/female), diabetes (yes/no), pre-existing respiratory condition (yes/no), hypertension (yes/no). Reference is patients without pre-existing cardiovascular disease. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model.32

Figure S4 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with pre-existing respiratory conditions. Models adjusted for: BMI categories (≥ 12 -<18, ≥ 18 -<25, ≥ 25 -<30, ≥ 30), age (<65, ≥ 65), sex (male/female), pre-existing cardiovascular disease (yes/no), diabetes (yes/no), hypertension (yes/no). Reference is patients without pre-existing respiratory conditions. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model.33

Table S5 – Site-specific and meta-analysis estimates using standard and Asian country specific BMI categories for Asian countries.....34

Table S5 - Invasive mechanical ventilation and in-hospital mortality site-specific estimates with additional adjustments for smoking &/or race/ethnicity35

List of Investigators

Main writing group

Danielle K. Longmore, Jessica E. Miller, Siroon Bekkering, Christoph Saner, Edin Mifsud, Yanshan Zhu, Richard Saffery, Alistair Nichol, Graham Colditz, Kirsty R. Short, David P. Burgner.

International BMI-COVID Consortium

F Anfasa MD, PhD (Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia; Department of Viroscience, Erasmus MC, Rotterdam, the Netherlands), TL Benfield MD (University of Copenhagen Denmark), MJT Blaauw MD (Department of Internal Medicine Bernhoven Hospital, Uden, the Netherlands), LJM Boonman-de Winter PhD (Amphia hospital, Department Amphia Academie, team Science, Breda, the Netherlands), AL Brucato MD (Department of Biomedical and Clinical Sciences “Sacco”, University of Milan, ASST Fatebenefratelli-Sacco, Milan, Italy), EA Buanes PhD (Department of Intensive Care, Haukeland University Hospital, Bergen, Norway, Norwegian Intensive Care and Pandemic Registry), E Burhan MD, PhD (Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Indonesia; Persahabatan Hospital, Jakarta Indonesia), E Calabro MD (Department of Internal Medicine, ASST Fatebenefratelli-Sacco, Milan, Italy), A Ceschi MD (Ente Ospedaliero Cantonale, Lugano, Switzerland; Biomedical Faculty, Università della Svizzera Italiana, Lugano, Switzerland; University Hospital and University of Zurich, Zurich, Switzerland), RL Chinhoyi MSc (Department of Medicine, University of Cape Town and Groote Schuur Hospital, Cape Town, South Africa), HFEW Cuijpers MSc (Amphia hospital, Department Amphia Academie, team Science, Breda, the Netherlands), A Dofferhoff MD PhD (Department of Internal Medicine, Canisius-Wilhelmina Hospital, the Netherlands), X Fang MD (Master, Department of Blood Transfusion, Fifth Affiliated Hospital, Sun Yat-Sen University, Zhuhai, Guangdong Province, China), L Favre MD (Service of endocrinology, diabetology and metabolism, Lausanne University Hospital, Lausanne, Switzerland), P Ferrari MD (Biomedical Faculty, Università della Svizzera Italiana, Lugano, Switzerland; Clinical School, University of New South Wales, Sydney, Australia; Ente Ospedaliero Cantonale, Lugano, Switzerland), T Fomina MSc (Department of Global Health and Primary Care, University of Bergen, Norway), JA Fulcher MD, PhD (Division of Infectious Diseases, David Geffen School of Medicine, University of California Los Angeles, United States of America), A Giacomelli MD (Department of Biomedical and Clinical Sciences “Sacco”, University of Milan, Italy), D Goodman-Meza MD (Division of Infectious Diseases, David Geffen School of Medicine, University of California Los Angeles, United States of America), P Goyal MSc (Weill Cornell Medicine, New York, NY, United States America), AL Groenendijk MD (Department of Medical Microbiology and Infectious Diseases, Erasmus MC, Rotterdam, the Netherlands), J Hoogerwerf MD PhD (Department of Internal Medicine and Radboudumc Center of Infectious Diseases, Radboudumc, Nijmegen, the Netherlands), SB Israelsen MD (University of Copenhagen, Denmark), M Karolyi MD (4th Medical Department with Infectious Diseases and Tropical Medicine, Klinik Favoriten, Vienna, Austria), APM Kerckhoffs MD PhD (Department of Internal Medicine and Geriatrics, Jeroen Bosch Hospital, the Netherlands), DM Kirkegaard-Klitbo MD (University of Copenhagen, Denmark), S Koesnoe MD, PhD (Division of Allergy and Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia; Universitas Indonesia Hospital, Depok, Indonesia), C Luo MD (Guangzhou Eighth People’s Hospital, Guangdong Province, China), D C Lye FRACP (National Centre for Infectious Diseases; Tan Tock Seng Hospital; Yong Loo Lin School of Medicine; Lee Kong Chian School of Medicine, Singapore), NAB Ntusi MD, DPhil (Division of Cardiology, Department of Medicine, University of Cape Town and Groote Schuur Hospital, Cape Town, South Africa), SWX Ong MMed (National Centre for Infectious Diseases; Tan Tock Seng Hospital; Singapore), L Oreni BIT (Department of Infectious Diseases, ASST Fatebenefratelli-Sacco, Milan, Italy), H Pangestu MD (Mochtar Riady Cancer Comprehensive Center; Siloam Mampang Hospital Jakarta, Indonesia), M Papadimitriou-Olivgeris PhD (Service of Infectious Diseases, Lausanne University Hospital, Lausanne, Switzerland), S Paramita MD, PhD (Faculty of Medicine, Mulawarman University, Samarinda, Indonesia), E Pawelka MD (4th Medical Department with Infectious Diseases and Tropical Medicine, Klinik Favoriten, Vienna, Austria), L Persani MD, PhD (Unit of Endocrinology, Istituto Auxologico Italiano, Milan, Italy, Department of Biotechnology and Translational Medicine University of Milan, Milan, Italy), CW Pitoyo MD (Division of Respiriology and Critical Care, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National General Hospital, Jakarta Indonesia), M

Plataki PhD (Weill Cornell Medicine, New York, NY, United States America), Prasenohadi MD, PhD (Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Indonesia; Persahabatan Hospital, Jakarta Indonesia), IB Prasetya MD (Department of Internal Medicine, Faculty of Medicine, Pelita Harapan University; Siloam Hospital Kelapa Dua, Tangerang, Indonesia), X Qu MD (Department of Medical, Fifth Affiliated Hospital, Sun Yat-Sen University, Zhuhai, Guangdong Province, China), M Rajan MBA (Weill Cornell Medicine, New York, NY, United States America), JB Ringel MPH (Weill Cornell Medicine, New York, NY, United States America), M Safford MD (Weill Cornell Medicine, New York, NY, United States America), T Santoso MD (Tasikmalaya Regional Hospital, Tasikmalaya, Indonesia), D Soranna PhD (Unit of Statistics, Istituto Auxologico Italiano, Milan, Italy), T Sprong MD PhD (Department of Internal Medicine, Canisius-Wilhelmina Hospital, the Netherlands), CRT Stoll MSW (Washington University School of Medicine, St Louis, United States of America), AD Susanto MD, PhD (Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Indonesia; Persahabatan Hospital, Jakarta Indonesia), AF Syam MD, PhD (Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National General Hospital, Jakarta Indonesia), C Torlasco MD (Unit of Cardiology, Istituto Auxologico Italiano, Milan, Italy), M van Apeldoorn PhD (Department of Internal Medicine, Jeroen Bosch Hospital, the Netherlands), JS van de Maat MD (Department of Internal Medicine and Radboud UMC Center of Infectious Diseases, Radboud UMC, the Netherlands), K Veerman MD (Department of Internal Medicine, Sint Maartenskliniek, the Netherlands), A Verbon PhD (Department of Medical Microbiology and Infectious Diseases, Erasmus MC, Rotterdam, the Netherlands), X Wen MD (Guangzhou Eighth People's Hospital, Guangzhou, Guangdong Province, China), M Westerman MD PhD (Department of Internal Medicine, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands), E-J Wils MD PhD (Department of Intensive Care, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands), Y Xia PhD (School of Science, Edith Cowan University, Australia; School of Biomedical Science, The University of Western Australia, Perth, Australia), BE Young MRCP (National Centre for Infectious Diseases; Tan Tock Seng Hospital; Lee Kong Chian School of Medicine, Singapore).

Statistical Analysis Plan (SAP)

Study aim:

- To assess the impact of obesity as a risk factor for severe COVID-19 in adult patients.

Study population:

- Patients aged 18 years and older admitted to hospital who test positive for SARS-CoV-2 by either PCR of nasopharyngeal secretions or saliva and/or serology and/or stool.

