Support-e
SUPPORTing high quality evaluation of covid-19 convalescent plasma throughout EUROPE

NHS Blood and Transplant

Support-E recommendations regarding the use of convalescent plasma in potential future pandemics

Lise Estcourt

Disclaimer: *The contents of this document reflects only the author's view and that the Commission is not responsible for any use that may be made of the information it contains. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 101015756.*

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ÉTABLISSEMENT FRANÇAIS DU SANG

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WP1 – Assessing CCP, conducting clinical evaluation and defining best practices

WP2 – Supporting high quality clinical evaluation and producing data-sets for inclusion in the database

WP3 – Collecting, monitoring and analysing EU-CCP Database data

WP4 – Improving plasma potency assessment

WP5 – Developing recommendations and preparing for the future

WP6 – Dissemination, exploitation and communication

WP7 – Project Management

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Recommendations

- Pandemic and the funding response
- Collection of data on convalescent plasma use
- Systematic reviews
- Collection of convalescent plasma
- Testing
- Clinical Trials

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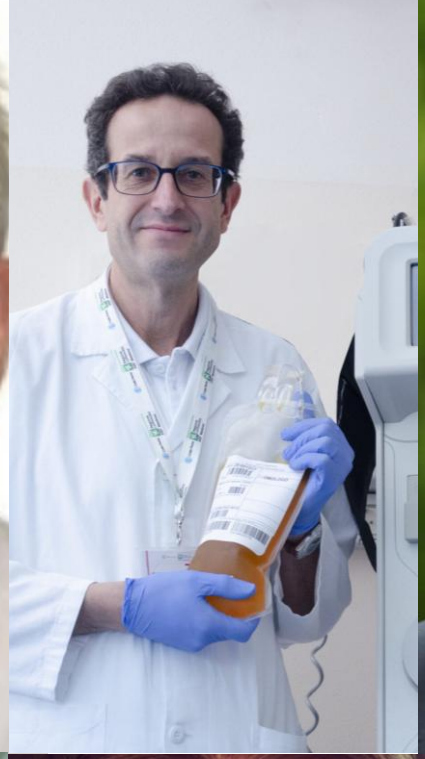






