DACCOVID

Anton Pottegård

Professor, Clinical Pharmacology and Pharmacy, University of Southern Denmark Head of Research, Hospital Pharmacy Funen, Odense University Hospital

apottegaard@health.sdu.dk

DACCOVID

Steering committee Danish Medicines Agency Danish Health Authority Statens Serum Institut Danish Health Data Authority **Danish** Patients Danish Regions Danish Regions Clinical Quality Program Danish Faculties of Health Science

DACCOVID

Expert group

Anton Pottegård, University of Southern Denmark Jesper Hallas, University of Southern Denmark Kasper Kristensen, University of Southern Denmark Lars Christian Lund, University of Southern Denmark Mette Reilev, University of Southern Denmark Henrik Toft Sørensen, Aarhus University Reimar W. Thomsen, Aarhus University Christian Fynbo Christiansen, Aarhus University Marianne Kragh Thomsen, Aarhus University Hospital Steffen Christensen, Aarhus University Hospital Henrik Støvring, Aarhus University Hospital Henrik Nielsen, Aalborg University Hospital Marianne Voldstedlund, Statens Serum Institut Anders Husby, Statens Serum Institut Nikolai C. Brun, The Danish Medicines Agency Nanna Borup Johansen, The Danish Medicines Agency

Aim

To provide rapid analyses of questions related to use of medicines in COVID-19 with potential important public health impact

Clinical Epidemiology

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Existing Data Sources in Clinical Epidemiology: The Danish COVID-19 Cohort

This article was published in the following Dove Press journal: Clinical Epidemiology

Anton Pottegård 10 Kasper Bruun Kristensen¹ Mette Reilev¹ Lars Christian Lund Martin Thomsen Ernst¹ Jesper Hallas (D^{1,2} Reimar Wernich Thomsen 103 Christian Fynbo Christiansen 103 Henrik Toft Sørensen 103,4 Nanna Borup Johansen⁵ Henrik Støvring Steffen Christensen⁷ Marianne Kragh Thomsen 108 Anders Husby⁹ Marianne Voldstedlund¹⁰ Jesper Kjær¹¹

Background: To facilitate research on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a prospective cohort of all Danish residents tested for SARS-CoV-2 in Denmark is established.

Data Structure: All Danish residents tested by reverse transcriptase polymerase chain reactions (RT-PCR) for SARS-CoV-2 in Denmark are included. The cohort is identified using the Danish Microbiology Database. Individual-level record linkage between administrative and health-care registries is facilitated by the Danish Civil Registration System. Information on outcomes related to SARS-CoV-2 infection includes hospital admission, intensive care unit admission, mechanical ventilation, and death and is retrieved from the five administrative Danish regions, the Danish National Patient Registry, and the Danish Register of Causes of Death. The Patient Registry further provides a complete hospital contact history of somatic and psychiatric conditions and procedures. Data on all prescriptions filled at community pharmacies are available from the Danish National Prescription Registry. Health-care authorization status is obtained from the Danish Register of Laboratory Results for Research. The cohort is governed

SARS-CoV-2 PCR results Prescription fills Hospital admissions Deaths Migrations Labdata; bloodtype Ethnicity; urban res.; marriage status



Hypothesis submitted Steering committee approval Expert group meeting Protocol development EU-PAS registration Programming Regulator note Submission



5 preparatory studies (all published)

Methods review Description of data sources Baseline characteristics NSAID in influenza ACE/ARB in influenza **5 preparatory studies** (all published)

11 hypothesis evaluating studies
4 being analysed
4 under review
1 accepted
2 published



International Journal of Epidemiology, 2020, 1–14 doi: 10.1093/ije/dyaa140 Original Article



Original Article

Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort

Mette Reilev ,¹ Kasper Bruun Kristensen,¹ Anton Pottegård,^{1,2} Lars Christian Lund,¹ Jesper Hallas,^{1,3} Martin Thomsen Ernst,¹ Christian Fynbo Christiansen,⁴ Henrik Toft Sørensen,^{4,5} Nanna Borup Johansen,⁶ Nikolai Constantin Brun,⁶ Marianne Voldstedlund,⁷ Henrik Støvring,^{1,8} Marianne Kragh Thomsen,⁹ Steffen Christensen,¹⁰ Sophie Gubbels,⁷ Tyra Grove Krause,⁷ Kåre Mølbak,⁷* and Reimar Wernich Thomsen⁴