Data:

- International critical care databases, national data on obesity prevalence or BMI, national COVID-19 data reporting, or hospital-based data reporting from multiple international sites

Exposure:

- Body mass index (BMI kg/ m²)
- BMI categories:
 - o **All sites:** normal, overweight, obese (may vary depending on country-specific ranges)
 - ≥ 12 -<18, ≥ 18 -<25 (reference), ≥ 25 -<30, ≥ 30 (upper limit 60)
 - Categories for Asian countries, if used: ≥ 12 -<18, ≥ 18 -<24 (reference), ≥ 24 -<28, ≥ 28
 - o If possible, based on site's sample size: (based on site's discretion to look at more categories) [to be done in addition to above categories]
 - ≥ 12 -<18, ≥ 18 -<25 (reference), ≥ 25 -<30, ≥ 30 -<35, ≥ 35 -<40, ≥ 40 (upper limit 60)
(note: may need to merge ≥ 40 and ≥ 35 -<40 groups if numbers are too small)

Outcomes (each to be analysed separately):

- **NOTE: All outcomes are among patients who test positive by PCR for SARS-CoV-2**
- 1. Patients with combined outcome of [oxygen use **without** invasive ventilation AND/OR non-invasive ventilation (e.g. CPAP)] (vs none) (yes=1/no=0)
- 2. Patients with combined outcome of [**invasive** mechanical ventilation (intubated and ventilated) AND/OR ECMO use] (vs none) (yes=1/no=0)
- 3. Patients with in-hospital mortality (yes=1/no=0)

Analysis:

1. **With the category values specified for all sites** [analysis code provided in 'BMI COVID code_SAS Stata R_FOR ALL SITES_11May' document]

1. **Risk of oxygen use without invasive ventilation AND/OR non-invasive ventilation; invasive mechanical ventilation (intubated and ventilated) AND/OR ECMO use; in-hospital mortality**
 - o Exposure: BMI categories compared to reference BMI group (≥ 18 -<25)
 - o Outcomes: **[NOTE: Modelling the odds of the outcome occurring (event=1), not event=0. For example, model the odds of death (mortality = 1), and not the odds of survival or (mortality = 0). SAS/Stata/R syntax reflect this.]**
 1. Combined outcome of [oxygen use **without** invasive ventilation AND/OR non-invasive ventilation (e.g. CPAP)]
YES (= 1) = people who have had this outcome
 - **NOTE:** it is ok if at some point these people had invasive mechanical ventilation or died
 - NO (= 0) = people who did not have this outcome nor a more severe outcome
 - **NOTE:** this group will only include people who were hospitalised and did not have any of the outcomes. DO NOT include people who have had invasive mechanical ventilation or died

2. Combined outcome of [**invasive** mechanical ventilation (intubated and ventilated) AND/OR ECMO use]
 YES (= 1) = people who have had this outcome
 - **NOTE:** it is ok if at some point these people had oxygen use **without** invasive ventilation AND/OR non-invasive ventilation or died
 NO (= 0) = people who did not have this outcome nor a more severe outcome
 - **NOTE:** this group will only include people who were hospitalised and did not have any of the outcomes or were hospitalised and only had oxygen use **without** invasive ventilation AND/OR non-invasive ventilation. DO NOT include people who have died
 3. In-hospital mortality
 YES (= 1) = people who have had this outcome
 - **NOTE:** it is ok if at some point these people had oxygen use **without** invasive ventilation AND/OR non-invasive ventilation or invasive mechanical ventilation
 NO (= 0) = people who did not have this outcome
 - **NOTE:** this group will include all patients who did not die
- Model - logistic regression
 - Overall non-stratified
 - [Results from below models to be entered into 'Overall' tab in excel file 'BMI COVID tables']
 - Crude and adjusted (2 levels) for:
 1. Age (<65/≥65); sex; pre-existing cardiovascular disease (y/n); diabetes (y/n); pre-existing respiratory conditions (y/n); hypertension (y/n)
 2. Above + current smoking status (if available); SES (if available); race/ethnicity (country-specific groups, if available)
2. **Table 1 – characteristics of study population (distribution of characteristics by exposure – n, %, median, IQR)** [Results to be entered into 'Table 1' tab in excel file 'BMI COVID tables']
 3. **Meta-analysis of overall, non-stratified results from logistic models – to be done by Murdoch Children's Research Institute**

Missing data:

No adjustments will be made for missing data. We do not anticipate a large % of missing data for the main analysis variables. The different levels of adjustments account for variables that might not be collected from all sites (ie smoking, socio-economic level, race/ethnicity).

Definition of variables:

Variable	Description	Coding
Required variables		
Age (years)	All sites:	<65 (reference) ≥65
		≥18-<50 (reference) ≥50-<65
	For larger sites to use, in addition to above category:	≥65-<75 ≥75
Sex		male = 1 female = 0
Body mass index (BMI = kg/ m ²)	All sites:	≥12-<18 ≥18-<25 (reference) ≥25-<30 ≥30 (upper limit 60)
		≥12-<18 ≥18-<25 (reference) ≥25-<30 ≥30-<35
	For larger sites to use, in addition to above category:	≥35-<40 ≥40 (upper limit 60)
Pre-existing cardiovascular disease	Doctor-diagnosed coronary heart disease, ischaemic stroke, heart failure, peripheral vascular disease, chronic kidney disease.	yes = 1 no = 0
Diabetes	Includes Type 1 or Type 2	yes = 1 no = 0
Pre-existing respiratory conditions	Doctor-diagnosed and currently on treatment (e.g. asthma, COPD, etc)	yes = 1 no = 0
Hypertension	Doctor-diagnosed and currently on treatment	yes = 1 no = 0
Hospital admission	Not required if data are from a hospital	yes = 1 no = 0
ICU admission	If there is a separate high dependency unit for non-invasive ventilation etc, it would be good to have these data	yes = 1 no = 0
Length of ICU admission		Number of days
Length of hospital stay	Optional: If patient is still in hospital at the time of data collection please indicate so	Number of days
In-hospital mortality	Patient died while in hospital	yes = 1 (died) no = 0 (survived)
Supplemental oxygen		yes = 1 no = 0
Non-invasive ventilation		yes = 1 no = 0

Number of days with non-invasive ventilation	if available	Number of days
Intubated/ventilated		yes = 1 no = 0
Number of days intubated/ventilated	if available	Number of days
<u>Desirable but optional</u>		
Current smoker	Is patient a current smoker, if available	yes = 1 no = 0
Socio-economic status (SES)	if available	quartiles or tertiles: (low, medium, high)
Race/ethnicity	if available	Use country-specific groups
Severity of illness marker (APACHE II)	Worst APACHE score during admission. For patients not admitted to ICU, list score as 0.	Number
CURB-65 pneumonia severity score		Number
Pneumonia severity index		Number

Table S1 - Types of hospitals for contributing sites and dates of data collection

Site	Type of hospital	Dates of data collection, 2020
Norway	19 public hospitals, of which 6 are university hospitals	26 February - 26 June
Denmark, Copenhagen	1 university hospital	20 February - 1 June
The Netherlands, Rotterdam ErasmusMC	1 university hospital	1 March - 26 June
The Netherlands, Rotterdam FG&V	1 non-academic teaching hospital	16 March - 28 April
The Netherlands, Amphia	1 non-academic teaching hospital	24 February - 6 May
The Netherlands, CliniCo Consortium	5 hospitals, including university and non-academic teaching hospitals	Depending on hospital, ranged from 16 March - 26 June
Austria	1 non-academic teaching hospital	1 March - 15 April
Switzerland, Lausanne	1 academic university hospital	28 February - 25 May
Switzerland, Ticino	5 non-academic teaching hospitals	1 March - 11 May
Italy, Milan Auxologico	2 university hospitals	27 March - June
Italy, Milan Sacco	1 academic hospital	21 February - 17 April
China, Guangdong Province	2 hospitals, including 1 university hospital	17 January - 1 May
Singapore	1 university teaching hospital	22 January to 4 April
Indonesia, Universitas Indonesia	7 hospitals, including public, private and university hospitals	10 March to 20 May
South Africa, Cape Town	1 university hospital	1 May to 1 July
United States, University of California Los Angeles	2 academic university hospitals	10 March -16 April
United States, Saint Louis Missouri	16 hospitals including 5 academic hospitals	1 March – 15 May
United States, Cornell University New York	2 academic university hospitals	3 March - 15 May

Table S2 – National obesity prevalence by site country¹

Site Country	Obesity prevalence 2016-2017 (%)
Norway	12.0
Denmark	16.8
The Netherlands	13.6
Austria	14.7
Switzerland	10.3
Italy	9.8
China	7.0
Singapore ²	8.9
Indonesia	5.7
South Africa	26.5
United States	40.0

1. OECD, (2017), Obesity Update 2017, Paris www.oecd.org/health/obesity-update.htm

2. Ministry of Health Singapore, Obesity trend and Programmes, 6 Jan 2020, Singapore, <https://www.moh.gov.sg/news-highlights/details/obesity-trend-and-programmes#:~:text=Written%20Answer,has%20remained%20stable%20since%202013>

Table S3 – Characteristics of the study population, by study site

	Norway		Denmark, Copenhagen		The Netherlands, Rotterdam ErasmusMC		The Netherlands, Rotterdam FG&V		The Netherlands, Amphia		The Netherlands, CliniCo Consortium	
Characteristic	n	%	n	%	n	%	n	%	n	%	n	%
Total	481	100	201	100	204	100	183	100	300	100	745	100

Sex	Male	287	59.7	100	49.8	143	70.1	105	57.4	193	64.3	487	65.4
Age	<65	261	54.3	66	32.8	112	54.9	101	55.2	108	36.0	269	36.1
	≥65	220	45.7	135	67.2	92	45.1	82	44.8	192	64.0	476	63.9
BMI	≥12-<18	14	2.9	0	0.0	2	1.0	3	1.6	2	0.7	6	0.8
	≥18-<25	161	33.5	71	35.3	59	28.9	52	28.4	84	28.0	199	26.7
	≥25-<30	189	39.3	61	30.3	71	34.8	62	33.9	125	41.7	307	41.2
	≥30	117	24.3	69	34.3	72	35.3	66	36.1	89	29.7	233	31.3
Pre-existing cardiovascular disease	Yes	260	54.1	120	59.7	59	28.9	37	20.2	129	43.0	298	40.0
Diabetes	Yes	67	13.9	65	32.3	53	26.0	48	26.2	57	19.0	182	24.4
Pre-existing respiratory condition	Yes	94	19.5	42	20.9	43	21.1	45	24.6	52	17.3	204	27.4
Hypertension	Yes	--	--	97	48.3	70	34.3	82	44.8	41	13.7	305	40.9
ICU admission	Yes	103	21.4	31	15.4	125	61.3	66	36.1	67	22.3	180	24.2
Death	Yes	41	8.5	55	27.4	45	22.0	29	15.8	90	30.0	166	22.3
Supplemental oxygen	Yes	--	--	144	71.6	191	93.6	162	88.5	--	--	671	90.1
Non-invasive ventilation	Yes	30	6.2	76	37.8	--	--	14	7.7	--	--	84	11.3

Intubated / ventilated		Yes	76	15·8	30	14·9	113	55·4	60	32·8	--	--	168	22·6
-------------------------------	--	------------	----	------	----	------	-----	------	----	------	----	----	-----	------