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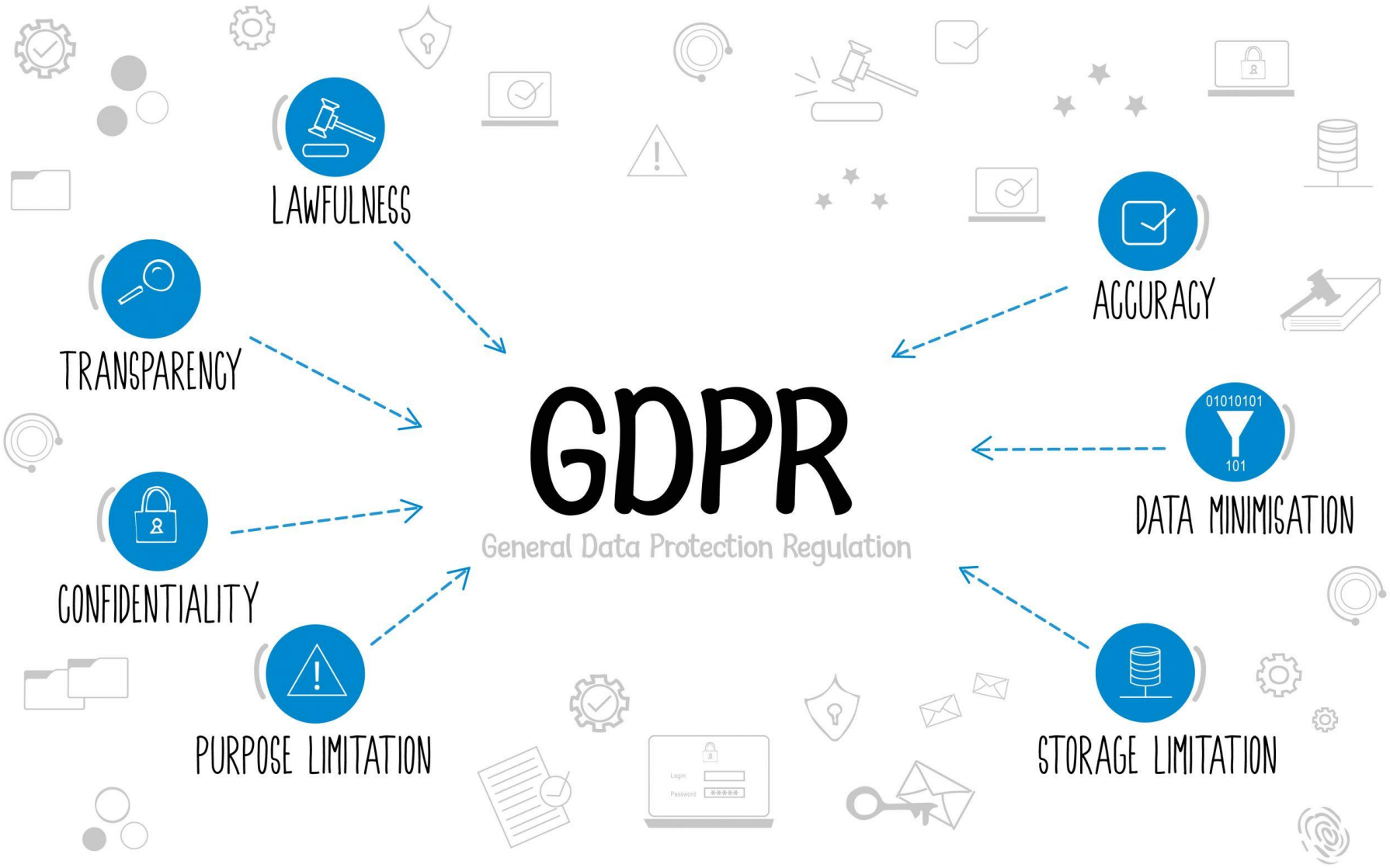
Pandemic and the funding response

- Support network of blood services and other experts to allow collection, testing, analysis, and trials of high-titre CP.
- Establish expert and timely review of research proposals.
- Maintain responsive and flexible funding as the pandemic evolves.
- Continue funding while valid and relevant scientific and technical questions remain to be answered.