¹Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark, ²Hospital Pharmacy Funen, Odense University Hospital, Odense, Denmark, ³Department of Clinical Biochemistry and Clinical Pharmacology, Odense University Hospital, Odense, Denmark, ⁴Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark, ⁵Center for Population Health and Sciences, Stanford University, Stanford, CA, USA, ⁶Department of Medical Evaluation and Biostatistics, Danish Medicines Agency, Copenhagen, Denmark, ⁷Statens Serum Institut, Copenhagen, Denmark, ⁸Department of Public Health—Biostatistics, Aarhus University, Aarhus, Denmark, ⁹Department of Clinical Microbiology, Aarhus University Hospital, Aarhus, Denmark and ¹⁰Department of Anaesthesia and Intensive Care Medicine, Aarhus University Hospital, Aarhus, Denmark

*Corresponding author, Department of Clinical Epidemiology, Aarhus, University, Hospital, Olof, Palmes Alle 43-45, DK-8200

	Danish SAI	RS-CoV-2 cohort		SARS	-CoV-2 PCR-positive	G2.905		of Isuoit				
					Hospi	talized		Jour				
Characteristic	SARS-CoV-2 test-negative individuals n = 410697	SARS-CoV-2 PCR-positive cases n = 11 122 (100%)	Community- managed n = 8868 (80%)	Hospitalized $n = 2254 (20\%)$	Hospitalized, non-ICU n = 1940 (17%)	Hospitalized, ICU n = 314 (2.8%)	Fatal disease within 30 days ^e n = 577 (5.2%)	nal of Epidem	SARS	CoV-2 PCR-positive	(2.95)	
Age years, median (IQR)	46 (30-60)	48 (33-62)	44 (30-56)	71 (56-80)	72 (55-81)	68 (58-75)	82 (75-88)	iolo				
0-9	23 295 (5.7%)	251 (2.3%)	240 (2.7%)	11 (0.5%)	11 (0.6%)	0 (-)	0 (-)	logy.		Hospi	talized	
10-19	25 256 (6.1%)	495 (4.5%)	481 (5.4%)	14 (0.6%)	14 (0.7%)	0 (-)	0 (-)	2020,	Hospitalized	Hospitalized,	Hospitalized,	Fatal disease
20-29	52 065 (13%)	1523 (14%)	1468 (17%)	55 (2.4%)	49 (2.5%)	6 (1.9%)	0 (-)	20,	1 roop room to a	non-ICU	ICU	within 30 days
30-39	60 638 (15%)	1588 (14%)	1498 (17%)	90 (4.0%)	80 (4.1%)	10 (3.2%)	16 (2.8%)	Vol		101-100	100	within 50 days
40-49	69 424 (17%)	1970 (18%)	1778 (20%)	192 (8.5%)	169 (8.7%)	23 (7.3%)		.00	n = 2254 (20%)	n = 1940 (17%)	n = 314 (2.8%)	n = 577 (5.2%)
50-59	72 603 (18%)	2035 (18%)	1698 (19%)	337 (15%)	285 (15%)	52 (17%)		, No	n = 220 4 (20 %)	n = 1240 (1770)	n = 514 (2.070)	n = 577 (52270)
60-69	51 445 (13%)	1305 (12%)	931 (10%)	374 (17%)	292 (15%)	82 (26%)	56 (9.7%)		88 (3.9%)	83 (4.3%)	5 (1.6%)	41 (7.1%)
70-79	33 740 (8.2%)	950 (8.5%)	372 (4.2%)	578 (26%)	471 (24%)	107 (34%)	165 (29%)	8	129 (5.7%)	115 (5.9%)	14 (4.5%)	46 (8.0%)
80-89	17 478 (4.3%)	762 (6.9%)	286 (3.2%)	476 (21%)	442 (23%)	34 (11%)	220 (38%)					
90+	4752 (1.2%)	243 (2.2%)	116 (1.3%)	127 (5.6%)	127 (6.5%)	0 (-)	120 (21%)		1105 (49%)	939 (48%)	166 (53%)	346 (60%)
Sex									727 (32%)	605 (31%)	122 (39%)	198 (34%)
Female	253 610 (62%)	6430 (58%)	5388 (61%)	1042 (46%)	956 (49%)	86 (27%)	249 (43%)		409 (18%)	346 (18%)	63 (20%)	105 (18%)