		Austria		Switzerland, Lausanne		Switzerland, Ticino		Italy, Milan Auxologico		Italy, Milan Sacco		China, Guangdong Province	
Characteristic		n	%	n	%	n	%	n	%	n	%	n	%
	Total	102	100	451	100	469	100	149	100	271	100	379	100
Sex	Male	66	64·7	258	57·2	295	62·9	98	65·8	184	67·9	174	45·9
Age	<65	44	43·1	197	43·7	140	29·9	63	42·3	154	56·8	320	84·4
	≥65	58	56·9	254	56·3	329	70·1	85	57·0	117	43·2	59	15·6
BMI	≥12-<18	2	2·0	12	2·7	4	0·9	7	4·7	5	1·8	17	4·5
	≥18-<25	32	31·4	182	40·4	135	28·8	40	26·8	99	36·5	211	55·7
	≥25-<30	42	41·2	145	32·2	179	38·2	54	36·2	111	41·0	110	29·0
	≥30	26	25·5	112	24·8	151	32·2	48	32·2	56	20·7	41	10·8
Pre-existing cardiovascular disease	Yes	31	30·4	163	36·1	188	40·1	54	36·2	146	53·9	25	6·6
Diabetes	Yes	20	19·6	111	24·6	119	25·4	32	21·5	29	10·7	26	6·9
Pre-existing respiratory condition	Yes	16	15·7	58	12·9	91	19·4	40	26·8	36	13·3	10	2·6

Hypertension	Yes	49	48·0	226	50·1	238	50·7	95	63·8	111	41·0	71	18·7
ICU admission	Yes	10	9·8	108	23·9	98	20·9	19	12·8	48	17·7	16	4·2
Death	Yes	16	15·7	64	14·2	91	19·4	30	20·1	37	13·7	1	0·3
Supplemental oxygen	Yes	--	--	311	69·0	391	83·4	103	69·1	222	81·9	166	43·8
Non-invasive ventilation	Yes	--	--	13	2·9	--	--	74	49·7	103	38·0	31	8·2
Intubated / ventilated	Yes	5	4·9	77	17·1	63	13·4	20	13·4	43	15·9	12	3·2

		Singapore		Indonesia, Universitas Indonesia		South Africa, Cape Town		United States, University of California Los Angeles		United States, Saint Louis Missouri		United States, Cornell University New York	
Characteristic		n	%	n	%	n	%	n	%	n	%	n	%
	Total	86	100	266	100	353	100	117	100	805	100	1682	100
Sex	Male	47	54·7	147	55·3	182	51·6	77	65·8	400	49·7	1003	59·6
Age	<65	67	77·9	221	83·1	270	76·5	67	57·3	346	43·0	785	46·7
	≥65	19	22·1	45	16·9	83	23·5	50	42·7	459	57·0	897	53·3
BMI	≥12-<18	2	2·3	3	1·1	0	0·0	4	3·4	32	4·0	47	2·8
	≥18-<25	46	53·5	164	61·7	92	26·1	46	39·3	222	27·6	558	33·2
	≥25-<30	28	32·6	70	26·3	114	32·3	28	23·9	202	25·1	557	33·1

	≥30	10	11·6	29	10·9	147	41·6	39	33·3	349	43·4	520	30·9
Pre-existing cardiovascular disease	Yes	9	10·5	37	13·9	72	20·4	12	10·3	453	56·3	417	24·8
Diabetes	Yes	17	19·8	50	18·8	147	41·6	31	26·5	369	45·8	526	31·3
Pre-existing respiratory condition	Yes	2	2·3	77	28·9	81	22·9	18	15·4	239	29·7	297	17·7
Hypertension	Yes	27	31·4	79	29·7	146	41·4	53	45·3	654	81·2	953	56·7
ICU admission	Yes	22	25·6	68	25·6	45	12·7	44	37·6	119	14·8	481	28·6
Death	Yes	4	4·7	63	23·7	81	22·9	9	7·7	192	23·9	300	17·8
Supplemental oxygen	Yes	30	34·9	68	25·6	353	100·0	117	100·0	211	26·2	--	--
Non-invasive ventilation	Yes	--	--	30	11·3	0	0·0	--	--	237	29·4	--	--
Intubated / ventilated	Yes	11	12·8	39	14·7	42	11·9	29	24·8	222	27·6	444	26·4

Table S4 - Characteristics of study population by study sites, detailed

		Norway, N=481				Denmark, Copenhagen, N=201				The Netherlands, Rotterdam ErasmusMC, N=204			
		BMI				BMI				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30
Characteristic	Total	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Sex	Total	14 (3)	161 (33)	189 (39)	117 (24)	0 (0)	71 (35)	61 (30)	69 (34)	2 (1)	59 (29)	71 (35)	72 (35)
	Male	9 (64)	99 (61)	120 (63)	59 (50)	--	29 (41)	37 (61)	34 (49)	0 (0)	38 (64)	57 (80)	48 (67)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	7 (50)	60 (37)	109 (58)	85 (73)	--	19 (27)	22 (36)	25 (36)	1 (50)	26 (44)	36 (51)	49 (68)
	≥65	7 (50)	101 (63)	80 (42)	32 (27)	--	52 (73)	39 (64)	44 (64)	1 (50)	33 (56)	35 (49)	23 (32)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	63(43)	68 (42)	78 (41)	51 (44)	--	41 (58)	34 (56)	45 (65)	1 (50)	20 (34)	12 (17)	26 (36)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Diabetes	Yes	1 (7)	20 (12)	22 (12)	24 (21)	--	16 (23)	18 (30)	31 (45)	0 (0)	18 (31)	20 (28)	15 (21)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing respiratory condition	Yes	4 (29)	29 (18)	37 (20)	24 (21)	--	20 (28)	9 (15)	13 (19)	0 (0)	14 (24)	15 (21)	14 (19)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Hypertension	Yes	--	--	--	--	--	31 (44)	27 (44)	39 (57)	0 (0)	17 (29)	26 (37)	27 (38)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
ICU admission	Yes	1 (7)	25 (16)	42 (22)	35 (30)	--	7 (10)	11 (18)	13 (19)	1 (50)	26 (44)	46 (65)	52 (72)
	Missing	--	--	--	--	--	1 (1)	0 (0)	0 (0)	--	--	--	--
Death	Yes	3 (21)	19 (12)	12 (6)	7 (6)	--	15 (21)	15 (26)	25 (36)	1 (50)	19 (32)	16 (23)	9 (13)
	Missing	--	--	--	--	--	--	--	--	--	6 (10)	9 (13)	16 (22)
Length of ICU admission (days)	Median [IQR]	2	16	14	13	--	18 [18-40]	25 [19-36]	16 [14-17]	--	--	--	--
	Missing	--	--	--	--	--	2 (3)	8 (13)	8 (12)	--	--	--	--
Length of hospital stay (days)	Median [IQR]	4	7	7	7	--	6 [1-16]	5 [1-9]	7 [3-13]	--	--	--	--

	Missing	--	--	--	--	--	16 (23)	17 (28)	25 (36)	--	--	--	--
Supplemental oxygen	Yes	--	--	--	--	--	43 (63)	42 (69)	59 (88)	2 (100)	54 (92)	66 (93)	69 (96)
	Missing	--	--	--	--	--	3 (4)	0 (0)	2 (3)	--	--	--	--
Non-invasive ventilation	Yes	0 (0)	7 (4)	9 (5)	14 (12)	--	26 (38)	21 (36)	29 (43)	--	--	--	--
	Median days [IQR]	--	1	1	0	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	3 (4)	2 (3)	2 (3)	--	--	--	--
Intubated/ventilated	Yes	0 (0)	21 (13)	31 (16)	24 (21)	--	7 (10)	11 (18)	12 (17)	1 (50)	24 (41)	43 (61)	45 (63)
	Median days [IQR]	--	16	13	12	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Current smoker	Yes	2 (14)	4 (2)	4 (2)	2 (2)	--	10 (14)	4 (7)	0 (0)	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Race/ethnicity	Black	--	--	--	--	--	--	--	--	--	--	--	--
	White	--	--	--	--	--	--	--	--	--	--	--	--
	Asian	--	--	--	--	--	--	--	--	--	--	--	--
	Latinx	--	--	--	--	--	--	--	--	--	--	--	--
	Other	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

The Netherlands, Rotterdam FG&V, N=183	The Netherlands, Amphia, N=300	The Netherlands, CliniCo Consortium, N=745
--	--------------------------------	--