LAWFULNESS
TRANSPARENCY
CONFIDENTIALITY
PURPOSE LIMITATION
ACCURACY
DATA MINIMISATION
STORAGE LIMITATION
GDPR
General Data Protection Regulation
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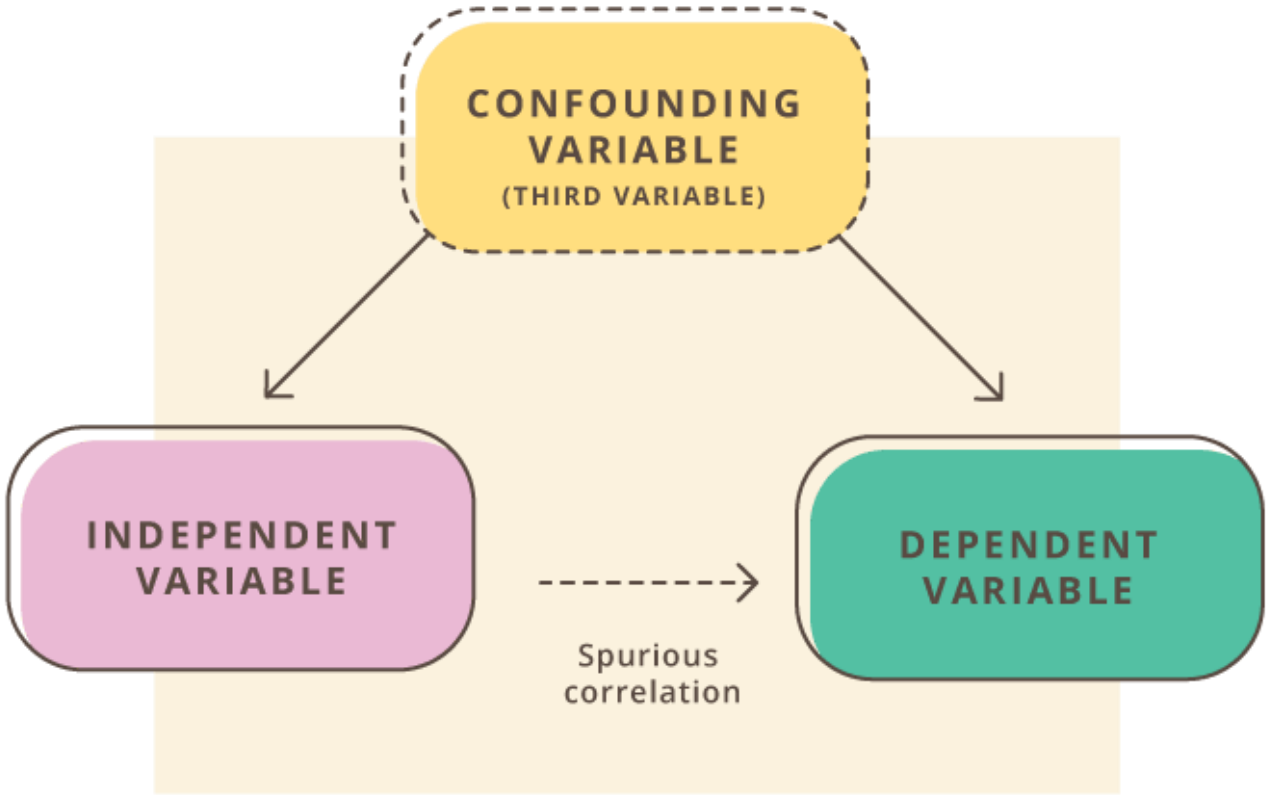

- Clinical status
- Pre-existing conditions of patients
- Demographic factors
- Viral variants
- Adjunctive care

What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

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Collection of data on convalescent plasma use

- Further work is needed to establish what data should be collected in future to maximise the value of the data

- Establish a national and/or **European collection system** of relevant and comparable data on CP production and use early in the pandemic.

Evidently Cochrane

Sharing health evidence you can trust

Chapman S. "Convalescent plasma to treat people with COVID-19: the evidence so far". Evidently Cochrane blog, 15 May 2020, last updated 21 May 2021. https://www.evidentlycochrane.net/convalescent-plasma

"Convalescent plasma to treat people with COVID-19: the evidence so far"

Weekly screening of studies

Published review updated four times within a year – significant changes in the evidence over very short time frame

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Systematic reviews

- Establish systematic reviews for continuous analysis of the efficacy of monoclonal and polyclonal antibodies in randomised controlled trials for prophylaxis and therapy of pre-hospital, hospitalised and ICU patients.

- Establish expert and timely review of recommendations for the use of CP (and other therapies).

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EU-CCP database

172,906 plasma donations of COVID-19 convalescent plasma from **16 European countries** were recorded in EU-CCP database.

The largest contributors were the **Netherlands (36%)** and **England (31%).**

The overall sex distribution showed a higher proportion of male donations (65%) compared to female donations (35%).

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Collection of convalescent plasma

- We recommend that if apheresis plasma production infrastructure already exists, then this should have the capacity to upscale production to meet the demand for CP.
- A **sample-first policy** is more cost-effective than collecting plasma and then testing to assess if high titre.
- Alternative uses for plasma that is not high titre should be sought – e.g., fresh frozen plasma (FFP), plasma for medicines (fractionation) or plasma for diagnostics if possible.