Male	157 087 (38%)	4692 (42%)	3480 (39%)	1212 (54%)	984 (51%)	228 (73%)	328 (57%)		493 (22%)	419 (22%)	74 (24%)	183 (32%)
Authorized healthcare workers	54 004 (13%)	2427 (22%)	2294 (26%)	133 (5.9%)	120 (6.2%)	13 (4.1%)	(n < 5)		187 (8.3%)	165 (8.5%)	22 (7.0%)	51 (8.8%)
Nurse	20 744 (38%)	1229 (51%)	1173 (51%)	56 (42%)	50 (42%)	6 (46%)	0 (-)		402 (18%)	355 (18%)	47 (15%)	195 (34%)
Physician	6335 (12%)	398 (16%)	371 (16%)	27 (20%)	2	(n < 5)	(n < 5)		367 (16%)	307 (16%)	60 (19%)	110 (19%)
Other	26 925 (50%)	800 (33%)	750 (33%)	50 (38%)		(n < 5)	(n < 5)		301 (13%)	254 (13%)	47 (15%)	89 (15%)
Number of co-morbidities"									162 (7.2%)	140 (7.2%)	22 (7.0%)	58 (10%)
Median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	2 (1-3)	2 (1-3)	2 (1-3)	3 (2-4)		66 (2.9%)	53 (2.7%)	13 (4.1%)	21 (3.6%)
0	215 795 (53%)	6034 (54%)	5532 (62%)	502 (22%)	433 (22%)	69 (22%)	30 (5.2%)		490 (22%)	417 (21%)	73 (23%)	198 (34%)
1	96 736 (24%)	2462 (22%)	1978 (22%)	484 (21%)	412 (21%)	72 (23%)	92 (16%)		343 (15%)	311 (16%)	32 (10%)	163 (28%)
2	45 590 (11%)	1140 (10%)	742 (8.4%)	398 (18%)	328 (17%)	70 (22%)	108 (19%)		414 (18%)	376 (19%)	38 (12%)	208 (36%)
3	25 312 (6.2%)	691 (6.2%)	327 (3.7%)	364 (16%)	317 (16%)	47 (15%)	122 (21%)		2.58 (11%)	231 (12%)	27 (8.6%)	115 (20%)
4+	27 264 (6.6%)	795 (7.1%)	289 (3.3%)	506 (22%)	450 (23%)	56 (18%)	225 (39%)		115 (5.1%)	102 (5.3%)	13 (4.1%)	68 (12%)
Hospital admissions within the last year ^b									392 (17%)	346 (18%)	46 (15%)	167 (29%)
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-1)	0 (0-0)	1 (0-2)		193 (8.6%)	170 (8.8%)	23 (7.3%)	78 (14%)
0	348 652 (85%)	9597 (86%)	8124 (92%)	1473 (65%)	1235 (64%)	238 (76%)	270 (47%)		307 (14%)	272 (14%)	35 (11%)	89 (15%)
1	38 080 (9.3%)	941 (8.5%)	539 (6.1%)	402 (18%)	357 (18%)	45 (14%)	149 (26%)		31 (1.4%)	2/2(14/6)	(n < 5)	(n < 5)
2	11 766 (2.9%)	269 (2.4%)	107 (1.2%)	162 (7.2%)	150 (7.7%)	12 (3.8%)	71 (12%)		661 (29%)	550 (28%)	(n < 5) 111 (35%)	(<i>n</i> < 3) 191 (33%)
-	11/00(20/0)	205 (21110)	101 (10010)	202 (1210)	200 (11 10)	12 (01010)						
							(Continued)	cn .	270 (12%)	220 (11%)	50 (16%)	54 (9.4%)
									17 (0.8%) 13 (0.6%)	2	(n < 5) (n < 5)	6 (1.0%) (n < 5)
									494 (22%)	433 (22%)	61 (19%)	153 (27%)
									1231 (55%)	1054 (54%)	177 (56%)	413 (72%)
									435 (19%)	377 (19%)	58 (18%)	156 (27%)
			Heart failure		9432 (2			(1.1%)	221 (9.8%)	206 (11%)	15 (4.8%)	101 (18%)

Table 1 Baseline characteristics for the overall Danish SARS-CoV-2 cohort and stratified by whether the infection was community-managed or led to any hospitalization, hospi-

(Continued)

6

lefined by hospital-discharge diagnoses in combination with drug use for the co-morbidity (i.e. filled prepplementary data at IJE on line.