		BMI				BMI ≥12- <18				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30
Characteristic	Total	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
		3 (2)	52 (28)	62 (34)	66 (36)	2 (1)	84 (28)	125 (42)	89 (30)	6 (1)	199 (27)	307 (41)	233 (31)
Sex	Male	2 (67)	36 (69)	42 (68)	25 (38)	1 (50)	52 (62)	90 (72)	50 (56)	4 (67)	135 (68)	215 (70)	133 (57)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	2 (67)	21 (40)	36 (58)	42 (64)	1 (50)	28 (33)	42 (34)	37 (42)	1 (17)	54 (27)	108 (35)	106 (45)
	≥65	1 (33)	31 (60)	26 (42)	24 (36)	1 (50)	56 (67)	83 (66)	52 (58)	5 (83)	145 (73)	199 (65)	127 (55)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	0 (0)	11 (21)	16 (26)	10 (15)	0 (0)	34 (40)	55 (44)	40 (45)	3 (50)	81 (41)	122 (40)	92 (40)
	Missing	--	1 (2)	--	--	--	--	--	--	0 (0)	0 (0)	2 (1)	0 (0)
Diabetes	Yes	1 (33)	11 (21)	16 (26)	20 (30)	0 (0)	7 (8)	25 (20)	25 (28)	1 (16.7)	37 (19)	65 (21)	79 (34)
	Missing	--	--	--	--	--	--	--	--	0 (0)	0 (0)	2 (1)	0 (0)
Pre-existing respiratory condition	Yes	2 (67)	12 (23)	12 (19)	19 (29)	0 (0)	18 (21)	17 (14)	17 (19)	5 (83)	51 (26)	65 (21)	83 (36)
	Missing	--	--	--	--	--	--	--	--	0 (0)	0 (0)	2 (1)	0 (0)
Hypertension	Yes	0 (0)	21 (40)	30 (48)	31 (47)	0 (0)	12 (14)	15 (12)	14 (16)	1 (17)	76 (38)	121 (39)	107 (46)
	Missing	--	5 (10)	8 (13)	10 (15)	--	--	--	--	0 (0)	0 (0)	2 (1)	0 (0)
ICU admission	Yes	0 (0)	15 (29)	24 (39)	27 (41)	0 (0)	17 (20)	34 (27)	16 (18)	0 (0)	45 (23)	83 (27)	52 (22)
	Missing	--	--	--	--	--	--	--	--	0 (0)	7 (4)	17 (6)	9 (4)
Death	Yes	1 (33)	11 (21)	10 (16)	7 (11)	1 (50)	25 (30)	37 (30)	27 (30)	0 (0)	51 (26)	68 (22)	47 (20)
	Missing	--	--	--	--	--	--	--	--	0 (0)	15 (8)	25 (8)	20 (9)
Length of ICU admission (days)	Median [IQR]	--	27 [1-53]	26 [1-84]	24 [1-56]	--	--	--	--	--	16 [10-26]	17 [9-26]	18 [10-32]
	Missing	--	--	--	--	--	--	--	--	--	2 (4)	4 (5)	6 (11)
Length of hospital stay (days)	Median [IQR]	3 [3-10]	9 [5-20]	7 [4-26]	7 [4-28]	--	--	--	--	4 [3-9]	6 [4-13]	7 [3-16]	6 [4-12]
	Missing	--	--	--	--	--	--	--	--	0 (0)	5 (3)	10 (3)	9 (3)
Supplemental oxygen	Yes	2 (67)	44 (85)	55 (89)	61 (92)	--	--	--	--	4 (67)	178 (89)	279 (91)	210 (90)

	Missing	--	--	--	--	--	--	--	--	0 (0)	1 (0)	0 (0)	1 (0)
Non-invasive ventilation	Yes	0 (0)	7 (13)	1 (2)	6 (9)	--	--	--	--	0 (0)	27 (14)	31 (10)	26 (11)
	Median days [IQR]	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	0 (0)	12 (6)	23 (8)	17 (7)
Intubated/ventilated	Yes	0 (0)	14 (27)	21 (34)	25 (38)	--	--	--	--	0 (0)	43 (22)	76 (25)	49 (21)
	Median days [IQR]	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	0 (0)	6 (3)	17 (6)	9 (4)
Current smoker	Yes	2 (67)	5 (10)	3 (5)	1 (2)	--	--	--	--	--	--	--	--
	Missing	--	4 (8)	--	4 (6)	--	--	--	--	--	--	--	--
Race/ethnicity	Black	0 (0)	12 (23)	11 (18)	14 (21)	--	--	--	--	--	--	--	--
	White	1 (33)	33 (63)	32 (52)	31 (47)	--	--	--	--	--	--	--	--
	Asian	--	--	--	--	--	--	--	--	--	--	--	--
	Latinx	--	--	--	--	--	--	--	--	--	--	--	--
	Other	0 (0)	2 (4)	2 (3)	0 (0)	--	--	--	--	--	--	--	--
	Missing	1 (33)	1 (2)	3 (5)	5 (8)	--	--	--	--	--	--	--	--
	Arab (NL site only)	1 (33)	4 (8)	14 (23)	16 (24)								

Austria, N=102	Switzerland, Lausanne, N=451	Switzerland, Ticino, N=469
----------------	------------------------------	----------------------------

		BMI				BMI				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30
Characteristic		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Total	2 (2)	32 (31)	42 (41)	26 (25)	12 (3)	182 (40)	145 (32)	112 (25)	4 (1)	135 (29)	179 (38)	151 (32)
Sex	Male	0 (0)	23 (72)	25 (60)	18 (69)	2 (17)	99 (54)	97 (67)	60 (54)	2 (50)	80 (59)	125 (70)	88 (58)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	2 (100)	9 (28)	18 (43)	15 (58)	0 (0)	68 (37)	69 (48)	60 (54)	0 (0)	34 (25)	48 (27)	58 (38)
	≥65	0 (0)	23 (72)	24 (57)	11 (42)	12 (100)	114 (63)	76 (52)	52 (46)	4 (100)	101 (75)	131 (73)	93 (62)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	0 (0)	10 (31)	9 (21)	12 (46)	8 (67)	70 (38)	51 (35)	34 (30)	1 (25)	62 (46)	73 (41)	52 (34)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Diabetes	Yes	0 (0)	7 (22)	7 (17)	6 (23)	1 (8)	23 (13)	41 (28)	46 (41)	1 (25)	23 (17)	47 (26)	48 (32)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing respiratory condition	Yes	0 (0)	4 (13)	9 (21)	3 (12)	1 (8)	25 (14)	15 (10)	17 (15)	2 (50)	22 (16)	37 (21)	30 (20)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Hypertension	Yes	0 (0)	16 (50)	17 (40)	16 (62)	6 (50)	72 (40)	78 (54)	70 (63)	1 (25)	59 (44)	100 (56)	78 (52)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
ICU admission	Yes	0 (0)	4 (13)	3 (7)	3 (12)	1 (8)	30 (16)	41 (28)	36 (32)	1 (25)	16 (12)	39 (22)	42 (28)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Death	Yes	0 (0)	8 (25)	3 (7)	5 (19)	1 (8)	26 (14)	25 (17)	12 (11)	0 (0)	27 (20)	33 (18)	31 (21)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Length of ICU admission (days)	Median [IQR]	0	8 [6-15]	6 [2-7]	5 [2-6]	0.2 [0-2]	2 [0-59]	3 [0-46]	4 [0-57]	7 [0-31]	2 [0-52]	3 [0-66]	6 [0-67]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Length of hospital stay (days)	Median [IQR]	9 [5-14]	10 [6-15]	11 [7-14]	9 [7-12]	8 [7-8]	7 [4-14]	8 [5-13]	7 [5-16]	19 [11-32]	13 [7-30]	16 [8-28]	16 [7-29]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Supplemental oxygen	Yes	--	--	--	--	6 (50)	108 (59)	110 (76)	87 (78)	4 (100)	108 (80)	150 (84)	129 (85)

	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Non-invasive ventilation	Yes	--	--	--	--	0 (0)	3 (2)	4 (3)	6 (5)	--	--	--	--
	Median days [IQR]	--	--	--	--	--	0.02 [0-1]	0.1 [0-6]	0.2 [0-17]	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Intubated/ventilated	Yes	0 (0)	3 (9)	1 (2)	1 (4)	0 (0)	21 (12)	30 (21)	26 (23)	1 (25)	14 (10)	19 (11)	29 (19)
	Median days [IQR]	--	--	--	--	0	1 [0-61]	2 [0-32]	3 [0-54]	1 [0-5]	1 [0-44]	1 [0-32]	2 [0-26]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Current smoker	Yes	0 (0)	12 (38)	14 (33)	4 (15)	--	--	--	--	--	--	--	--
	Missing	0	3 (9)	3 (7)	3 (12)	--	--	--	--	--	--	--	--
Race/ethnicity	Black	--	--	--	--	--	--	--	--	--	--	--	--
	White	--	--	--	--	--	--	--	--	--	--	--	--
	Asian	--	--	--	--	--	--	--	--	--	--	--	--
	Latinx	--	--	--	--	--	--	--	--	--	--	--	--
	Other	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

		Italy, Milan Auxologico, N=149				Italy, Milan Sacco, N=271				China, Guangdong Province, N=379			
		BMI				BMI				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18.5	≥18.5-<24	≥24-<28	≥28
Characteristic	Total	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
		7 (5)	40 (27)	54 (36)	48 (32)	5 (2)	99 (37)	111 (41)	56 (21)	17 (4)	211 (56)	110 (29)	41 (11)
Sex	Male	1 (14)	30 (75)	38 (70)	29 (60)	0 (0)	61 (62)	83 (75)	40 (71)	3 (18)	81 (38)	62 (56)	28 (68)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	0 (0)	12 (30)	22 (41)	29 (60)	3 (60)	53 (54)	63 (57)	35 (63)	16 (94)	179 (85)	90 (82)	35 (85)
	≥65	7 (100)	28 (33)	32 (59)	18 (48)	2 (40)	46 (47)	48 (43)	21 (38)	1 (6)	32 (15)	20 (18)	6 (15)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	3 (43)	20 (50)	19 (35)	12 (25)	1 (20)	48 (49)	65 (59)	32 (57)	0 (0)	11 (5)	11 (10)	3 (7)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Diabetes	Yes	1 (14)	7 (18)	10 (18)	14 (29)	0 (0)	6 (6)	17 (15)	6 (11)	0 (0)	16 (8)	8 (7)	2 (5)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing respiratory condition	Yes	2 (29)	5 (13)	14 (26)	19 (40)	1 (20)	21 (21)	10 (9)	4 (7)	0 (0)	7 (3)	0 (0)	3 (7)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Hypertension	Yes	5 (71)	23 (58)	37 (69)	30 (63)	1 (20)	35 (35)	50 (45)	25 (45)	1 (6)	36 (17)	23 (21)	11 (27)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
ICU admission	Yes	0 (0)	6 (15)	7 (13)	6 (13)	0 (0)	10 (10)	21 (19)	17 (30)	0 (0)	12 (6)	1 (1)	3 (7)
	Missing	4 (57)	9 (23)	10 (19)	15 (31)	--	--	--	--	--	--	--	--
Death	Yes	2 (29)	13 (33)	11 (20)	4 (8)	2 (40)	10 (10)	14 (13)	11 (20)	0 (0)	1 (0)	0 (0)	0 (0)
	Missing	1 (14)	2 (5)	4 (7)	1 (2)	--	--	--	--	--	--	--	--
Length of ICU admission (days)	Median [IQR]	0	9 [2-10]	11 [6-19]	3 [2-9]	--	17 [7-23]	10 [7-14]	9 [3-19]	--	--	--	--
	Missing	7 (100)	34 (85)	48 (89)	43 (89)	--	--	--	--	--	--	--	--
Length of hospital stay (days)	Median [IQR]	12 [5-19]	13 [7-21]	18 [12-28]	24 [12-37]	5 [0-7]	12 [7-22]	14 [8-24]	12 [7-24]	--	--	--	--
	Missing	1 (14)	11 (27)	15 (28)	9 (19)	--	--	--	--	--	--	--	--
Supplemental oxygen	Yes	3 (43)	28 (70)	40 (74)	32 (67)	3 (60)	73 (74)	97 (87)	49 (88)	6 (35)	83 (39)	58 (53)	19 (46)

