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Countermeasures against COVID-19: Navigating Medical Practice through a nascent, evolving Evidence Base

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ABSTRACT

Objectives

The European Pediatric Dialysis Working Group reported widely variable counteractive responses to COVID-19 during the first week of statutory public curfews in 11 European countries with caseloads of 4 to 680 infected patients per million. In this study we applied the *capability, opportunity, motivation model of behavior* (COM-B) to describe determinants of countermeasure implementation rates.

Design

This is an international multi-center mixed methods study.

Setting

This study was conducted in 14 Pediatric Nephrology centers across 12 European countries during the COVID-19 pandemic.

Participants

The participants were pediatric nephrologists, all members of the EPDWG, of 14 European centers.

Main outcome measures

52 countermeasures clustered into eight response domains (Access Control, Patient Testing, Personnel Testing, Personal Protective Equipment Policy, Patient Cohorting, Personnel Cohorting, Suspension of Routine Care, Remote Work) were categorized by implementation status, drivers (expert opinion, hospital regulations) and resource dependency. Governmental Strictness and Media Attitude were independently assessed for each country and correlated with relevant countermeasure implementation factors.

Results

Implementation rates varied widely among response domains (median 49.5%, range 20%-71%) and centers (median 46%, range 31%-62%). Caseloads were insufficient to explain response rate variability. Increasing caseloads resulted in shifts from expert opinion-based to hospital regulation-based decisions to implement additional countermeasures despite increased resource dependency. Higher Governmental Strictness and positive Media Attitude toward countermeasure implementation were associated with higher implementation rates.

Conclusions

COVID-19 countermeasure implementation by pediatric tertiary care centers did not reflect caseloads but rather reflected heterogeneity of local rules and of perceived resources. These data highlight the

need of ongoing reassessment of current practices, facilitating rapid change in ‘institutional behavior’ in response to emerging evidence of countermeasure efficacy.

Strengths and limitations of this study

- This is the first study evaluating the most important drivers of behaviors conducive to counteracting the COVID-19 pandemic during the first week of public curfews.
- We explored a unique snapshot of 14 pediatric dialysis centers in 12 European countries with caseloads ranging from 4 to 680 infected patients per million.
- Using the capability, opportunity, motivation model of behavior (COM-B) to understand the generic mechanisms of our responses to COVID-19, might help to review our current practices with a more critical appraisal.
- Accepting limitations of the complex reasoning behind implementation rates, on individual and institutional level, might enable rapid change of ‘institutional behavior’ in response to the ongoing emergence of evidence on efficacy of countermeasures and treatments for COVID-19.

Public and Patient Involvement Statement: This paper was co-produced with members of different non-medical specialties, including information technology analytical experts and qualitative research experts, contributing analysis of public realms, such as news(papers) and governmental (law) enforcements.

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INTRODUCTION

SARS-CoV-2-related disease (COVID-19) spread throughout Europe when minimal evidence was available to support efficacy of then available countermeasures.[1-4] The European Pediatric Dialysis Working Group (EPDWG) conducted a Delphi exercise over five days during the first week of statutory public curfews in 13 pediatric nephrology centers from 11 European countries[5] using 'crowd intelligence' to define countermeasures in several relevant response domains, and to assess their implementation rates.[5] Whereas some countermeasures (replacement of routine visits by telephone calls) were widely implemented, others (asymptomatic staff member testing) were rarely implemented, and implementation rates varied widely among countermeasures and centers.[5] This heterogeneity may have reflected country-specific infection rates and pandemic stage-dependent measures to decrease infection rates.

However, the mechanisms underlying COVID-19 countermeasure implementation by individual centers were not studied. Therefore, to explain response variability among these tertiary care centers, we investigated why practice behaviors changed or did not change in each pediatric dialysis center.

The *capability, opportunity and motivation model of behavior* (COM-B) [6] describes determinants of behavior [7], including *capability* (physical and psychological capacity to engage in an activity, such as knowledge and skills), *opportunity* (physical and social factors outside the individual that permit or prevent a certain behavior), and *motivation* (brain processes that energize and direct behavior).[6] In 2011 *the Behavior Change Wheel* (BCW) was added to the COM-B to distinguish between *interventions* (activities aimed at changing behavior) and *policies* (actions of responsible authorities or the government that enable interventions, respectively change of behavior).[6] In this study, we used the COM-B and the BCW to describe determinants of behavioral change in pediatric tertiary care centers relating to COVID-19 countermeasure implementation rates during the first week of statutory public curfews in Europe. Such insights may permit improved management of impending COVID-19 resurgence(s) and of future pandemic events.