SARS-CoV-2 PCR-positive cases

Hospitalized,

non-ICU

n = 1940 (17%)

321 (17%)

269 (14%)

364 (19%)

139 (7.2%)

317 (16%)

54 (2.8%)

172 (8.9%)

99 (5.1%)

27 (1.4%)

239 (12%)

127 (6.5%)

Hospitalized

n = 2254 (20%)

354 (16%)

299 (13%)

436 (19%)

139 (6.2%)

374 (17%)

65 (2.9%)

194 (8.6%)

114 (5.1%)

57 (2.5%)

33 (1.5%)

23 (1.0%)

277 (12%)

145 (6.4%)

nmunity-

anaged

868 (80%)

(2.8%)

3 (2.7%)

2 (5.0%)

2(1.9%)

l (4.6%)

(1.0%)

)(1.1%)

+(2.1%)

3 (1.4%)

(0.5%)

(0.2%)

\$ (7.5%)

3 (2.3%)

Hospitalized

Hospitalized,

ICU

n = 314 (2.8%)

33 (11%)

30 (9.6%)

72 (23%)

0 (-)

57 (18%)

11 (3.5%)

22 (7.0%)

15 (4.8%)

(n < 5)

6 (1.9%)

(n < 5)

38 (12%)

18 (5.7%)

Fatal disease

within 30 days^e

n = 577 (5.2%)

170 (29%)

137 (24%)

144 (25%)

117 (20%)

137 (24%)

15 (2.6%)

80 (14%)

37 (6.4%)

21 (3.6%)

13 (2.3%)

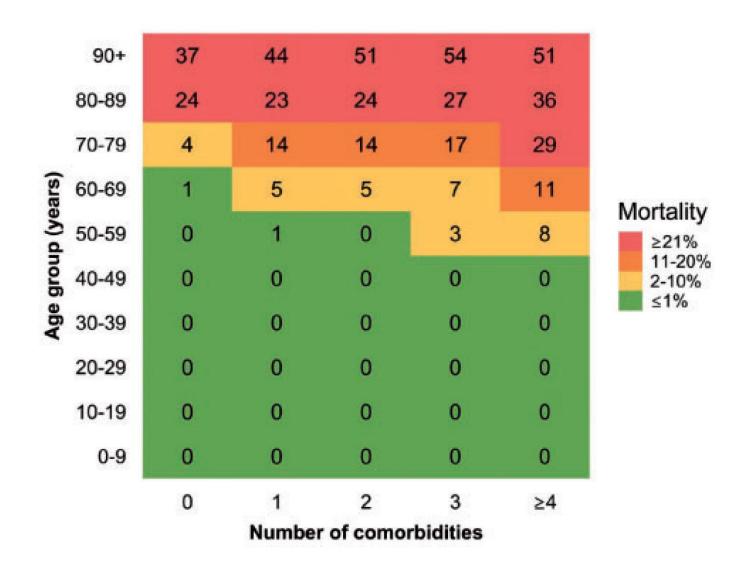
7 (1.2%)

57 (9.9%)

50 (8.7%)

*** "To ensure anonymity, Danish law prohibits reporting of exact n= measures (-) in some cases where this could lead to inferring of low n results (n < 5) in other categories.

ICU, intensive care unit; IQR, interquartile nange; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker, NSAID, non-steroidal anti-inflammatory drugs.



ABO bloodtype **NSAIDs** ACE/ARB VTE risk Inhaled steroids Immunosuppr. PPIs Antidiabetics Thyroid function Psychotropics Complications

PLOS MEDICINE

RESEARCH ARTICLE

Adverse outcomes and mortality in users of non-steroidal anti-inflammatory drugs who tested positive for SARS-CoV-2: A Danish nationwide cohort study

Lars Christian Lund^{1°}, Kasper Bruun Kristensen^{1°}, Mette Reilev¹, Steffen Christensen², Reimar Wernich Thomsen³, Christian Fynbo Christiansen³, Henrik Støvring^{1,4}, Nanna Borup Johansen⁵, Nikolai Constantin Brun⁵, Jesper Hallas¹, Anton Pottegård^{1*}

 Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark, 2 Department of Anaesthesia and Intensive Care Medicine, Aarhus University Hospital, Aarhus, Denmark, 3 Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark,
 Biostatistics, Department of Public Health, Aarhus University, Aarhus, Denmark, 5 Department of Medical Evaluation and Biostatistics, Danish Medicines Agency, Copenhagen, Denmark