	Missing	1 (14)	6 (15)	8 (15)	2 (4)	--	--	--	--	--	--	--	--
Non-invasive ventilation	Yes	1	24 (60)	30 (55)	19 (39)	3 (60)	25 (25)	54 (49)	21 (38)	1 (6)	18 (9)	8 (7)	4 (10)
	Median days	11 [11-11]	1 [0-6]	6 [2-9]	3 [1-8]	--	--	--	--	--	--	--	--
	[IQR]	6 (86)	16 (40)	24 (44)	19 (39)	--	--	--	--	--	--	--	--
Intubated/ventilated	Yes	0 (0)	4 (10)	9 (17)	7 (15)	0 (0)	10 (10)	18 (16)	15 (27)	0	9 (4)	1 (1)	2 (5)
	Median days	0	9 [8-10]	13 [9-17]	9 [2-15]	--	17 [6-23]	10 [4-13]	11 [4-18]	--	--	--	--
	[IQR]	3 (43)	11 (28)	10 (19)	2 (4)	--	--	--	--	--	--	--	--
Current smoker	Yes	0 (0)	3 (8)	4 (7)	3 (6)	--	--	--	--	--	--	--	--
	Missing	2 (29)	9 (23)	9 (17)	7 (15)	--	--	--	--	--	--	--	--
Race/ethnicity	Black	0 (0)	0 (0)	1 (2)	0 (0)	--	--	--	--	--	--	--	--
	White	5 (71)	38 (95)	51 (94)	45 (94)	--	--	--	--	--	--	--	--
	Asian	0 (0)	1 (3)	0 (0)	1 (2)	--	--	--	--	--	--	--	--
	Latinx	1 (14)	1 (3)	1 (2)	2 (4)	--	--	--	--	--	--	--	--
	Other	1 (14)	0 (0)	1 (2)	0 (0)	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

		Singapore, N=86				Indonesia, Universitas Indonesia, N=266				South Africa, Cape Town, N=353			
		BMI				BMI				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30
Characteristic	Total	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
		2 (2)	46 (53)	28 (33)	10 (12)	3 (1)	164 (62)	70 (26)	29 (11)	0 (0)	92 (26)	114 (32)	147 (42)
Sex	Male	0 (0)	22 (48)	17 (61)	8 (80)	1 (33)	84 (51)	47 (67)	15 (52)	--	71 (77)	66 (58)	45 (31)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	2 (100)	34 (74)	21 (75)	10 (100)	3 (100)	132 (80)	60 (86)	26 (90)	--	63 (69)	91 (80)	116 (79)
	≥65	0 (0)	12 (26)	7 (25)	0 (0)	0 (0)	32 (20)	10 (14)	3 (10)	--	29 (32)	23 (20)	31 (21)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	0 (0)	4 (9)	3 (11)	2 (20)	0 (0)	26 (16)	5 (7)	6 (21)	--	23 (25)	22 (19)	27 (18)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Diabetes	Yes	0 (0)	11 (24)	4 (14)	2 (20)	0 (0)	29 (18)	13 (19)	8 (28)	--	36 (39)	35 (31)	76 (52)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing respiratory condition	Yes	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	61 (37)	10 (14)	6 (21)	--	19 (21)	32 (28)	30 (20)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Hypertension	Yes	0 (0)	13 (28)	9 (32)	5 (50)	0 (0)	49 (30)	18 (26)	12 (41)	--	46 (50)	45 (40)	55 (37)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
ICU admission	Yes	0 (0)	12 (26)	7 (25)	3 (30)	0 (0)	36 (22)	20 (29)	12 (41)	--	4 (4)	8 (7)	33 (23)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Death	Yes	0 (0)	3 (7)	1 (4)	0 (0)	0 (0)	38 (23)	16 (23)	9 (31)	--	14 (15)	16 (14)	51 (35)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Length of ICU admission (days)	Median [IQR]	--	--	--	--	0	0 [0-3]	4 [2-14]	4 [1-10]	--	0 [0-0]	0 [0-0]	0 [0-0]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Length of hospital stay (days)	Median [IQR]	10 [7-14]	13 [10-18]	14 [11-17]	13 [10-17]	9 [5-18]	8 [6-16]	8 [5-13]	7 [4-20]	--	11 [8-14]	11 [8-15]	11 [8-16]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

Supplemental oxygen	Yes	0 (0)	14 (30)	11 (39)	5 (50)	0 (0)	40 (24)	15 (21)	13 (45)	--	92 (100)	114 (100)	147 (100)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Non-invasive ventilation	Yes	--	--	--	--	0 (0)	14 (9)	11 (16)	5 (17)	--	0 (0)	0 (0)	0 (0)
	Median days [IQR]	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Intubated/ventilated	Yes	0 (0)	5 (11)	5 (18)	1 (10)	0 (0)	24 (15)	10 (14)	5 (17)	--	5 (5)	7 (6)	30 (20)
	Median days [IQR]	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Current smoker	Yes	0 (0)	1 (2)	3 (11)	0 (0)	0 (0)	25 (15)	3 (4)	4 (14)	--	13 (14)	13 (11)	18 (12)
	Missing	0 (0)	2 (4)	1 (4)	1 (10)	1 (33)	74 (45)	51 (73)	14 (48)	--	--	--	--
Race/ethnicity	Black	--	--	--	--	--	--	--	--	--	--	--	--
	White	--	--	--	--	--	--	--	--	--	--	--	--
	Asian	--	--	--	--	--	--	--	--	--	--	--	--
	Latinx	--	--	--	--	--	--	--	--	--	--	--	--
	Other	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

		United States, University of California Los Angeles, N=117				United States, Saint Louis Missouri, N=805				United States, Cornell University New York, N=1682			
		BMI				BMI				BMI			
		≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30	≥12-<18	≥18-<25	≥25-<30	≥30
Characteristic	Total	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
		4 (3)	46 (39)	28 (24)	39 (33)	32 (4)	222 (28)	202 (25)	349 (43)	47 (3)	558 (33)	557 (33)	520 (31)
Sex	Male	3 (75)	30 (65)	18 (64)	26 (67)	16 (50)	128 (58)	109 (54)	147 (42)	24 (51)	336 (60)	359 (64)	284 (55)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Age	<65	1 (25)	22 (48)	15 (54)	29 (74)	3 (9)	61 (27)	70 (35)	212 (61)	13 (28)	180 (32)	264 (47)	328 (63)
	≥65	3 (75)	24 (52)	13 (46)	10 (26)	29 (91)	161 (73)	132 (65)	137 (39)	34 (72)	378 (68)	293 (53)	192 (37)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing cardiovascular disease	Yes	3 (75)	5 (11)	1 (4)	3 (8)	18 (56)	136 (61)	123 (61)	176 (50)	18 (38)	154 (28)	131 (24)	114 (22)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Diabetes	Yes	3 (75)	8 (17)	7 (25)	13 (33)	12 (38)	78 (35)	95 (47)	184 (53)	15 (32)	152 (27)	181 (33)	178 (34)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Pre-existing respiratory condition	Yes	0 (0)	8 (17)	4 (14)	6 (15)	15 (47)	62 (28)	48 (24)	114 (33)	8 (17)	96 (17)	78 (14)	115 (22)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Hypertension	Yes	3 (75)	21 (46)	10 (36)	19 (49)	28 (88)	175 (79)	168 (83)	283 (81)	28 (60)	312 (56)	306 (55)	307 (59)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
ICU admission	Yes	1 (25)	14 (30)	11 (39)	18 (46)	0 (0)	33 (15)	21 (10)	65 (19)	9 (19)	135 (24)	162 (29)	175 (34)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Death	Yes	2 (50)	3 (7)	1 (4)	3 (8)	10 (31)	50 (23)	43 (21)	89 (26)	17 (36)	128 (23)	78 (14)	77 (15)
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Length of ICU admission (days)	Median [IQR]	--	--	--	--	--	--	--	--	2 [1-3]	13 [5-28]	19.5 [9-31]	18 [9-32]
	Missing	--	--	--	--	--	--	--	--	38 (81)	423 (76)	395 (71)	345 (66)
Length of hospital stay (days)	Median [IQR]	13 [12-19]	7 [2-14]	5 [3-15]	8 [3-17]	--	--	--	--	5 [3-11]	7 [3-15]	8 [4-20]	8 [4-19]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--