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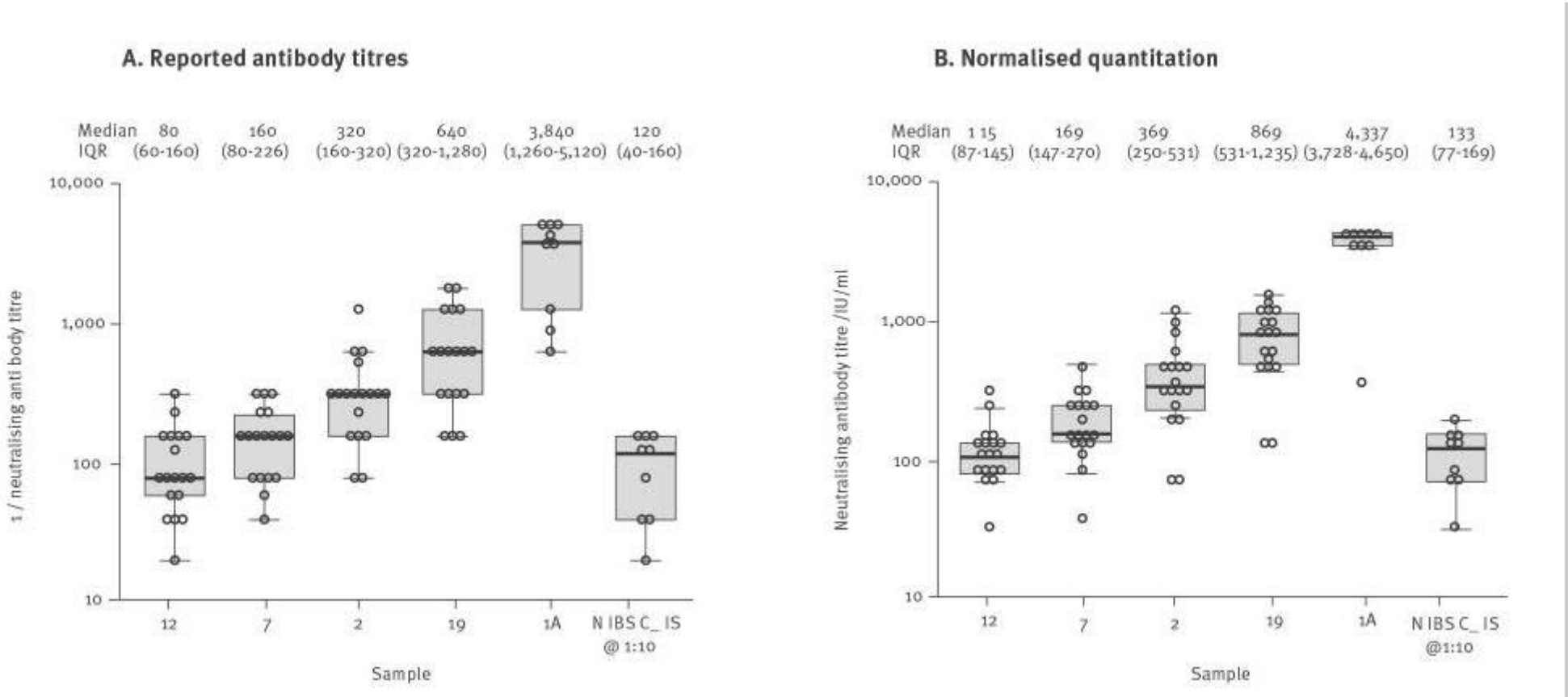
SARS-CoV-2 neutralising antibody testing between 12 European laboratories involved in convalescent plasma trials. Raw titres differed almost **100-fold differences** between laboratories when blind-testing 15 plasma samples



Nguyen et al. SARS-CoV-2 neutralising antibody testing in Europe: towards harmonisation of neutralising antibody titres for better use of convalescent plasma and comparability of trial data. Euro Surveill. 2021 Jul;26(27):2100568. doi: 10.2807/1560-7917.ES.2021.26.27.2100568. PMID: 34240697; PMCID: PMC8268650.