These authors contributed equally to this work.
* apottegaard@health.sdu.dk

Abstract

Background

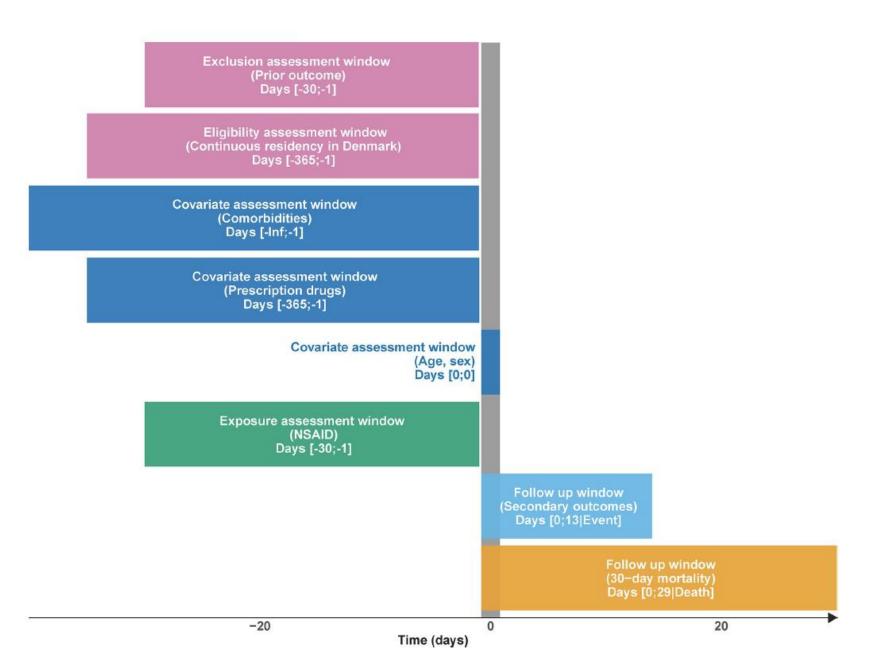
Concerns over the safety of non-steroidal anti-inflammatory drug (NSAID) use during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been raised. We studied whether use of NSAIDs was associated with adverse outcomes and mortality during SARS-CoV-2 infection.



OPEN ACCESS

Citation: Lund LC, Kristensen KB, Reilev M, Christensen S, Thomsen RW, Christiansen CF, et al. (2020) Adverse outcomes and mortality in users of non-steroidal anti-inflammatory drugs who tested positive for SARS-CoV-2: A Danish nationwide cohort study. PLoS Med 17(9): e1003308. <u>https://doi.org/10.1371/journal. pmed.1003308</u>

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Outcome	NSAID users		Non-users		Comparison				
	Number of events/ sample size	Risk (%) (95% CI)	Number of events/ sample size	Risk (%) (95% CI)	Risk difference (%) (95% CI)	p- Value	Risk ratio (95% CI)	p- Value	
Unmatched cohort									
Death	14/248	5.6 (2.8, 8.5)	521/8,988	5.8 (5.3, 6.3)	-0.2 (-3.1, 2.8)	0.92	0.97 (0.58, 1.63)	0.92	
Hospitalization*	56/228	24.6 (19.0, 30.2)	1,456/8,414	17.3 (16.5, 18.1)	7.3 (1.6, 12.9)	0.01	1.42 (1.13, 1.79)	< 0.01	
ICU admission*	11/247	4.5 (1.9, 7.0)	279/8,956	3.1 (2.8, 3.5)	1.3 (-1.3, 3.9)	0.31	1.43 (0.79, 2.58)	0.23	
Mechanical ventilation*	10/248	4.0 (1.6, 6.5)	225/8,970	2.5 (2.2, 2.8)	1.5 (-0.9, 4.0)	0.23	1.61 (0.86, 2.99)	0.13	
Renal replacement therapy*	n < 5/248	-**	**	_**	0.6 (-0.8, 1.9)	0.42	1.87 (0.59, 5.94)	0.29	
Matched cohort					-				
Death	14/224	6.3 (3.1, 9.4)	55/896	6.1 (4.4, 7.8)	0.1 (-3.5, 3.7)	0.95	1.02 (0.57, 1.82)	0.95	
Hospitalization*	50/204	24.5 (18.6, 30.4)	175/826	21.2 (18.1, 24.3)	3.3 (-3.4, 10.0)	0.33	1.16 (0.87, 1.53)	0.31	
ICU admission*	11/223	4.9 (2.1, 7.8)	42/889	4.7 (3.2, 6.2)	0.2 (-3.0, 3.4)	0.90	1.04 (0.54, 2.02)	0.90	
Mechanical ventilation*	10/224	4.5 (1.8, 7.2)	35/891	3.9 (2.5, 5.3)	0.5 (-2.5, 3.6)	0.73	1.14 (0.56, 2.30)	0.72	
Renal replacement therapy*	<i>n</i> < 5/224	-**	**	**	-0.2 (-2.0, 1.6)	0.81	0.86 (0.24, 3.09)	0.81	