MATERIALS AND METHODS

The methodology of the Delphi exercise conducted among the EPDWG in March, 2020 was recently described.[5] This follow-up study examines 14 EPDWG centers from 12 countries (Austria, Belgium, Czech Republic, France, Germany, Greece, Italy, Lithuania, Poland, Spain, Turkey and the United Kingdom). Individual sets of 52 countermeasures (see[5]) were mailed to each center to validate countermeasure implementation rates on March 20, and to assess altered rates on April 3, 2020. Participants were asked whether implementation decisions concerning individual countermeasures were based on expert opinion and/or hospital regulations and/or resource availability. Country-specific caseloads from the European Centre for Disease Prevention and Control [8] were calculated as case number per million (from Eurostat [9]). Pandemic phase was expressed as binary logarithm of caseloads per million, since exponential case doubling times in the EPDWG countries (~two days at this phase) transitioned gradually to a logistic function.

Behavior change determinants

COM-B and BCW components were mapped to concepts derived from anonymized EPDWG experts' initial open email replies to the first Delphi exercise.[5] Mapping was conducted by component definitions and experts' wording, using modified meaning condensation analysis to aggregate experts' statements in terms of underlying concepts. For example, the email statement *'Timely recipient testing should be feasible in our center'* was mapped to *Opportunity (physical)* and to BCW policy *'environmental/social planning'*, whereas the statement *'I read a lot about this, but to my knowledge we cannot draw any firm conclusions'* was assigned to *Capability (psychological)* and to BCW policy *'guidelines'*. To ensure accuracy and rigor, initial mapping performed by one researcher (FE) was independently reviewed by a second, senior qualitative researcher (VR). In cases of disagreement, consensus was achieved through discussion.

Governmental Strictness

Country-specific online news agencies and governmental information websites were searched for governmental interventions in response to COVID-19. Relative frequencies of 23 defined governmental interventions to achieve 'social distancing' were combined to yield a Governmental Strictness score (Table 1). Interventions included *restriction of free public movement, restriction of hospital access, restriction of prison access, recommended or mandatory teleworking, requirements for adequate mouth and nose coverage in public, closure of parks and playgrounds, closure of governmental facilities (e.g. schools, universities), closure of mass events, recommendation to limit gatherings to five people, prohibition of gatherings exceeding five people, police surveillance, closure of non-essential businesses, closure of restaurants, local quarantine, nationwide quarantine, selective border closure, complete border closure, state of emergency, vacation ban for health care professionals, implementation of tele-*

medicine, export and sales ban on all FFP3-type respirators and selected medications, ban on minors leaving home unaccompanied by a legal guardian, censorship of medical personnel.

Media Attitude

Cover page articles during the week of March 20, 2020 from the three widest-circulating newspapers in each EPDWG country and text blocks containing COVID-19-related news and/or opinion pieces were manually classified. Transcribed, translated and anonymized excerpts from the selected articles were rated by participants (n=5) for positivity of reporting attitude on COVID-19 countermeasures on a scale from 1 (lowest) to 5 (highest). Excerpts were uniformly formatted without country identifiers. Mean values yielded a country-specific Media Attitude score (Table 1).

Data analysis and Statistics

Data were clustered into eight response domains (*Access Control, Patient Testing, Testing Health Care Personnel [HCP], Personal Protective Equipment [PPE] Policy, Patient Cohorting, HCP Cohorting, Suspension of Routine Care, Remote Work*) and visualized as implementation rates and their rates of change (Supplemental Figure 1). Response rates (%) were calculated as numbers of implemented countermeasures divided by numbers of total identified countermeasures for March 20 and April 3, 2020. Resource dependency (%) for March 20, 2020 was calculated as numbers of decisions for which resources were decisive for implementation, divided by numbers of total identified countermeasures.

Expert decisions and hospital authority decisions were expressed as the Hospital-authority-decisions-to-Expert-decisions (H/E) ratio for March 20, 2020:

$$\frac{H}{E}\,Ratio = \frac{(Hospital\ authority\ decisions\ (n) - Expert\ decisions\ (n))}{total\ countermeasures\ (n)}$$

The H/E-Ratio expresses the degree to which response rates are influenced by hospital authority decisions (resulting in positive values to +1) or by expert decisions (resulting in negative values to -1), with the balanced H/E-Ratio of zero reflecting equivalent contributions of hospital authority and experts' decisions.