Supplemental oxygen	Yes	4 (100)	46(100)	28 (100)	39 (100)	8 (25)	63 (28)	52 (26)	88 (25)	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Non-invasive ventilation	Yes	--	--	--	--	7 (22)	71 (32)	53 (26)	106 (30)	--	--	--	--
	Median days [IQR]	--	--	--	--	--	--	--	--	--	--	--	--
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Intubated/ventilated	Yes	1 (25)	7 (15)	5 (18)	16 (41)	7 (22)	67 (30)	55 (27)	93 (27)	3 (6)	119 (21)	152 (27)	170 (33)
	Median days [IQR]	--	--	--	--	--	--	--	--	5 [1-9]	12 [5-23]	15 [9-23.5]	15.5 [8-27]
	Missing	--	--	--	--	--	--	--	--	--	--	--	--
Current smoker	Yes	0 (0)	2 (4)	0 (0)	1 (3)	7 (22)	25 (11)	15 (7)	25 (7)	3 (6)	19 (3)	24 (4)	25 (5)
	Missing	--	--	--	--	2 (6)	17 (8)	9 (4)	7 (2)	--	--	--	--
Race/ethnicity	Black	0 (0)	4 (9)	1 (4)	2 (5)	16 (50)	144 (65)	127 (63)	245 (70)	16 (34)	165 (30)	168 (30)	155 (30)
	White	1 (25)	24 (52)	15 (54)	13 (33)	16 (50)	65 (29)	62 (31)	93 (27)	6 (13)	53 (10)	65 (12)	83 (16)
	Asian	1 (25)	7 (15)	1 (4)	0 (0)					16 (34)	144 (26)	105 (19)	33 (6)
	Latinx	2 (50)	6 (13)	8 (29)	18 (46)	0 (0)*	6 (3)*	7 (3)*	6 (2)*	2 (4)	22 (4)	26 (5)	29 (6)
	Other	0 (0)	5 (11)	3 (11)	6 (15)					2 (4)	118 (21)	128 (23)	139 (27)
	Missing	--	--	--	--	0 (0)	7 (3)	6 (3)	5 (1)	5 (11)	56 (10)	65 (12)	81 (16)

* Combined group of Asian, Latinx and Other

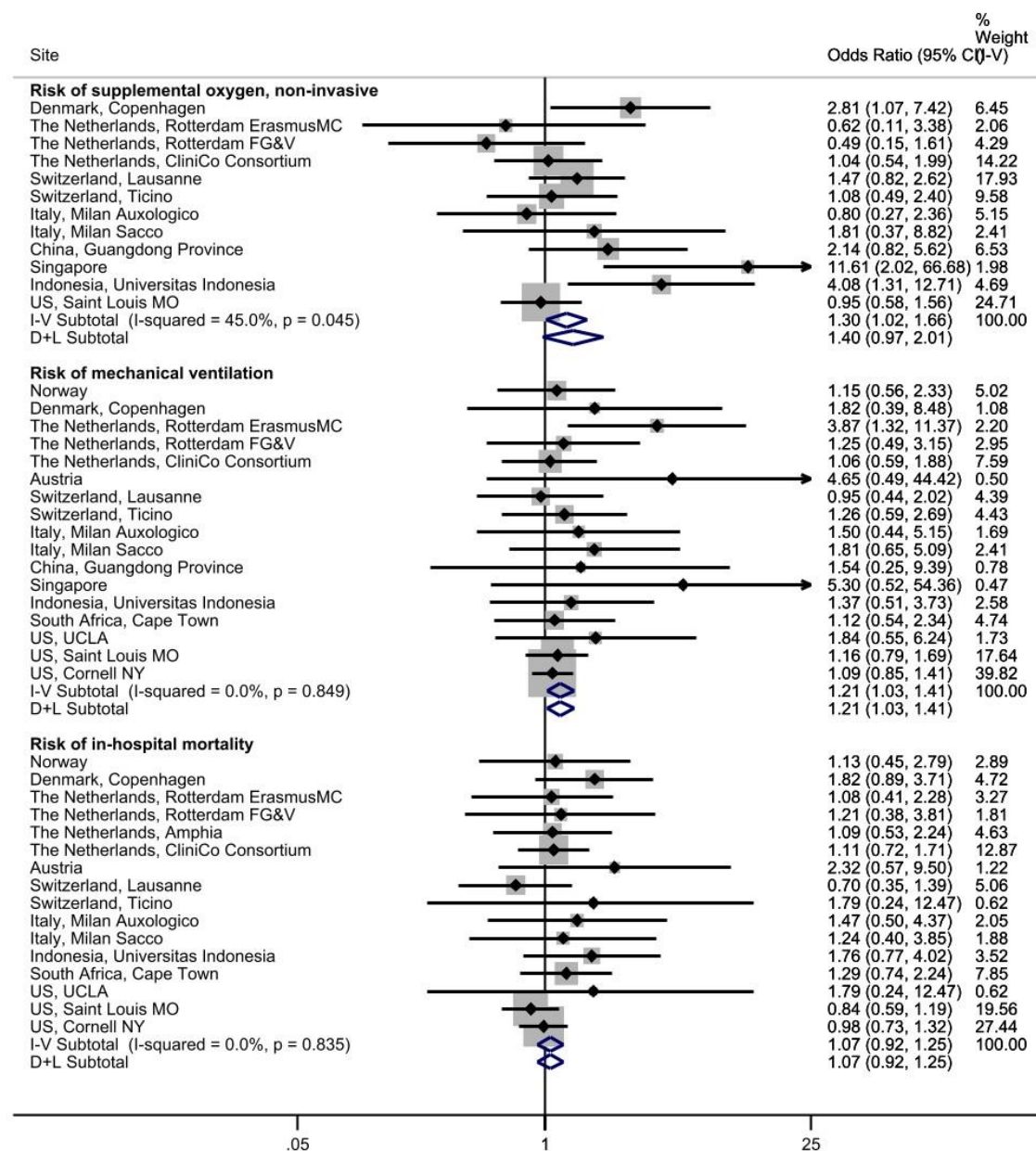
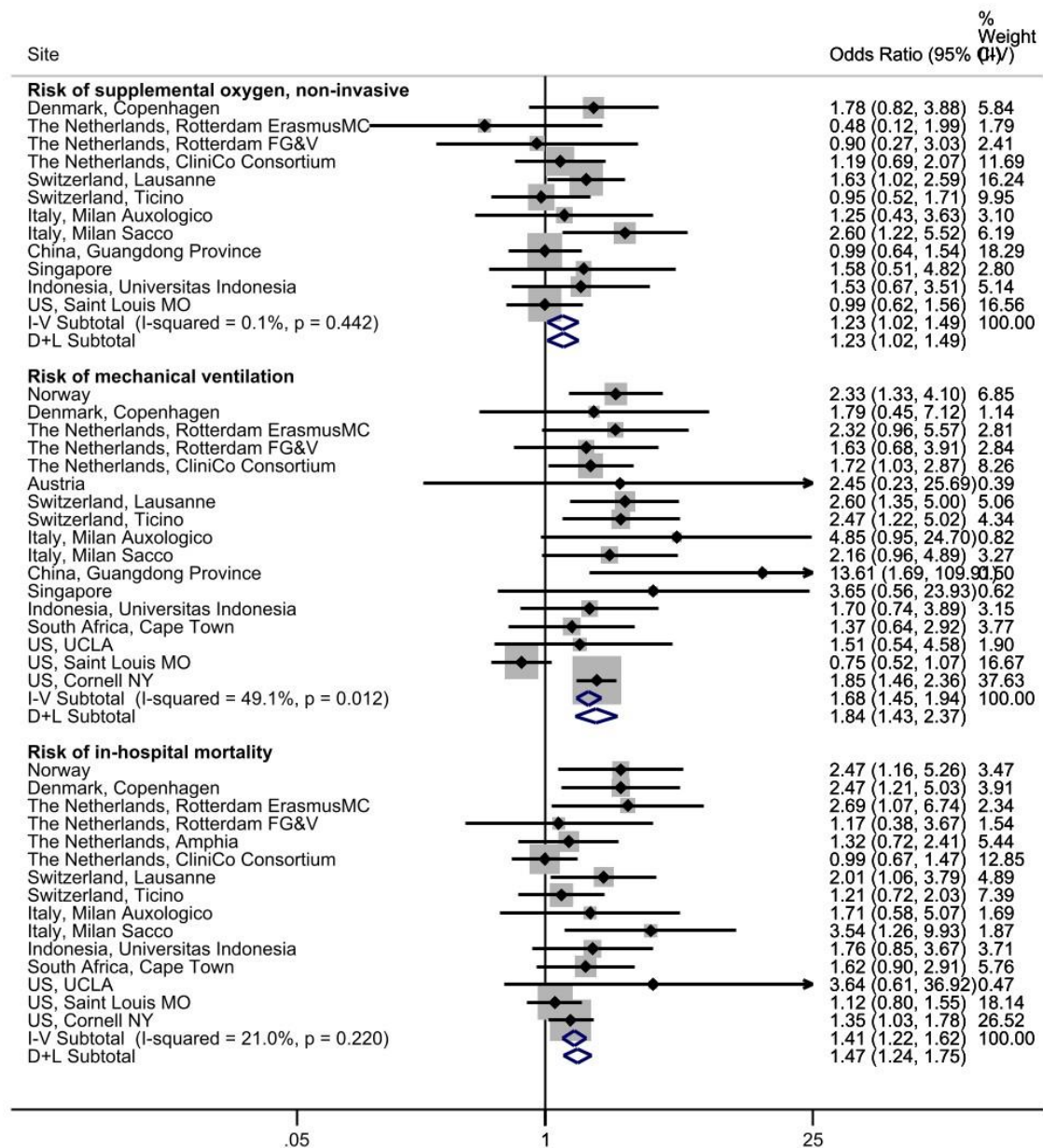


Figure S1 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with diabetes. Models adjusted for: BMI categories (≥ 12 - <18 , ≥ 18 - <25 , ≥ 25 - <30 , ≥ 30), age (<65 , ≥ 65), sex (male/female), pre-existing cardiovascular disease (yes/no), hypertension (yes/no), pre-existing respiratory condition (yes/no). Reference is patients without diabetes. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model.

