



The real-world data response to a changing world

Dr Jennifer Lane

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Vision

The European Health Data & Evidence Network (EHDEN) aspires to be the trusted observational research ecosystem to enable better health decisions, outcomes and care

Mission

Our mission is to provide a new paradigm for the discovery and analysis of health data in Europe, by building a large-scale, federated network of data sources standardized to a common data model



EHDEN IS ABOUT...

FEDERATION

Creation of an EU-wide architecture for federated analyses of real world data

HARMONISATION

Harmonise more than 100 million anonymised health records to the OMOP common data model



COMMUNITY

Establish a self-sustaining open science collaboration in Europe, supporting academia, industry, regulators, payers, government, NGOs and others

OUTCOMES

Enabling outcomes driven healthcare at a European level

EDUCATION

The establishment of an EHDEN Academy, webinars and face-to-face training sessions to train all stakeholders



EHDEN CONSORTIUM



Start date: 1 Nov 2018
End date: 30 Apr 2024
Duration: 66 months



22 partners



Almost €29 million

Universities, public bodies and research organisations

Erasmus MC Academic coordinator



SME & Mid-sized companies



Non-profit organisations



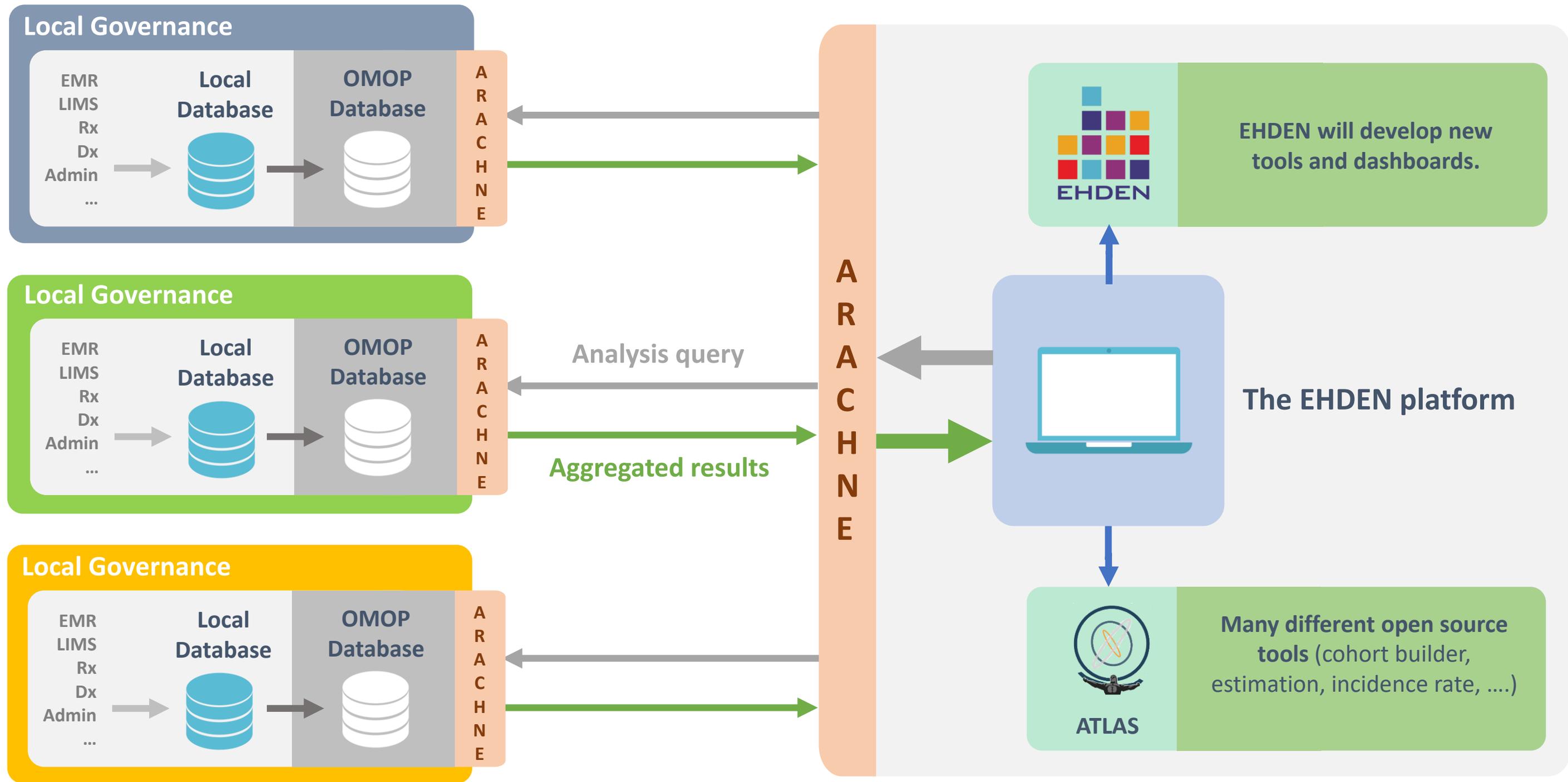
EFPIA & Associated partners



EFPIA Lead

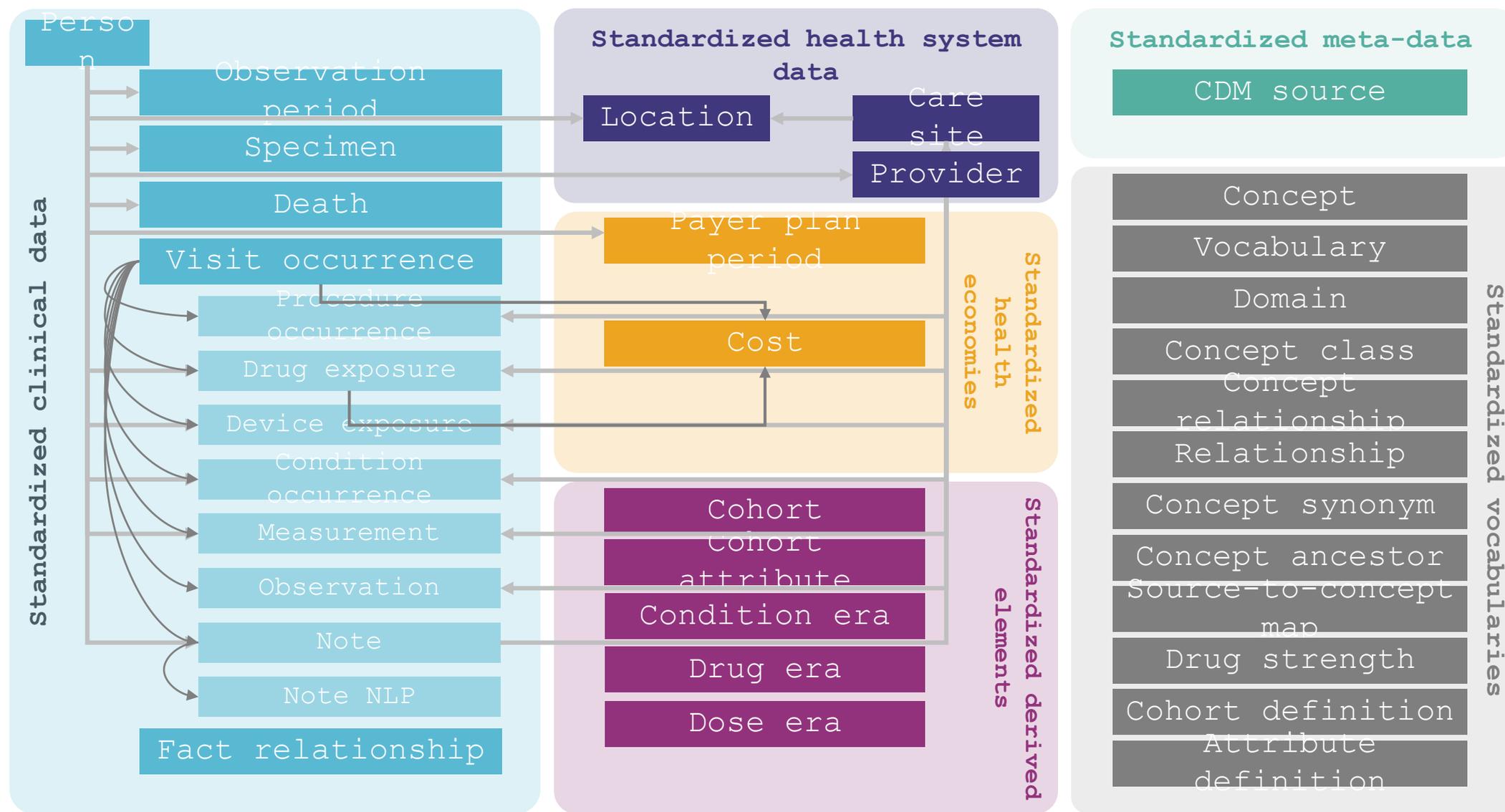


THE EHDEN FEDERATED DATA NETWORK





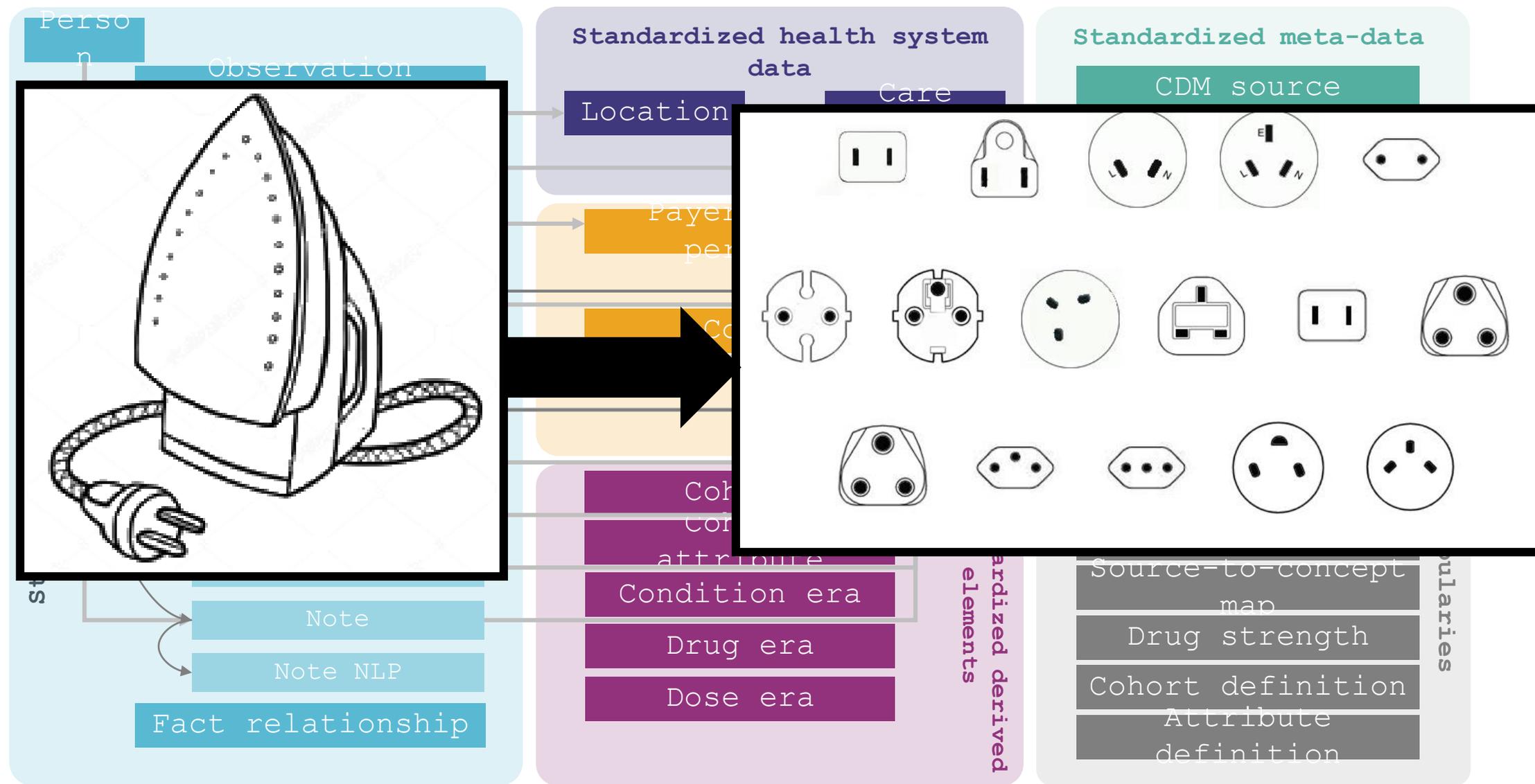
THE OMOP COMMON DATA MODEL



Patient-centric
 Tabular
 Extendable
 Built for analytics
 Relational design

v 5.0.1

THE OMOP COMMON DATA MODEL



Patient-centric
 Tabular
 Extendable
 Built for analytics
 Relational design

v 5.0.1



EHDEN WILL ENSURE COMPLIANCE WITH E.G., GDPR/DGA



Compliance with citizen and data protection regulations

Ethical Advisory Board

Development of a FDN code of conduct (concentric circles of trust view)

'Privacy by design'

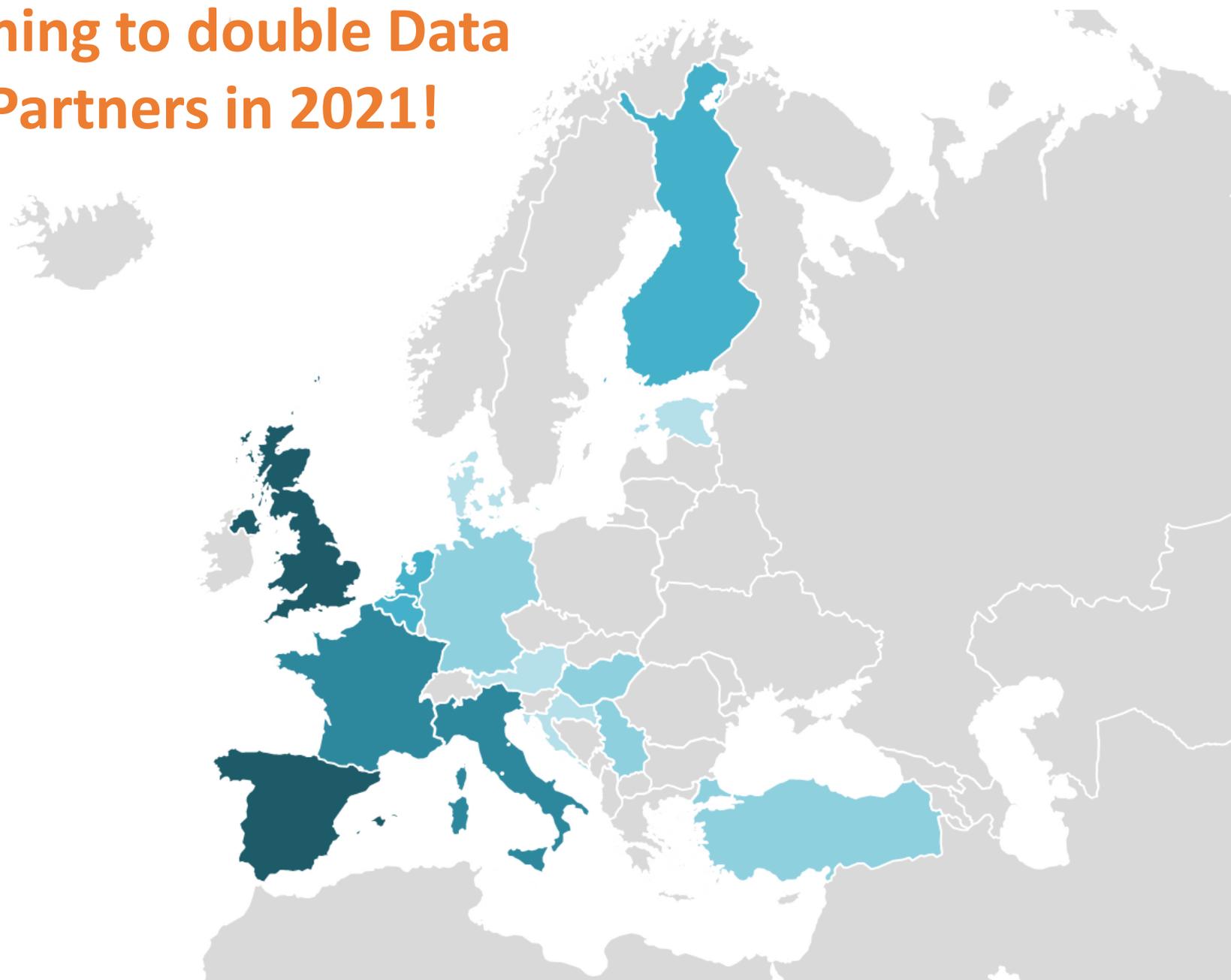
(data remains local behind socio-technical firewalls)