Each of these variables was calculated (I) on the domain level, as mean for each domain across all centers, and (II) on the center level, as mean for each center across all domains. Data was analyzed with descriptive statistics utilizing scatter plot matrices, bar plots, histograms and heat maps. Kendall's tau correlation analysis was conducted within a correlation matrix for each dependent and independent variable on each level. Correction for multiple testing was not performed, reflecting the exploratory character of this analysis. For Kendall's tau, correlation analysis between Response Rates and Pandemic Phase outliers was omitted post-hoc (high response despite low caseload, or relatively low responses despite highest caseloads).

RESULTS

Implementation of individual counteractive measures varied widely among response domains and centers in the March 20, 2020 cross-sectional analysis. Domain response rates ranged from 20% (28/140) to 71% (59/84); median 49.5%. Center response rates ranged from 31% (16/52) to 62% (32/52); median 46%. Re-assessment of response rates on April 3 demonstrated increased countermeasure implementation, particularly in centers with lower initial response rates ('catch-up implementation').

<u>'Snapshot' of implemented COVID-19 countermeasures (March 20)</u>: Center response rates or individual countermeasure response rates correlated weakly with center caseloads. Figure 1 demonstrates that centers at both ends of the pandemic phase spectrum markedly deviated from the assumption of correlation. Although overall correlations between center responses and pandemic phase were statistically significant, country/center-specific caseloads correlated with implemented countermeasures only after outlier exclusion (Table 2).

<u>Policy measures influencing implementation of countermeasures per BCW</u>: Five of seven BCW-defined policy measures [6] were reported as reasons for behavior change in the clinical setting (Supplemental Figure 2). As expected, 'regulation' by employers (establishing rules of principles of behavior) and/or governmental 'legislation' were important reasons for behavioral changes at the centers. However, information from mass media ('communication'), missing 'guidelines' and 'environmental/social'-related restrictions were equally often determinative for change in behavioral patterns. 'Fiscal measures' and 'service provision' were not mentioned as influencing behavioral changes. Mass media information indicated increasing pressure from growing caseloads in the EPDWG centers ('communication'), corresponding to correlation of pandemic phase with average countermeasure implementation rates (Table 2). Respondents often noted that recommendations ('guidelines') for clinical decision-making remained lacking, likely explaining why rules and principles established by hospital management ('regulation') contributed more as important drivers for implementation than did 'guidelines' (Table 2). Growing mass media pressure ('communication') in most centers resulted in a pandemic phase-dependent shift from expert opinion (missing 'guidelines') to hospital-based 'regulations' (Figure 2, Table 2).

Resource dependency was a major inhibitor of countermeasure implementation ('environmental/social' restrictions). Estimated resource dependency of eight individual measures correlated negatively with their implementation rates at the domain level (Figure 2, Table 2). Increasing resource dependency associated with an increasing ratio of hospital rules ('regulations') over expert opinion (missing 'guidelines') as a driver of countermeasure implementation (Table 2). Interestingly, implementation rates for countermeasures of comparable resource dependency ('environmental/social' restrictions) increased in direct proportion to the H/E ratio ('regulations'; compare, for example, 'Suspension of Routine Care/Remote Work" with comparably low resource dependency and 'Testing HCP/Patients" with comparably high resource dependency; Figure 2).

Longitudinal assessment of 'catch-up' implementation of COVID-19 countermeasures: The above cross-sectional assessment describes associations between individual factors and countermeasure implementation rates in different centers/countries at different pandemic phases. Longitudinal changes in countermeasure implementation rates were assessed by another survey on April 3, 2020 and plotted as a function of pandemic phase. Figure 3 shows that pandemic progression resulted in globally increased rates of countermeasure implementation from March 20 to April 3 in almost all centers (Table 2). At the center level, mean changes of response rates were negatively influenced by cumulative local perception of resource dependency on March 20 (= 'resource awareness', perceived 'costs'; Table 2). However, 'catch-up implementation' of counteractive measures from March 20 to April 3 positively correlated with higher H/E ratio (between hospital rule and expert opinion as drivers), and with resource dependency of particular measures (Table 2). Thus, growing pressures of increased country-specific caseloads increased local implementation of hospital rules, thereby overcoming the initially inhibitory effects of locally perceived resource dependency for these measures in a center-specific way.