A)



B)

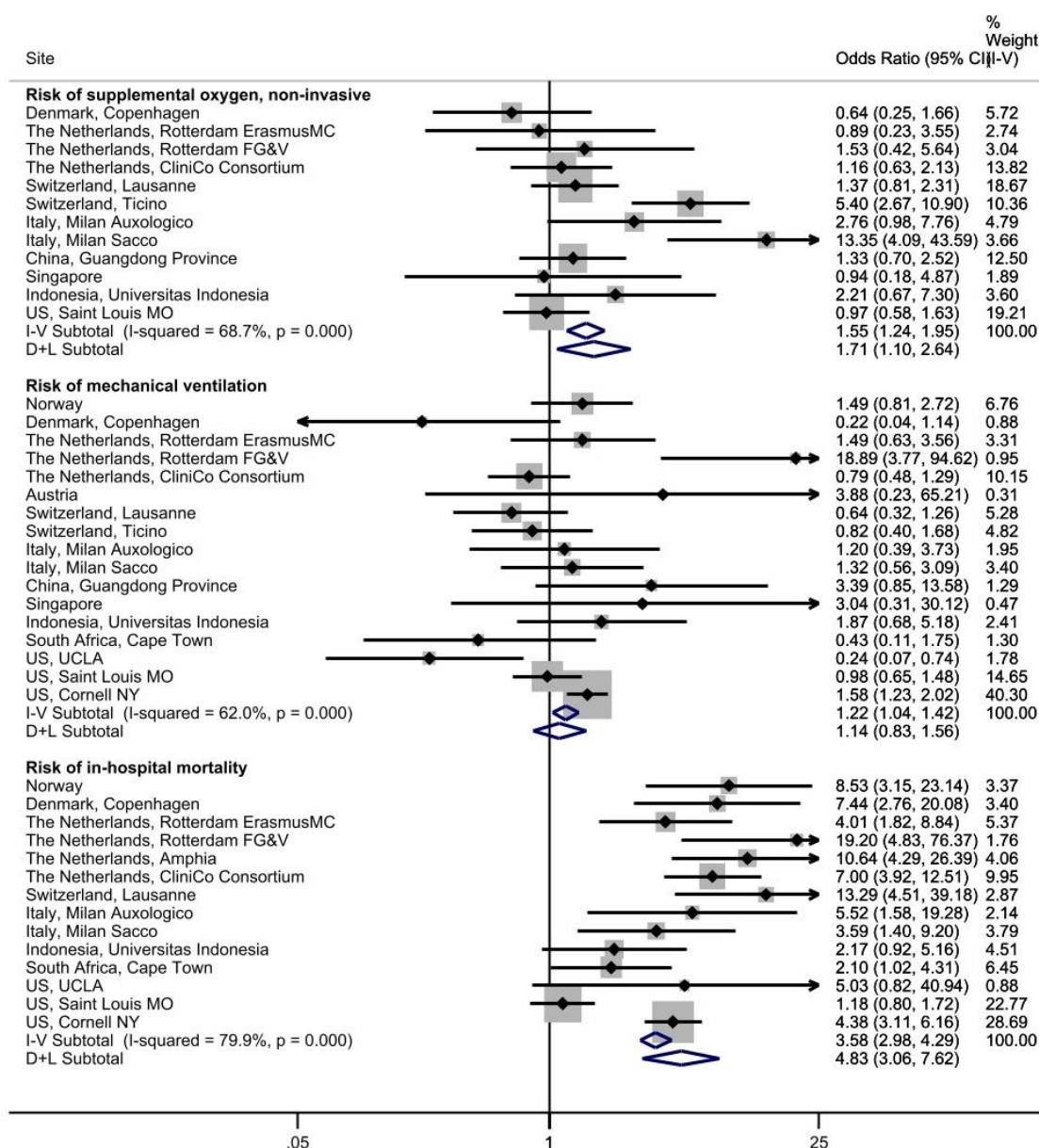


Figure S2. Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality male compared to female (panel A) and patients ≥65 years of age compared to <65 years of age (panel B). Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among males (panel A) and patients ≥65 years of age (panel B)

Models adjusted for: BMI categories (≥12-<18, ≥18-<25, ≥25-<30, ≥30), age (<65, ≥65) (panel A only), sex (male/female) (panel B only), pre-existing cardiovascular disease (yes/no), diabetes (yes/no), pre-existing respiratory conditions (yes/no), hypertension (yes/no). Reference is female (panel A) and patients <65 years of age (panel B). I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model. The 95% confidence intervals (CIs) of the odds ratios have not been adjusted for multiple testing and should not be used to infer definitive effects.

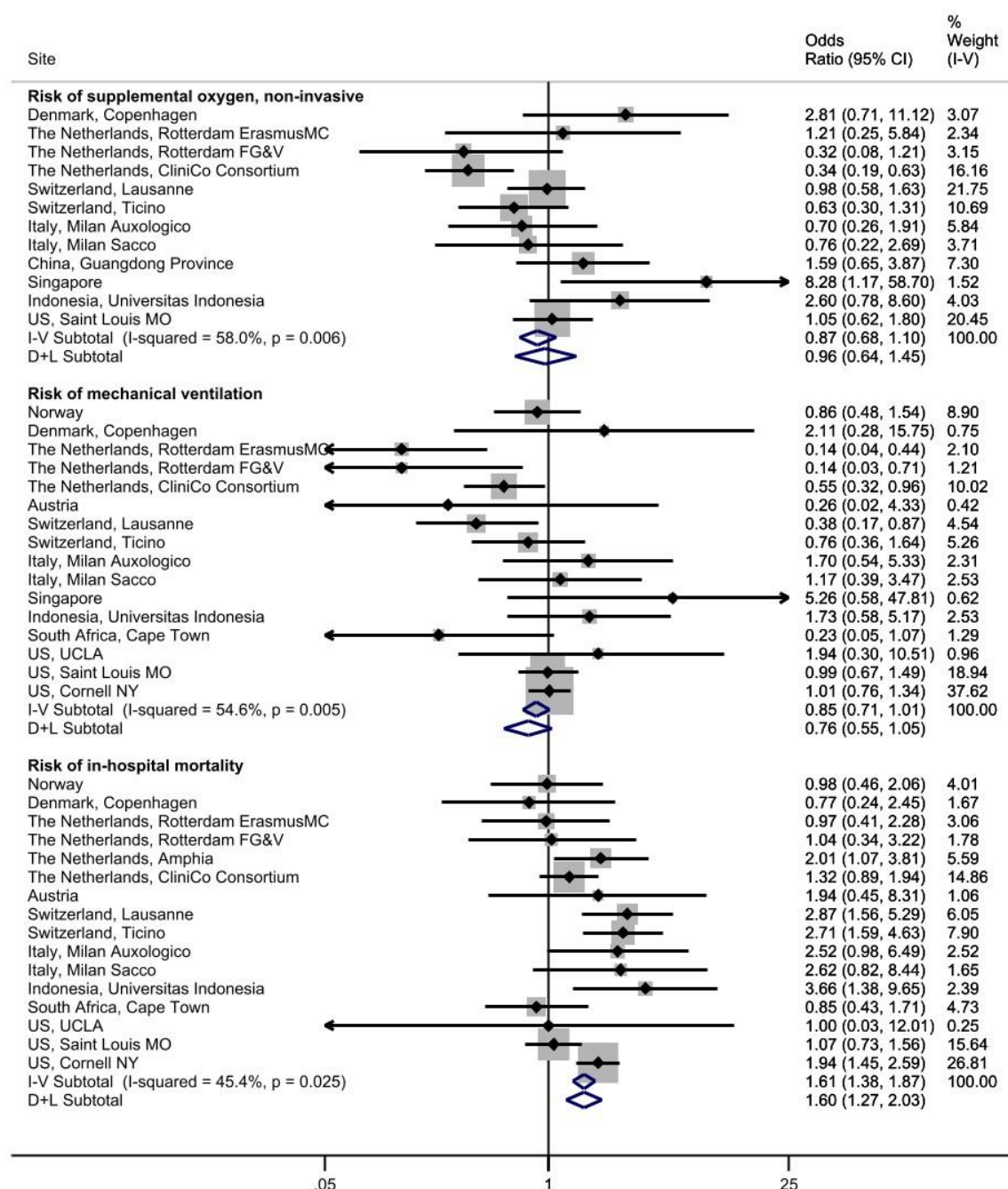


Figure S3 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with pre-existing cardiovascular disease. Models adjusted for: BMI categories (≥ 12 - <18 , ≥ 18 - <25 , ≥ 25 - <30 , ≥ 30), age (<65 , ≥ 65), sex (male/female), diabetes (yes/no), pre-existing respiratory condition (yes/no), hypertension (yes/no). Reference is patients without pre-existing cardiovascular disease. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model.