Evolving framework for data protection as regulation and implementation evolves

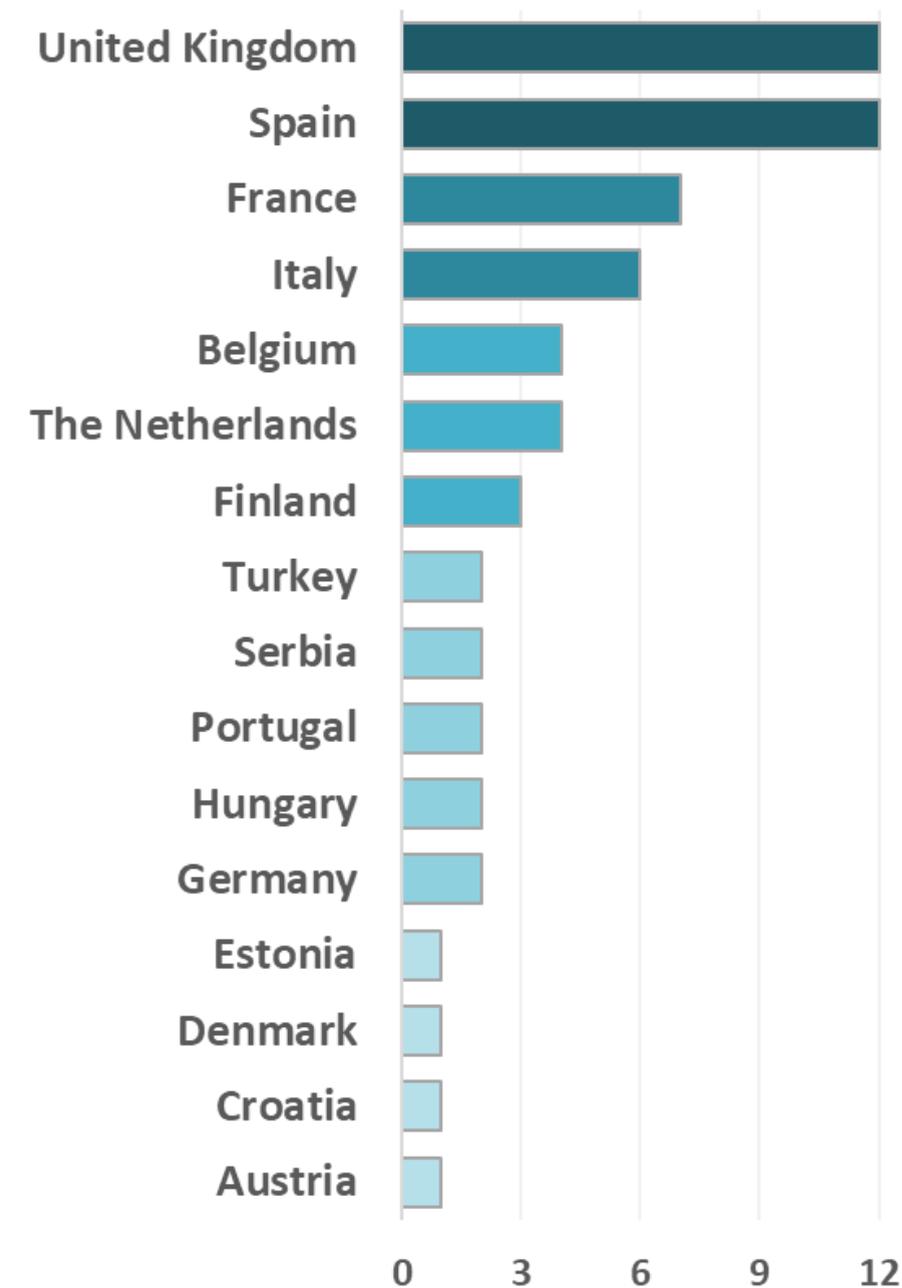


AFTER THREE CALLS WE SELECTED 60 DATA PARTNERS IN 16 COUNTRIES

Aiming to double Data Partners in 2021!



Geographic spread of data partners. The shade of blue indicates the # of data partners in that country (darker = more)





FAST OBSERVATIONAL RESEARCH IS FEASIBLE (STUDY-A-THON)

“To compare the **risk** of post-operative **complications** and **mortality** between unicompartmental vs total knee replacement.”

Monday

Group consensus on the **problem**

Draft cohort definitions

Wednesday

Review patient-level prediction results

Externally validate prediction model

Friday

Review of results

Plan for completing **publications**

Tuesday

Review clinical characterisation

Draft patient-level prediction design

Thursday

Draft population-level effect estimation design

Review population-level effect estimation diagnostics



(EHDEN 1st Study-a-thon, Oxford, December 2018); published Lancet Rheumatology Dec 2019



COVID-19 PANDEMIC BEGINS

Home Info Symposium 2020 Forum Github Past Events Photos Contact

EHDEN [Login](#)

 **OHDSI**
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

We regret to inform you that the 2020 European Symposium "From data to impact: the journey towards improving clinical practice" is cancelled due to the COVID-19 outbreak

[More Info](#)



HOW COULD WE HELP?

What is the phenotype, prognosis and care needs? *[characterization]*

Who is at high or low risk? *[prediction]*

What is the safety of the most commonly used medications repurposed for treatment? *[causal inference/estimation]*





OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

#OHDSICOVID19

OHDSI COVID-19 International Study-A-Thon

Follow our
COVID19 Updates

[www.ohdsi.org/
covid-19-updates](http://www.ohdsi.org/covid-19-updates)

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#JoinTheJourney

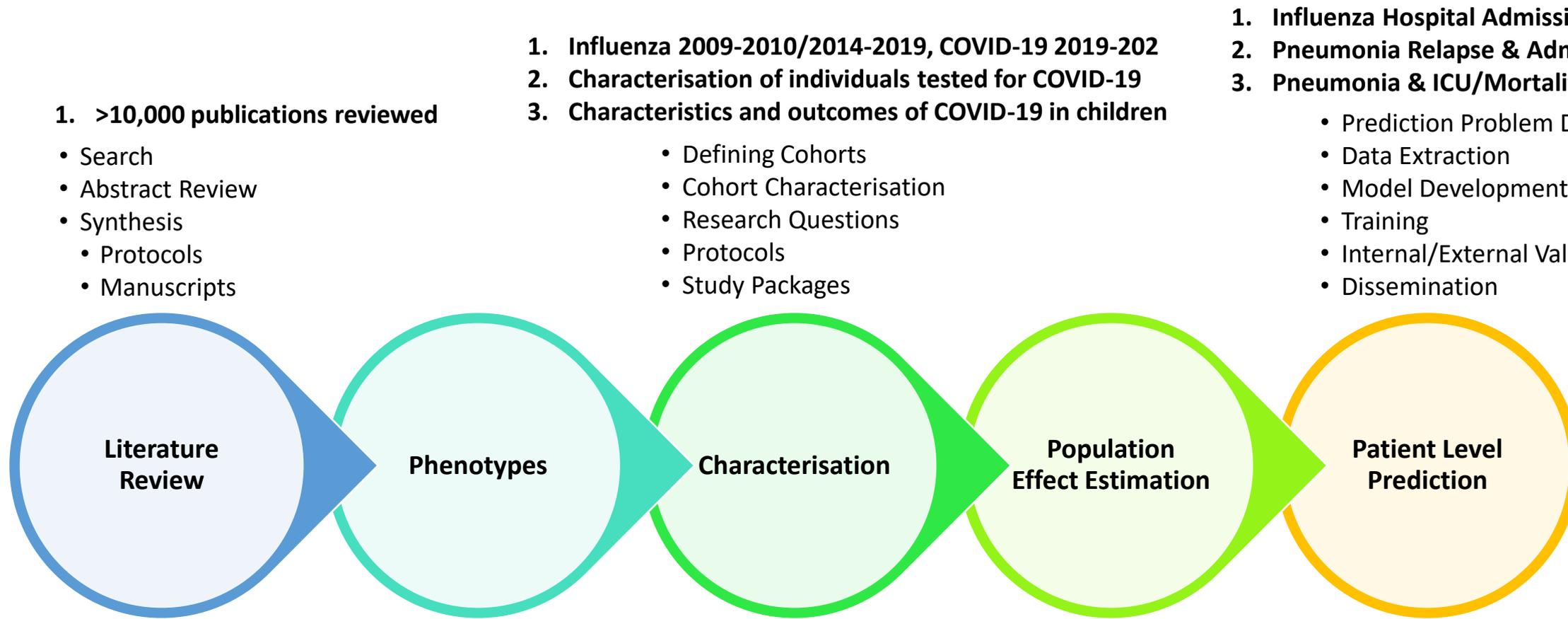
Collaborating to design and execute observational research and generate real-world evidence to inform the global pandemic