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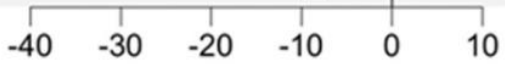
Testing

- Establish plasma standards that can be calibrated to international standards from WHO (World Health Organization) or NIBSC (National Institute for Biological Care).
- Establish reliable virological assays for nAb to new variant variants in a few centres that include rapid assessment of new viral variants.
- Establish calibration between the different high-throughput serological available tests to enhance the resilience of the supply of testing kits.
- Provide quality control scheme and reagents for serological assays.

Early, very high-titre convalescent plasma therapy in clinically vulnerable individuals with mild COVID-19: an international, randomised, open-label trial

Simone Hoffmann,[a,s] Eva Schrezenmeier,[b,s] Maxime Desmarets,[c,d] Fabian Halleck,[b] Antoine Durrbach,[e,f] Lynn Peters,[g] Anna-Teresa Tremmel,[h] Alina Seidel,[i] Marita Führer,[a] Friederike Bachmann,[b] Jens Schrezenmeier,[j] Jochen Greiner,[k] Sixten Körper,[a] Henrike Hofmann,[a] Carolin Ludwig,[a] Christiane Vieweg,[a] Bernd Jahrsdörfer,[a] Klemens Budde,[b] Michael Schmidt,[j] Jan Münch,[j] Nizar Joher,[e] Etienne Daguindau,[c,m] Beate Grüner,[g] Gaelle Brunotte,[d] Charline Vauchy,[c,d] Erhard Seifried,[l] Daniel Bradshaw,[n] Lise J. Estcourt,[o,p] David J. Roberts,[o,p] Eric Toussirot,[c,d] Bart Rijnders,[q] Pierre Tiberghien,[c,r,t] and Hubert Schrezenmeier[a,t,*]

Group	N	Standard*	Plasma*	Diff. (95% CI)	p-value
All patients	117	5 (8.6)	0 (0)	-8.6% (-19.0% – -0.8%)	0.027



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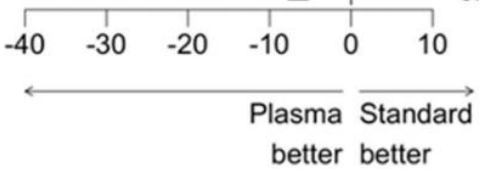
Group	N	Standard*	Plasma*	Diff. (95% CI)
Age				
[25,57]	61	3 (10)	0 (0)	-10.0% (-26.0% – 2.3%)
(57,82]	56	2 (6.9)	0 (0)	-6.9% (-22.0% – 6.5%)
Sex				
Male	68	2 (6.1)	0 (0)	-6.1% (-20.0% – 4.8%)
Female	49	3 (12)	0 (0)	-12.0% (-30.0% – 3.9%)
Monoclonal antibodies				
Yes	77	1 (2.6)	0 (0)	-2.6% (-13.0% – 6.9%)
No	40	4 (21)	0 (0)	-21.0% (-43.0% – -1.1%)
Antivirals				
Yes	26	2 (17)	0 (0)	-17.0% (-45.0% – 8.0%)
No	91	3 (6.5)	0 (0)	-6.5% (-18.0% – 2.4%)

*Events (%)



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Clinical trials

- Encourage and maintain international trial platforms for testing of CP.
- Support countries and sites to open sites for international trial platforms for example COVIC-19 and REMAP-CAP to gather definitive evidence as quickly as possible.
- Encourage enrolment of all patients receiving CP into adequately powered large-scale trials to examine the use of CP prophylaxis and therapy of pre-hospital, hospitalised and ICU patients.
- Establish analysis of trials for sub-groups based on the most vulnerable groups, for example in this pandemic, older age, pre-existing disease, immunocompromised patients, and negative serological status.

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