Table 2. Association between current NSAID use and 30-day mortality, hospitalization, ICU admission, mechanical ventilation, and renal replacement therapy in unmatched and propensity-score-matched cohorts.

Outcome

Death Hospitalization ICU admission Mechanical ventilation Renal replacement therapy

Risk ratio (95% CI) 1.02 (0.57-1.82) 1.16 (0.87-1.53) 1.04 (0.54-2.02) 1.14 (0.56-2.30)

0.86 (0.24-3.09)

Conclusions

Use of NSAIDs was not associated with an increased risk of 30-day mortality or adverse outcomes in patients infected with SARS-CoV-2.

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REVIEW

WILEY

Considerations for pharmacoepidemiological analyses in the SARS-CoV-2 pandemic

Anton Pottegård¹ | Xavier Kurz² | Nicholas Moore³ | Christian F. Christiansen⁴ | Olaf Klungel^{1,5}

¹Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark ²Data Analytics and Methods Task Force, European Medicines Agency, Amsterdam, The

Netherlands ³Bordeaux PharmacoEpi, University of Bordeaux, Bordeaux, France

⁴Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

⁵Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, The Netherlands

Correspondence

Anton Pottegård, Clinical Pharmacology and Pharmacy, University of Southern Denmark, JB Winsløwsvej 19, 2, DK-5000 Odense C, Denmark. Email: apottegaard@health.sdu.dk

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has triggered several hypotheses regarding use of specific medicines and risk of infection as well as prognosis. Under these unique circumstances, rapid answers require quick engagement in data collection and analyses; however, appropriate design and conduct of pharmacoepidemiologic studies are needed to generate valid and reliable evidence. In this paper, endorsed by the International Society for Pharmacoepidemiological studies in relation to the pandemic across eight domains: (1) timeliness of evidence, including the need to prioritise some questions over others in the acute phase of the pandemic; (2) the need to align observational and interventional research on efficacy; (3) the specific challenges related to "real-time epidemiology" during an ongoing pandemic; (4) what design to use to answer a specific question; (5) considerations on the definition of exposures; (6) what covariates to collect; (7) considerations on the definition of out-

Project	Main responsible entity	Reference
ABO Bloodtype	Odense University Hospital (Torben Barrington)	<u>LINK</u>
NSAID in COVID19	University of Southern Denmark (Anton Pottegård)	<u>LINK</u>
Methods review (ISPE)	International Society for Pharmacoepidemiology (Anton Pottegård)	<u>LINK</u>
Description of DACCOVID	Expert group (Anton Pottegård)	<u>LINK</u>
Baseline paper	Expert group (Reimar W. Thomsen)	<u>LINK</u>
NSAID in influenza	University of Southern Denmark (Anton Pottegård)	<u>LINK</u>
ACE/ARB in influenza	Aarhus University (Christian Fynbo Christiansen)	<u>LINK</u>

THANK YOU!

Jesper Hallas, University of Southern Denmark Kasper Kristensen, University of Southern Denmark Lars Christian Lund, University of Southern Denmark Mette Reilev, University of Southern Denmark Henrik Toft Sørensen, Aarhus University Reimar W. Thomsen, Aarhus University Christian Fynbo Christiansen, Aarhus University Marianne Kragh Thomsen, Aarhus University Hospital Steffen Christensen, Aarhus University Hospital Henrik Støvring, Aarhus University Hospital Henrik Nielsen, Aalborg University Hospital Marianne Voldstedlund, Statens Serum Institut Anders Husby, Statens Serum Institut Nikolai C. Brun, The Danish Medicines Agency Nanna Borup Johansen, The Danish Medicines Agency





Anton Pottegård apottegaard@health.sdu.dk www.antonpottegaard.dk @Pottegard