March 26-29, 2020



3RD STUDY-A-THON: COVID-19 AIMS & PROCESS

March 26th
2020



1. >10,000 publications reviewed

- Search
- Abstract Review
- Synthesis
 - Protocols
 - Manuscripts

1. Influenza 2009-2010/2014-2019, COVID-19 2019-202
2. Characterisation of individuals tested for COVID-19
3. Characteristics and outcomes of COVID-19 in children

- Defining Cohorts
- Cohort Characterisation
- Research Questions
- Protocols
- Study Packages

1. Influenza Hospital Admission in next 30 days
2. Pneumonia Relapse & Admission in next 30 days
3. Pneumonia & ICU/Mortality

- Prediction Problem Definition
- Data Extraction
- Model Development
- Training
- Internal/External Validation
- Dissemination

March 29th
2020

- Comprehensive Concept Sets
- Capturing Coding Practices
- Cohort Creation
- Cohort Diagnostics
- Building Blocks for Composite Phenotypes

1. Literature review 36 phenotypes
2. 355 cohorts
3. 114 validated and reviewed cohorts for prediction, estimation and characterisation on atlas.ohdsi.org

- Research Questions
 - AEs
 - Efficacy
- Comparative Cohorts
- Participants
- Outcomes
- Analyses
- Diagnostics
- Results

1. DMARDs
2. Antivirals
3. ACEi/ARBs



HCQ SAFETY: DISTRIBUTED DATABASE NETWORK STUDY

Source	Population	Patients	Type
VA	US (Veterans)	12M	Claims
DAGermany	Germany (general population)	37M	EHR
IMRD	UK (general population)	15M	EHR
AmbEMR	US (general population)	49M	EHR
OpenClaims	US (general population)	300M	Claims
CPRD	UK (general population)	13M	EHR
CCAE	US (commercially insured, <65y)	142M	Claims
MDCD	US (Medicaid enrollees)	26M	Claims
MDCR	US (commercially insured, ≥65y)	10M	Claims
IPCI	Netherlands (general population)	2.5M	EHR
JMDC	Japan (insured general population)	5.5M	Claims
Clinformatics	US (commercially insured)	85M	Claims
OptumEHR	US (general population)	93M	EHR
SIDIAP	Catalonia (general population)	7.7M	EHR

14 database

6 countries

7 administrative claims

7 electronic health records

Real world heterogeneity of patient experience

Data partners contributing to this study remain custodians of their individual patient-level health information and hold either exemption from institutional review boards or approval for participation



HCQ SAFETY: COMPARATIVE COHORT STUDY DESIGN

Eligibility criteria:

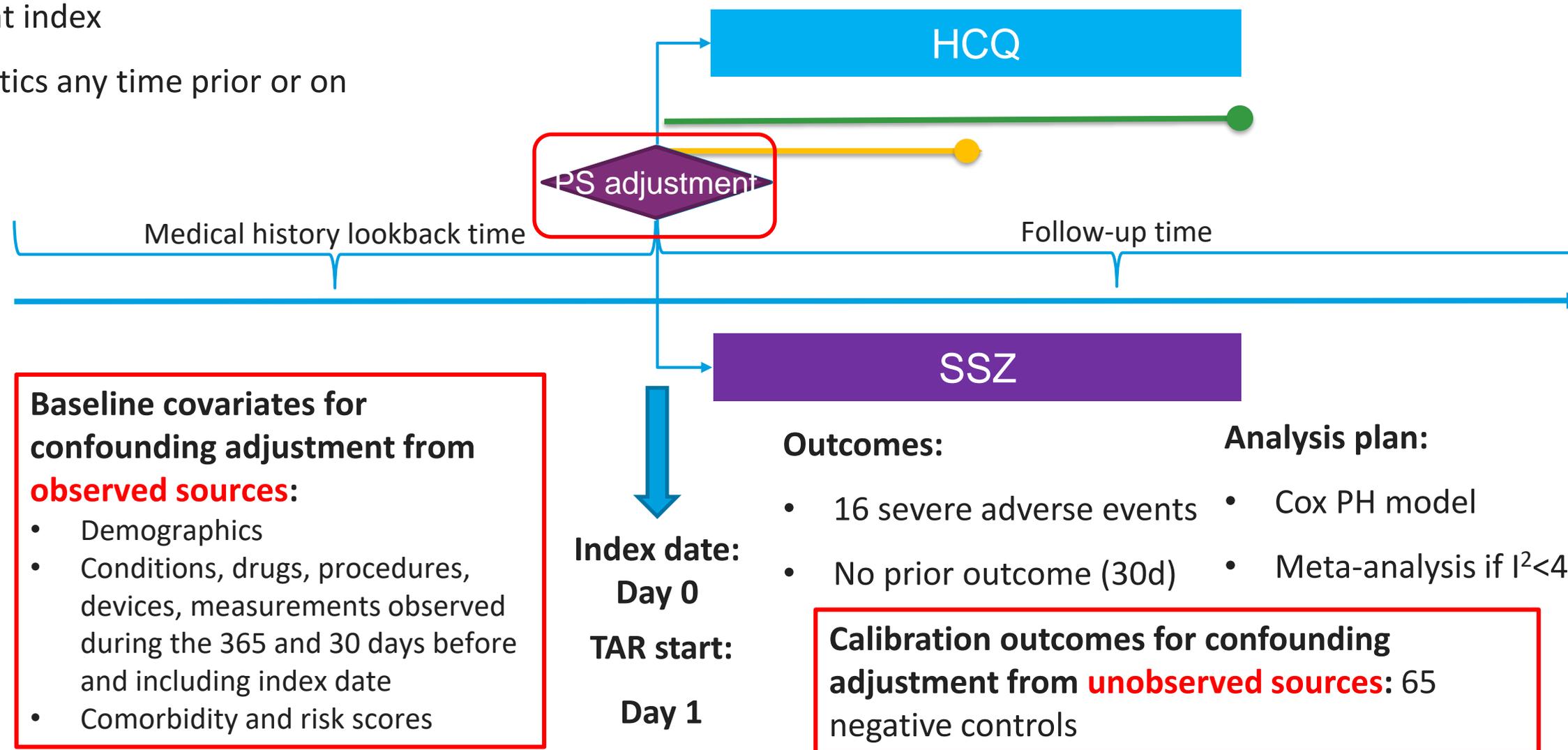
- First exposure after Sept 1, 2000
- ≥365 days prior observation
- ≥18 years at index
- RA diagnostics any time prior or on index

Treatment strategies:

1. HCQ vs SSZ
2. HCQ+AZM vs HCQ+AMX

Causal contrasts:

- On-treatment effect
- Fixed 30d effect





HYDROXYCHLOROQUINE & CV RISK

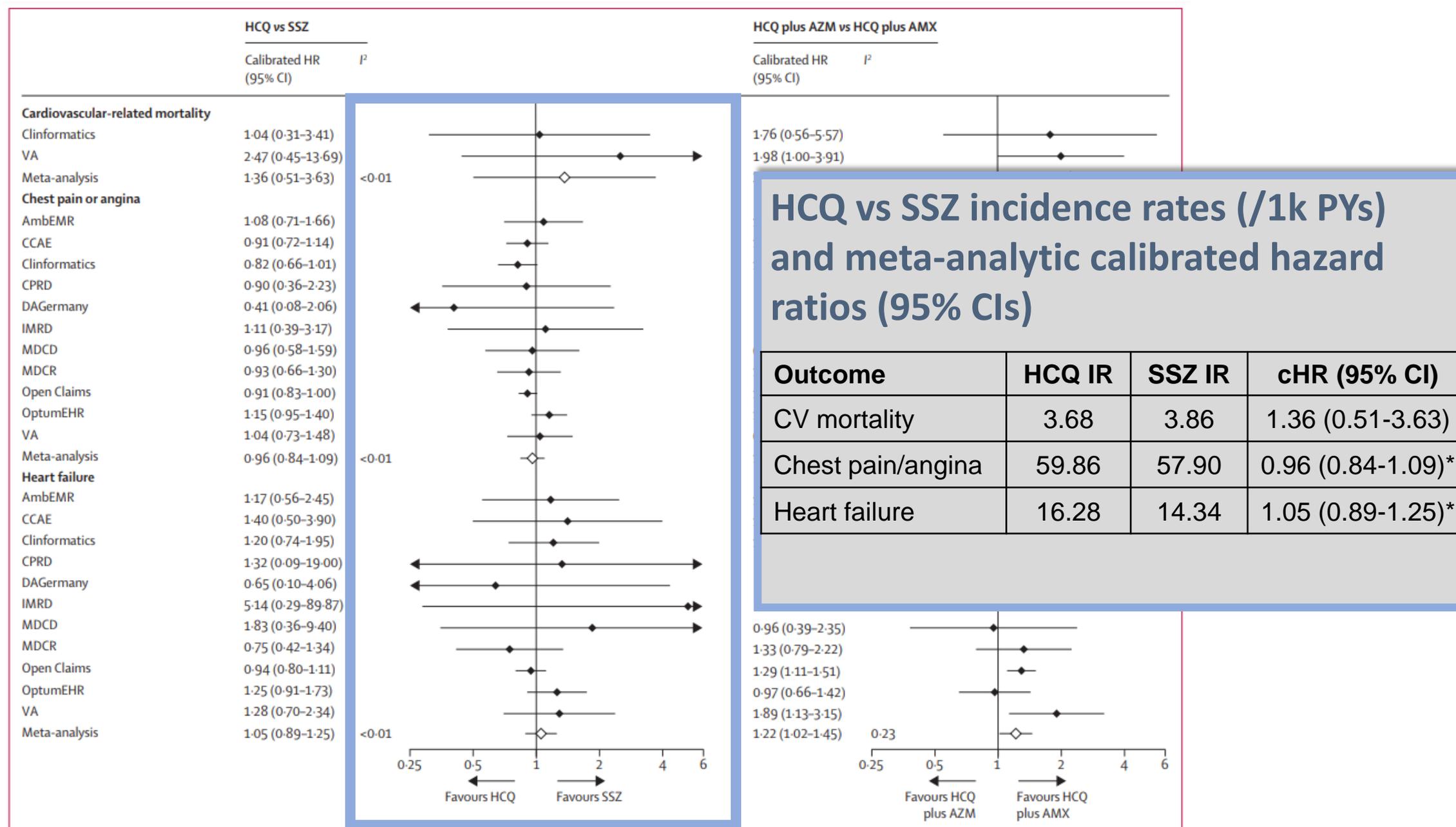


Figure 2: Source-specific and meta-analytic-specific severe adverse event risk estimates for HCQ versus SSZ and HCQ plus AZM versus HCQ plus AMX new users during 30-day (intention-to-treat) follow-up

AmbEMR=IQVIA Ambulatory EMR. AMX=amoxicillin. AZM=azithromycin. CCAE=IBM Commercial Claims and Encounters. CPRD=Clinical Practice Research Datalink. DAGermany=IQVIA Disease Analyzer Germany. EMR=electronic medical record. HCQ=hydroxychloroquine. HR=hazard ratio. IMRD=IQVIA UK Integrated Medical Record Data. MDCD=IBM Multi-state Medicaid. MDCR=IBM Medicare Supplemental Database. OptumEHR=Optum de-identified Electronic Health Record. SSZ=sulfasalazine. VA=US Department of Veterans Affairs.



HYDROXYCHLOROQUINE & CV RISK

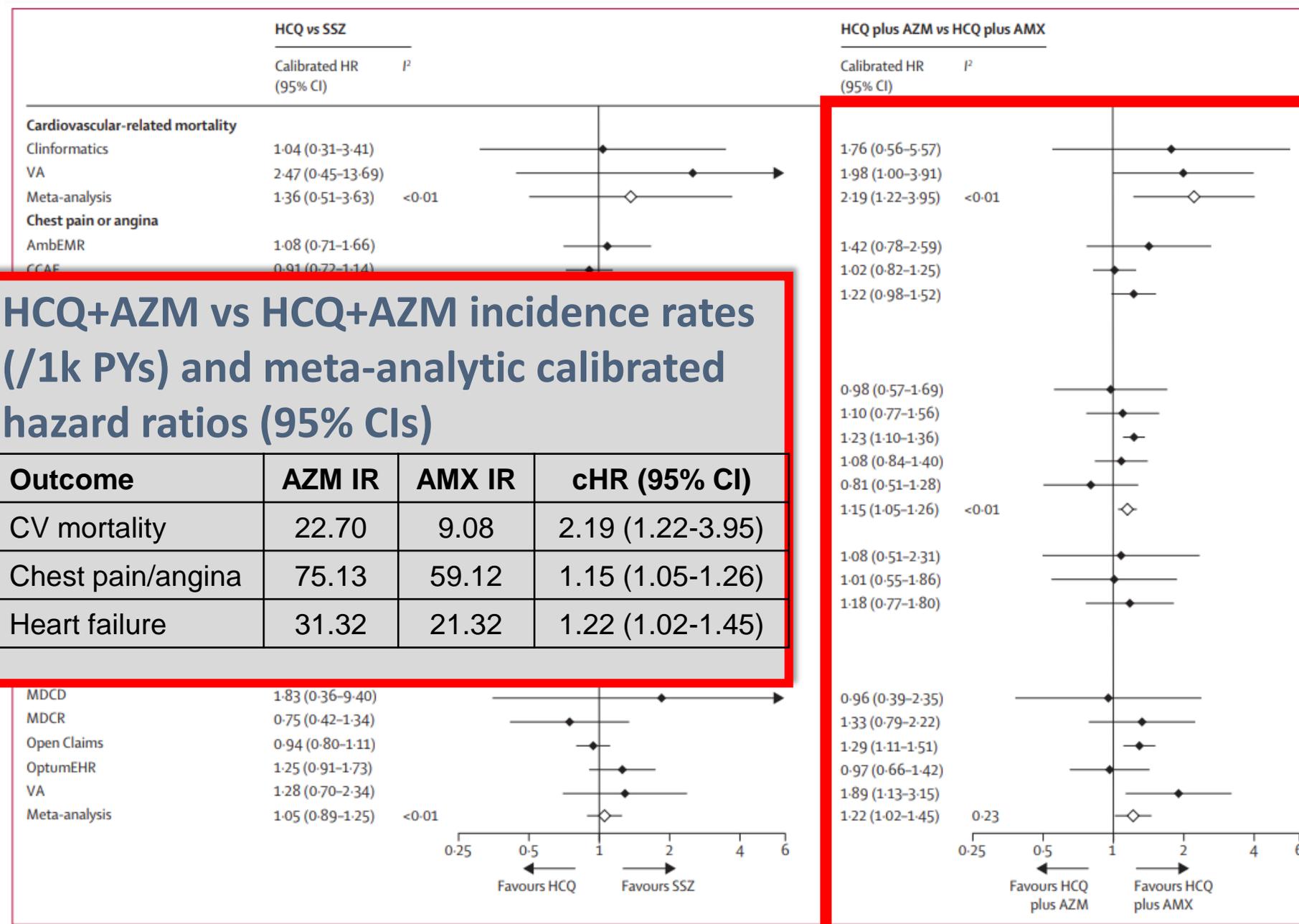


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Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study