Role of country-specific, non-medical influencers on countermeasure implementation: Center-specific patterns of longitudinal changes suggest that local countermeasure implementation rates represent a balance of local influences only poorly modulated by global medical evidence, allowing study of the influence of non-medical drivers such as Media and Government. Media Attitude Table 1 shows scores for implementation of COVID-19 countermeasures in the 11 EPDWG countries. Cover page articles from the three widest-circulation newspapers during the week of March 20 each contained >75% of COVID-19-related text. Media Attitude was only weakly associated with center response rates (Table 2). However, centers in countries with higher Media Attitude scores demonstrated significantly lower ratios of hospital rules over expert opinion (Table 2), in turn associated with higher implementation rates and catch-up (Table 2). Indeed, the two centers with the highest Media Attitude Scores demonstrated the highest response rates (see Figure 4). Table 1 also shows Governmental Strictness Scores of the 11 EPDWG countries. As for Media Attitude, Governmental Strictness associated only weakly with response rates (Table 2). However, centers in countries with higher Governmental Strictness scores demonstrated lower perceptions of resource dependency regarding countermeasure implementation (Table 2), in turn associated with higher implementation rates and catch-up implementation (Table 2). Interestingly, positive Media Attitude (potentially enhancing motivation) paired with high Governmental Strictness (potentially reducing resource dependency) was found in the two countries with the highest response rates (at intermediate caseload).

DISCUSSION

During the COVID-19 pandemic, the most important motivational driver of behaviors conducive to counteracting the pandemic has been the magnitude of pandemic growth. In the absence of prior evidence, many interventions were rapidly executed on local, national and international levels with different degrees of coordination.[1 4] The recent Delphi study from the European Pediatric Dialysis Working Group (EPDWG) confirmed marked heterogeneity of COVID-19 countermeasure implementation as of March 20, 2020, across 13 Pediatric Nephrology centers in 11 European countries,[5] with caseloads ranging from 4 to 680 infected patients per million (median 161 per million). This variability led us to hypothesize that growing pressures from increasing, country-specific caseloads were the main drivers for countermeasure implementation in our centers, and that differing numbers of infected patients might explain the heterogeneity in response rates among centers.[5]

However, the present study's comparisons of center caseloads with mean center responses or with mean response rates of individual measures found no close correlation. Thus, pandemic phase alone cannot explain the observed heterogeneity of COVID-19 countermeasure implementation rates across European centers. We therefore treated countermeasure implementation as a complex process with multiple influencers.[6 10] In the conceptual framework of COM-B, countermeasure implementation rates likely represent the 'capability' (as 'regulation' and/or 'guideline' policies) of their drivers (experts and/or hospital authorities) to allocate resources by opinion or rules, balancing pressure of the pandemic phase ('motivation' as 'communication' policies) and availability of resources ('opportunity' as 'environmental/social' policies).

Complex interactions between these factors in the BCW (Supplemental Figure 2) might better explain observed heterogeneities of implementation rates among different centers and measures. In this context, increased pressure from pandemic progression shifted expert opinion-based decisions towards more formal hospital rules, likely to overcome growing barriers to additional countermeasure implementation that in part reflected increasing awareness of growth in resource dependency. EPDWG center implementation rates of COVID-19 countermeasures, when regarded as changes of 'institutional behavior,' thus reflected the ability of drivers at each center to overcome local resource dependency. These changes motivated by local perception of growing global medical need led to diverse local rules and heterogeneous responses. Longitudinal assessment of countermeasure implementation from March 20 to April 3 supports the hypothesis that pressure from growing country-specific caseloads increased local implementation of hospital rules, overcoming the initially inhibitory effects of locally perceived resource dependency of these measures, particularly measures with lower initial response rates.

Ordinarily, a shared body of scientific evidence ('what is right') underlies consensus procedures to harmonize 'institutional behavior' in response to medical challenges. However, whereas COVID-19 countermeasure implementation rates increased at almost all EPDWG centers, overall response patterns among centers with similar caseloads or at similar pandemic phase did not converge. Despite the pressure of pandemic progression, individual within-center drivers appeared influenced by different perceptions of this pressure, and by different local resource dependencies (and/or awareness of those dependencies). This suggests other center- and/or country-specific factors, beyond pandemic phase progression, that significantly influence countermeasure implementation. The COM-B and BCW model also allows systematic analysis of drivers for different behaviors and interventions on all levels, from individuals to national governments and civil societies.