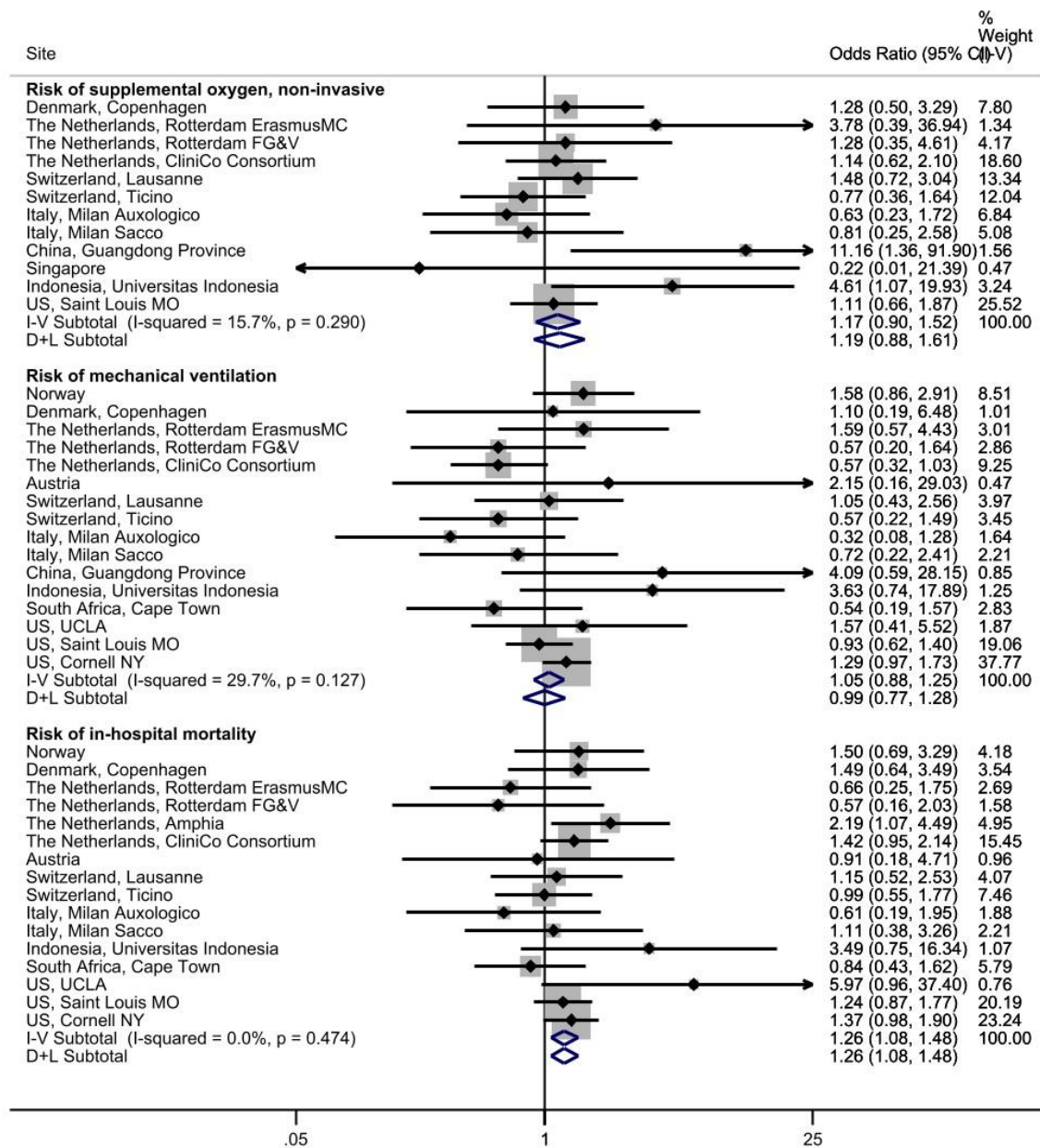


Figure S4 - Meta-analysis odds ratios for supplemental oxygen/non-invasive ventilation, invasive mechanical ventilation, and in-hospital mortality among patients with pre-existing respiratory conditions. Models adjusted for: BMI categories (≥ 12 - <18 , ≥ 18 - <25 , ≥ 25 - <30 , ≥ 30), age (<65 , ≥ 65), sex (male/female), pre-existing cardiovascular disease (yes/no), diabetes (yes/no), hypertension (yes/no). Reference is patients without pre-existing respiratory conditions. I-V: inverse-variance weighted fixed effects model, D+L: DerSimonian and Laird random effects model.

Table S5 – Site-specific and meta-analysis estimates using standard and Asian country specific BMI categories for Asian countries

	BMI categories	Indonesia	Singapore	China	Meta-analysis estimates
		Adj OR (95% CI)	Adj OR (95% CI)	Adj OR (95% CI)	Random effects Adj OR (95% CI)
Supplemental oxygen, non-invasive	Standard				
	≥12-<18	--	--	0.88 (0.25-3.09)	--
	≥18-<25	ref	ref	ref	ref
	≥25-<30	1.72 (0.55-5.32)	2.41 (0.70-8.32)	1.57 (0.93-2.64)	1.44 (1.15-1.80)
	≥30	3.55 (0.91-13.89)	2.10 (0.36-12.29)	1.15 (0.45-2.97)	1.75 (1.33-2.30)
	Asian country specific				
	≥12-<18.5	2.13 (0.21-21.2)	5.04 (0.34-74.9)	0.9 (0.32-2.56)	0.74 (0.42-1.33)
	≥18.5-<24	ref	ref	ref	ref
	≥24-<28	1.84 (0.65-5.24)	1.58 (0.41-6.14)	1.75 (1.07-2.84)	1.46 (1.17-1.83)
	≥28	3.51 (1.11-11.11)	3.88 (0.87-17.29)	1.27 (0.62-2.60)	1.81 (1.37-2.40)
Invasive mechanical ventilation	Standard				
	≥12-<18	--	--	--	--
	≥18-<25	ref	ref	ref	ref
	≥25-<30	0.94 (0.34-2.61)	3.48 (0.6-20.28)	0.21 (0.03-1.81)	1.23 (1.03-1.46)
	≥30	0.86 (0.23-3.15)	1.06 (0.06-17.81)	0.67 (0.07-6.37)	1.73 (1.29-2.32)
	Asian country specific				
	≥12-<18.5	--	--	--	--
	≥18.5-<24	ref	ref	ref	ref
	≥24-<28	0.43 (0.15-1.20)	2.06 (0.35-11.99)	0.16 (0.02-1.37)	1.18 (0.97-1.43)
	≥28	0.84 (0.28-2.49)	2.24 (0.28-18.17)	0.76 (0.14-4.19)	1.72 (1.28-2.30)
In-hospital mortality	Standard				
	≥12-<18	--	--	--	--
	≥18-<25	ref	--	--	ref
	≥25-<30	1.09 (0.44-2.72)	--	--	0.88 (0.74-1.04)
	≥30	1.80 (0.60-5.37)	--	--	1.23 (0.92-1.64)
	Asian country specific				
	≥12-<18.5	0.86 (0.07-10.85)	--	--	--
	≥18.5-<24	ref	--	--	ref
	≥24-<28	0.49 (0.20-1.22)	--	--	0.85 (0.72-1.01)
	≥28	1.14 (0.43-3.06)	--	--	1.20 (0.90-1.60)

Table S5 - Invasive mechanical ventilation and in-hospital mortality site-specific estimates with additional adjustments for smoking &/or race/ethnicity

	Invasive mechanical ventilation		In-hospital mortality	
	Adjusted OR (95% CI)	Adjusted OR (95% CI) + smoking &/or race/ethnicity	Adjusted OR (95% CI)	Adjusted OR (95% CI) + smoking &/or race/ethnicity
BMI	United States, University of California Los Angeles			
≥12-<18	1.62 (0.04-70.27)	1.58 (0.03-80.47)	0	0
≥18-<25	ref	ref	ref	ref
≥25-<30	1.23 (0.32-4.57)	1.68 (0.39-7.26)	0.35 (0.01-3.69)	0.56 (0.01-29.19)
≥30	2.59 (0.85-8.35)	3.2 (0.88-13.00)	1.95 (0.28-14.59)	--
	United States, Saint Louis Missouri			
≥12-<18	0.7 (0.24-2.03)	0.56 (0.17-1.78)	1.47 (0.65-3.35)	1.77 (0.76-4.15)
≥18-<25	ref	ref	ref	ref
≥25-<30	0.92 (0.56-1.48)	0.87 (0.53-1.44)	0.97 (0.61-1.55)	0.88 (0.54-1.43)
≥30	0.83 (0.52-1.31)	0.73 (0.45-1.18)	1.3 (0.85-1.99)	1.19 (0.76-1.86)
	United States, Cornell University New York			
≥12-<18	0.36 (0.11-1.23)	0.47 (0.14-1.62)	1.84 (0.94-3.58)	1.92 (0.93-3.93)
≥18-<25	ref	ref	ref	ref
≥25-<30	1.31 (0.99-1.74)	1.31 (0.96-1.79)	0.65 (0.47-0.9)	0.62 (0.44-0.87)
≥30	1.90 (1.41-2.54)	2.19 (1.57-3.04)	0.88 (0.63-1.24)	0.92 (0.64-1.34)
	South Africa, Cape Town			
≥12-<18	0	0	0	0
≥18-<25	ref	ref	ref	ref
≥25-<30	1.17 (0.34-3.98)	1.17 (0.34-4)	1.16 (0.52-2.59)	1.16 (0.52-2.59)
≥30	5.59 (1.91-16.35)	5.59 (1.91-16.35)	4.28 (2.03-9.05)	4.28 (2.03-9.05)
	Norway			
≥12-<18	0	0	2.87 (0.64-12.83)	2.67 (0.6-11.85)
≥18-<25	ref	ref	ref	ref
≥25-<30	1.39 (0.75-2.58)	1.43 (0.76-2.66)	0.72 (0.33-1.59)	0.75 (0.34-1.66)
≥30	2.11 (1.05-4.26)	2.17 (1.07-4.4)	1 (0.37-2.69)	1.03 (0.38-2.8)
	Italy, Milan Auxologico			
≥12-<18	0	0	1.19 (0.16-9.01)	0.99 (0.11-8.67)
≥18-<25	ref	ref	ref	ref
≥25-<30	2.34 (0.6-9.15)	2.45 (0.6-10)	0.79 (0.27-2.29)	0.76 (0.26-2.24)
≥30	2.16 (0.49-9.59)	2.72 (0.57-12.97)	0.37 (0.09-1.46)	0.36 (0.09-1.43)
	Switzerland, Lausanne			
≥12-<18	0	0	0.33 (0.04-2.81)	0.32 (0.04-2.76)
≥18-<25	ref	ref	ref	ref
≥25-<30	1.78 (0.83-3.83)	1.75 (0.81-3.79)	1.63 (0.82-3.42)	1.62 (0.82-3.23)
≥30	2.62 (1.16-5.91)	2.83 (1.24-6.44)	1.11 (0.49-2.51)	1.11 (0.49-2.52)
	The Netherlands, Amphia			
≥12-<18	--	--	0	0
≥18-<25	--	--	ref	ref
≥25-<30	--	--	1.03 (0.52-2.05)	1.04 (0.52-2.09)
≥30	--	--	1.23 (0.57-2.66)	1.31 (0.60-2.86)

	The Netherlands, Rotterdam FG&V			
	0	0	0	0
	ref	ref	ref	ref
≥12-<18				
≥18-<25				
≥25-<30	1.86 (0.67-5.18)	2.36 (0.77-7.25)	0.74 (0.22-2.46)	0.65 (0.18-2.4)
≥30	2.19 (0.75-6.33)	2.36 (0.74-7.47)	0.46 (0.12-1.75)	0.66 (0.14-3.14)

Models adjusted for: age (<65, ≥65), sex (male/female), pre-existing cardiovascular disease (yes/no), diabetes (yes/no), pre-existing respiratory conditions (yes/no), hypertension (yes/no)