Jennifer C.E Lane, James Weaver, Kristin Kostka, Talita Duarte-Salles, Maria Tereza F. Abrahao, Heba Alghoul, Osaid Alser, Thamir M Alshammari, Patricia Biedermann, Edward Burn, Paula Casajust, Mitch Conover, Aedin C. Culhane, Alexander Davydov, Scott L. DuVall, Dmitry Dymshyts, Sergio Fernández Bertolín, Kristina Fišter, Jill Hardin, Laura Hester, George Hripcsak, Seamus Kent, Sajan Khosla, Spyros Kolovos, Christophe G. Lambert, Johan ver der Lei, Kristine E. Lynch, Rupa Makadia, Andrea V. Margulis, Michael E. Matheny, Paras Mehta, Daniel R. Morales, Henry Morgan-Stewart, Mees Mosseveld, Danielle Newby, Fredrik Nyberg, Anna Ostropelets, Rae Woong Park, Albert Prats-Uribe, Gowtham A. Rao, Christian Reich, Jenna Reys, Peter Rijnbeek, Selva Muthu Kumaran Sathappan, Martijn Schuemie, Sarah Seager, Anthony Sena, Azza Shoaibi, Matthew Spotnitz, Marc A. Suchard, Joel Swerdel, Carmen Olga Torre, David Vizcaya, Haini Wen, Marcel de Wilde, Seng Chan You, Lin Zhang, Oleg Zhuk, Patrick Ryan, Daniel Prieto-Alhambra

doi: <https://doi.org/10.1101/2020.04.08.20054551>

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

KEY PUBLICATIONS

Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study



Journal article

LANE J. et al, (2020)

Forbes

36,377 views | Apr 10, 2020, 05:59pm EDT

Hydroxychloroquine And Azithromycin For COVID-19: Benefits TBD, Risks Clear



Harlan Krumholz Former Contributor Healthcare



IMPACT ON REGULATORY BODIES



- Medicines ▾
- Human regulatory ▾
- Veterinary regulatory ▾
- Committees ▾
- News & events ▾
- Partners & networks ▾

COVID-19: reminder of risk of serious side effects with chloroquine and hydroxychloroquine [Share](#)

News 23/04/2020



Chloroquine and hydroxychloroquine are known to potentially cause heart rhythm problems, and these could be exacerbated if treatment is combined with other medicines, such as the antibiotic azithromycin, that have similar effects on the heart.

Recent studies^{1,2} have reported serious, in some cases fatal, heart rhythm problems with chloroquine or hydroxychloroquine, particularly when taken at high doses or in combination with the antibiotic azithromycin.

Chloroquine and hydroxychloroquine are currently authorised for treating malaria and certain autoimmune diseases. In addition to side effects affecting the heart, they are known to potentially cause liver and kidney problems, nerve cell damage that can lead to seizures (fits) and low blood sugar (hypoglycaemia).



← Home / Drugs / Drug Safety and Availability / FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems

FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems

Does not affect FDA-approved uses for malaria, lupus, and rheumatoid arthritis

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Drug Safety and Availability

[Information about Nitrosamine Impurities in Medications](#)

[Drug Alerts and Statements](#)

[Medication Guides](#)

[Drug Safety Communications](#)

July 1, 2020 Update: A summary of the FDA [review of safety issues](#) with the use of hydroxychloroquine and chloroquine to treat hospitalized patients with COVID-19 is now available. This includes reports of serious heart rhythm problems and other safety issues, including blood and lymph system disorders, kidney injuries, and liver problems and failure.

June 15, 2020 Update: Based on ongoing analysis and emerging scientific data, FDA has revoked the emergency use authorization (EUA) to use hydroxychloroquine and chloroquine to treat COVID-19 in certain hospitalized patients when a clinical trial is

Content current as of:
07/01/2020

Regulated Product(s)
Drugs

Topic(s)
Safety - Issues, Errors, and Problems

Health Topic(s)
Infectious Disease
Coronavirus



RESPONSE TO PSYCHIATRIC EFFECTS OF HCQ



AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

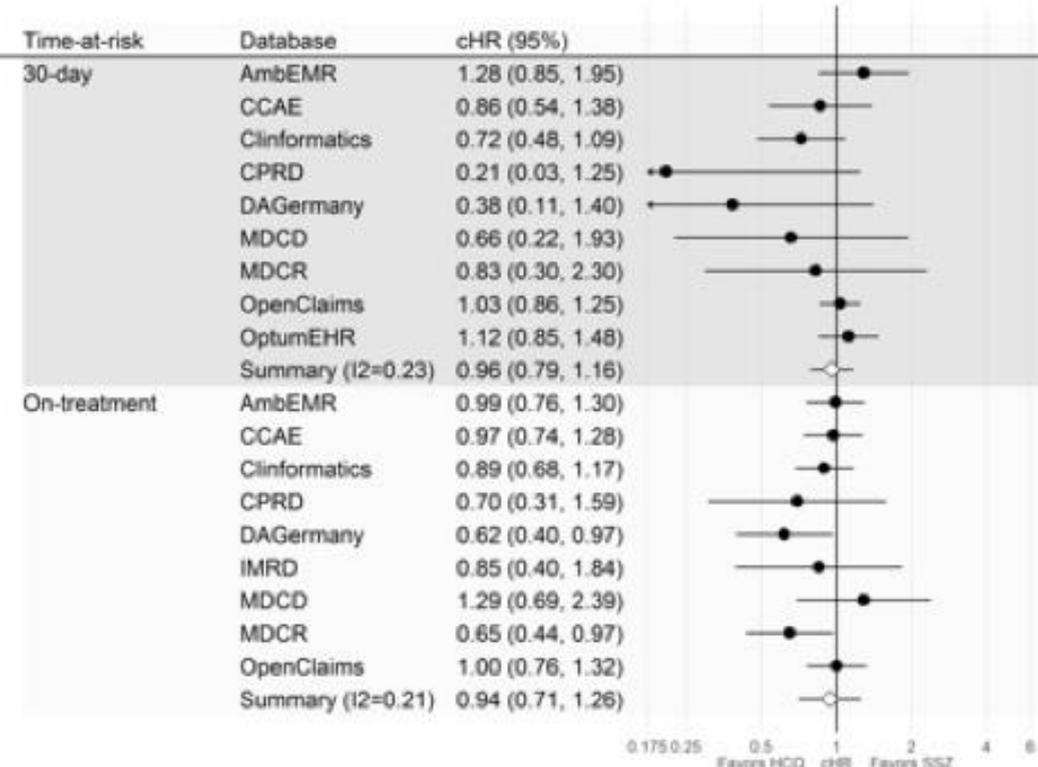
NOTA DE SEGURIDAD

Cloroquina/Hidroxiclороquina: precauciones y vigilancia de posibles reacciones adversas en pacientes con COVID-19

Fecha de publicación: 22 de abril de 2020
 Categoría: medicamentos de uso humano, farmacovigilancia
 Referencia: MUH (FV) 07/2020

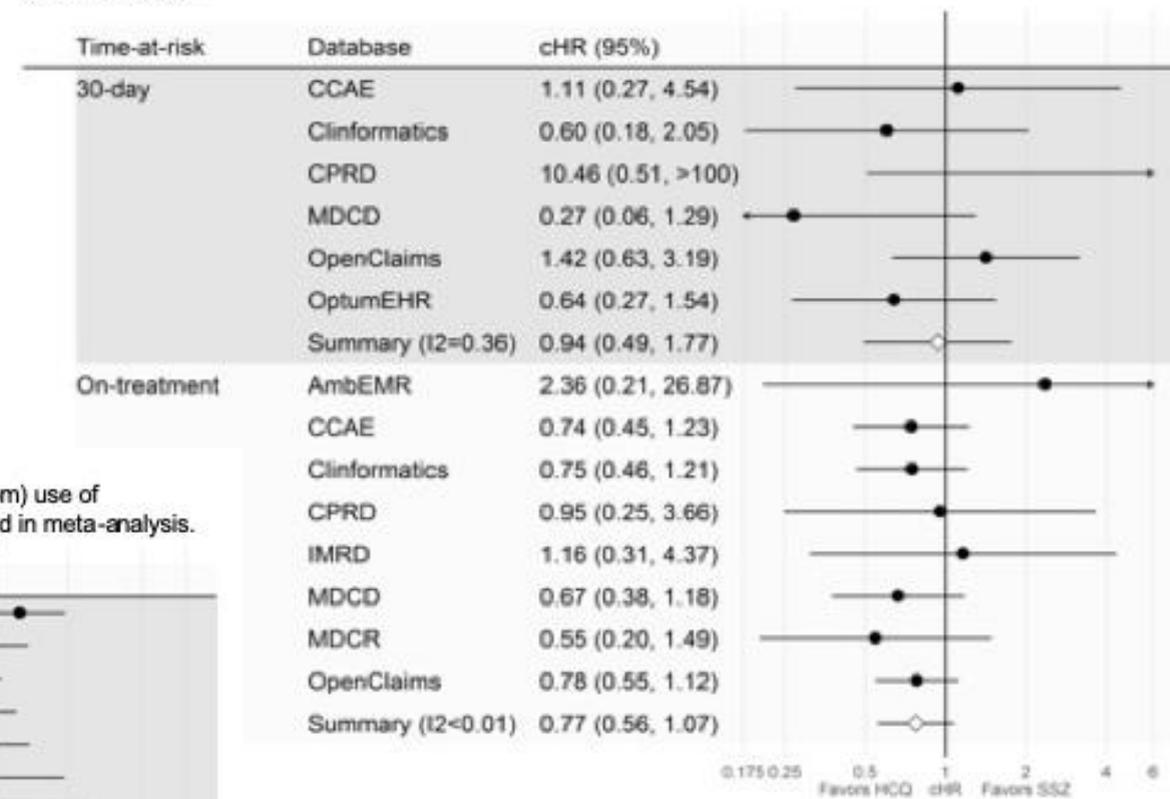
- Estos medicamentos pueden ocasionar trastornos del ritmo cardíaco, específicamente prolongación del intervalo QT del ECG. Este riesgo aumenta con dosis altas y cuando se administra con otros medicamentos que también comparten este posible riesgo como azitromicina.
- No es aconsejable por tanto la combinación de cloroquina o hidroxiclороquina con otros medicamentos que comparten el riesgo de prolongar el intervalo QT del ECG, especialmente en pacientes con factores de riesgo de un intervalo QT prolongado. En caso de necesidad, administrarlo en alguna de estas condiciones, se realizará una vigilancia estrecha del paciente.
- Se recomienda informar a los pacientes que comienzan el tratamiento sobre los posibles signos y síntomas que sugieren un trastorno del ritmo recomendándoles que consulten con el médico que les realiza seguimiento en caso de que aparezcan.

Figure 1. Forest plot of the association between short- (top) and long-term (bottom) use of Hydroxychloroquine versus Sulfasalazine and risk of depression, by database and in meta-analysis.



cHR=calibrated hazard ratio; 95%=95% confidence interval; I²=estimate heterogeneity statistic.

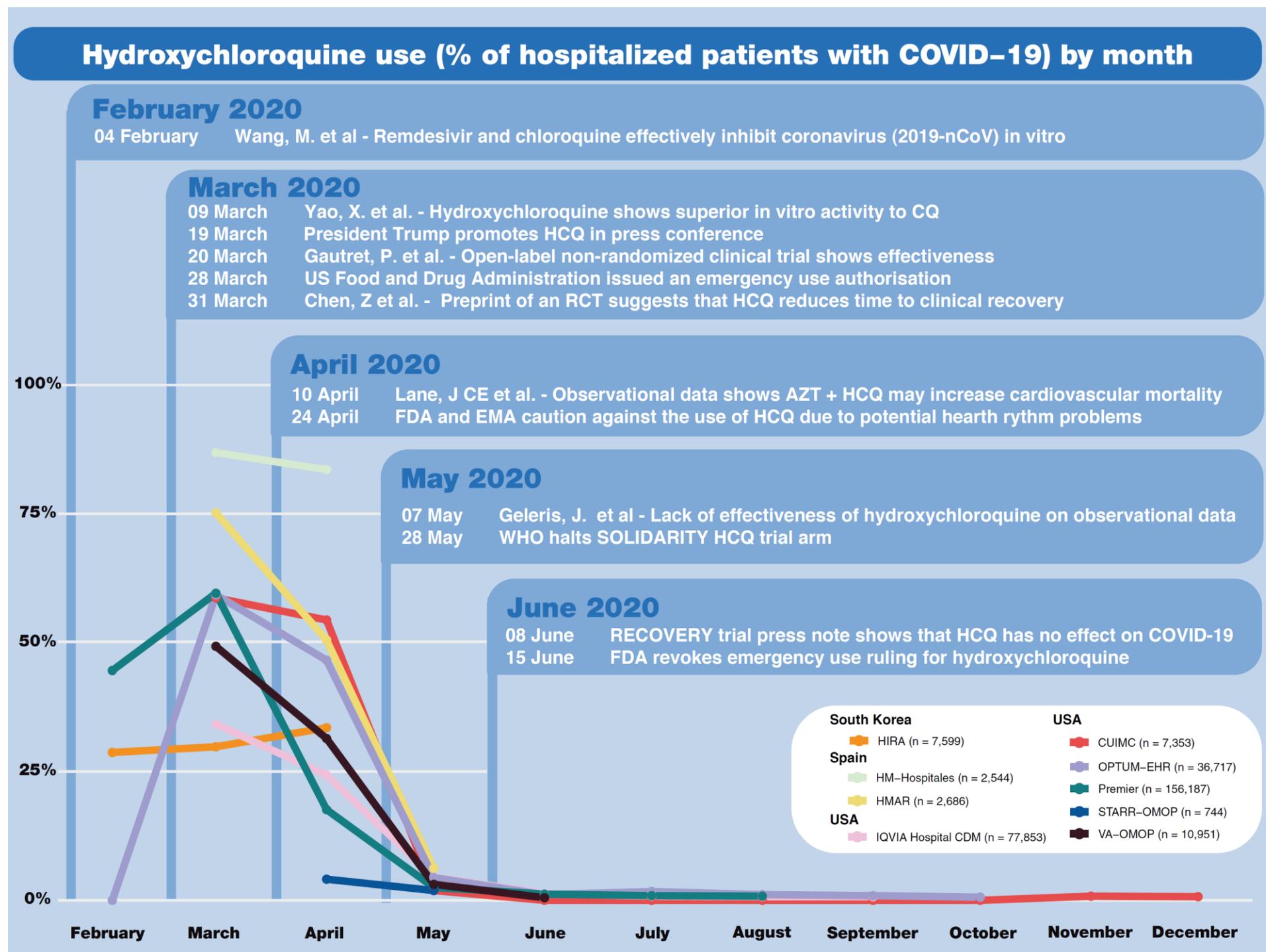
Figure 2. Forest plot of the association between short- (top) and long-term (bottom) use of Hydroxychloroquine versus Sulfasalazine and risk of suicidal ideation or suicide, by database and in meta-analysis.



cHR=calibrated hazard ratio; 95%=95% confidence interval; I²=estimate heterogeneity statistic.



RISE AND FALL OF HYDROXYCHLOROQUINE



Prats-Urbe et al 2021 BMJ





READ ALL ABOUT IT!

THE LANCET
Rheumatology

ARTICLES | VOLUME 2, ISSUE 11, E698-E711, NOVEMBER 01, 2020

Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study

Jennifer C E Lane, MRCS [†] • James Weaver, MSc [†] • Kristin Kostka, MPH • Talita Duarte-Salles, PhD • Maria Tereza F Abrahao, PhD • Heba Alghoul, MD • Osaid Alser, MD • Thamir M Alshammari, PhD • Patricia Biedermann, MSc • Juan M Banda, PhD • Edward Burn, MSc • Paula Casajust, MSc • Mitchell M Conover, PhD • Aedin C Culhane, PhD • Alexander Davydov, MD • Scott L DuVall, PhD • Dmitry Dymshyts, MD • Sergio Fernandez-Bertolin, MSc • Kristina Fišter, PhD • Jill Hardin, PhD • Laura Hester, PhD • Prof George Hripcsak, MD • Benjamin Skov Kaas-Hansen, MD • Seamus Kent, PhD • Sajan Khosla, MSc • Spyros Kolovos, PhD • Christophe G Lambert, PhD • Prof Johan van der Lei, PhD • Kristine E Lynch, PhD • Rupa Makadia, PhD • Andrea V Margulis, ScD • Michael E Matheny, MD • Paras Mehta, BA • Daniel R Morales, PhD • Henry Morgan-Stewart, PhD • Mees Mosseveld, MSc • Danielle Newby, PhD • Prof Fredrik Nyberg, PhD • Anna Ostropolets, MD • Prof Rae Woong Park, MD • Albert Prats-Urbe, MPH • Gowtham A Rao, MD • Christian Reich, MD • Jenna Reps, PhD • Peter Rijnbeek, PhD • Selva Muthu Kumaran Sathappan, MSc • Martijn Schuemie, PhD • Sarah Seager, BA • Anthony G Sena, BA • Azza Shoaibi, PhD • Matthew Spotnitz, MD • Prof Marc A Suchard, MD • Carmen O Torre, MSc • David Vizcaya, PhD • Haini Wen, MSc • Marcel de Wilde, BSc • Junqing Xie, MSc • Seng Chan You, MD • Lin Zhang, MD • Oleg Zhuk, MD • Patrick Ryan, PhD   • Prof Daniel Prieto-Alhambra, PhD • on behalf of the OHDSI-COVID-19 consortium • [Show less](#) • [Show footnotes](#)

Open Access • Published: August 21, 2020 • DOI: [https://doi.org/10.1016/S2665-9913\(20\)30276-9](https://doi.org/10.1016/S2665-9913(20)30276-9)



RHEUMATOLOGY

Rheumatology 2020;00:1-13
doi:10.1093/rheumatology/keaa771

Original article

Risk of depression, suicide and psychosis with hydroxychloroquine treatment for rheumatoid arthritis: a multinational network cohort study

Jennifer C. E. Lane ^{1,*}, James Weaver^{2,*}, Kristin Kostka³, Talita Duarte-Salles⁴, Maria Tereza F. Abrahao⁵, Heba Alghoul⁶, Osaid Alser⁷, Thamir M. Alshammari⁸, Carlos Areia⁹, Patricia Biedermann¹⁰, Juan M. Banda¹¹, Edward Burn ^{1,4}, Paula Casajust¹², Kristina Fister¹³, Jill Hardin², Laura Hester², George Hripcsak^{14,15}, Benjamin Skov Kaas-Hansen^{16,17}, Sajan Khosla¹⁸, Spyros Kolovos¹, Kristine E. Lynch^{19,20}, Rupa Makadia², Paras P. Mehta²¹, Daniel R. Morales²², Henry Morgan-Stewart³, Mees Mosseveld²³, Danielle Newby²⁴, Fredrik Nyberg²⁵, Anna Ostropolets¹⁴, Rae Woong Park²⁶, Albert Prats-Urbe ¹, Gowtham A. Rao², Christian Reich³, Peter Rijnbeek²³, Anthony G. Sena^{2,23}, Azza Shoaibi², Matthew Spotnitz¹⁴, Subbian Vignesh²⁷, Marc A. Suchard²⁸, David Vizcaya²⁹, Haini Wen³⁰, Marcel de Wilde²³, Junqing Xie¹, Seng Chan You²⁶, Lin Zhang^{31,32}, Simon Lovestone³³, Patrick Ryan^{2,14} and Daniel Prieto-Alhambra¹, for the OHDSI-COVID-19 consortium





3 NEW THINGS, 4 DAYS

First large-scale characterisation of COVID-19 patients in Europe, Asia & US

First prediction model externally validated on COVID-19 patients to inform shielding strategies

Largest study ever conducted on the safety of hydroxychloroquine





RAPID EXPANSION OF COLLABORATIVE COMMUNITY

RAPID & AVAILABLE EVIDENCE

REGULATORY CHANGE

PEER REVIEW PUBLICATIONS

1 Drug Utilisation Study

3 PLEs (HCQ; HCQ psych effects; ARBs)

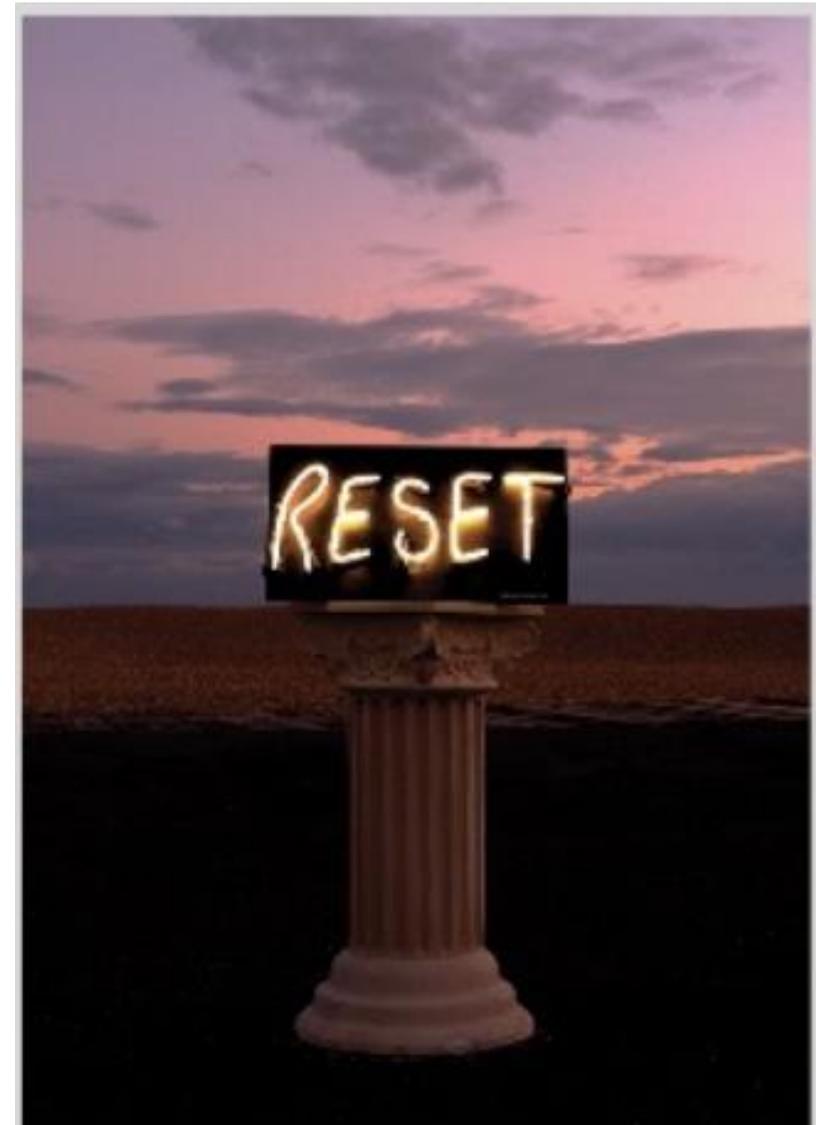
1 Phenotyping hospitalized patients with COVID-19

Characterisations- obesity, paediatrics, cancer

More to come:

Drug use during pandemic

Characterisation, HIV, pregnancy, summary of all



@rebecca_mason_art



KEY CONTACT POINTS

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- EHDEN Coordinator: Nigel Hughes, Janssen: nhughes@its.inj.com



EHDEN
EUROPEAN HEALTH DATA & EVIDENCE NETWORK

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github.com/EHDEN



This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 806968. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.