Our analysis identified the non-medical influencers, Media Attitude and Government Strictness, as important determinants of EPDWG center responses to COVID-19 which might foster effective implementation of other medically relevant measures.[11] Governmental interventions, in particular those aimed at social distancing, were recognized early in China as the most effective non-medical tool to 'flatten the curve' of the pandemic.[1] Similar interventions, ranging from banning large events to strict curfews, were implemented to varying degrees in European countries during the week of March 20. Our study quantified these interventions and found that higher 'Governmental Strictness' correlated with increased center responses, associated with reduced perception of resource dependency ('resource/cost awareness') of countermeasure implementation. Media dissemination of information can be incorporated in the COM-B and BCW model as a motivational driver for behavior and decision making on all social levels.[11] This pertains especially to European countries attempting to contain the pandemic to the degree achieved in China, but in settings where Governmental Strictness effects on social distancing depend more on individual decisions and actions.[1] During the week of March 20, the three widest-circulation newspapers in each participating European country covered COVID-19 with >75% of front page text. Centers in countries with more positive Media Attitude towards Governmental Strictness (based on front page articles) also demonstrated higher response rates, associated with higher perception of importance of expert opinion as driver for countermeasure implementation.

The rapidly evolving shared knowledge base and emerging 'best practices' for counteracting COVID-19 in the European context allowed our study on EPDWG center practice patterns, utilizing COM-B and BCW models to describe behavioral drivers, to serve as a case study of institutional 'behavioral changes' under high pressure with insufficient available information. Under such conditions, we might expect that skills (but not knowledge) and tactics (but not strategy) will guide an individual's decisions and (measurable) actions. The same held true at the institutional level where, for example, varied initial policies on PPE and testing material led to nationwide export bans, prioritizing local demand and production.[3] Such mechanisms and interdependencies detected by our targeted statistical approach might increase understanding of still heterogeneous response patterns among countries with similar infection rates.

Another major study finding was that as COVID-19 countermeasure implementation in the European context was not based on ‘hard’ scientific evidence, none of the implemented local policies can be objectively judged from a medical viewpoint as ’right‘ or ’wrong’. At time of submission four months after the initial Delphi exercise, there remains no strong evidence on efficacy of individual COVID-19 countermeasures pertaining to the European pediatric dialysis population. Recent Chinese consensus guidelines [12] mentioned neither suspension of routine care nor testing strategies (for HCP and patients), although these measures were advocated as important to COVID-19 control.[13] The COVID-19 outbreak in a German pediatric dialysis center [14] also highlights the importance of adequate testing, tracing and monitoring strategies for successful outbreak containment and prevention in the hospital setting.

Nevertheless, continued heterogeneity of countermeasure implementation can be expected to continue among European centers until ongoing ’catch-up implementation‘ saturates response rates, as limited by local availability and resources. Although our study provides no solutions to that problem, our ‘mechanistic’ work does provide a mirror for the weak evidence basis underlying current practice patterns.[1] Understanding limitations of current approaches to selection and implementation of COVID-19 countermeasures might help re-assess those practices with open minds, allowing rapid ‘institutional behavior changes’ in response to emerging evidence on efficacy from controlled clinical trials. These will also provide evidence-based knowledge to optimize non-medical interventions during the COVID-19 pandemic.

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TABLES

Table 1. Media Attitude scores and Governmental Strictness scores in the countries of the EPDWG

Country	Media Attitude score (rank)		Governmental Strictness score (rank)	
Austria	***3.38**	***1**	***52**	***1**
Belgium	2.64	8	***43**	***3**
Czech Republic	2.8	4	***48**	***2**
France	2.73	5	17	7
Germany	2.65	7	26	6
Greece	2.56	10	39	4
Italy	2.62	9	35	5
Lithuania	2.2	11	***43**	***3**
Poland	2.67	6	17	7
Spain	***3.13**	***3**	***43**	***3**
United Kingdom	***3.17**	***2**	4	8

**) top three highest ranking countries for Media Attitude score and Governmental Strictness score*
EPDWG = European Pediatric Dialysis Working Group

Table 2. Statistical analysis of the COM-B model as applied to the EPDWGs decisions

COM – Variable	Variable (B or COM)	Kendall's tau	p-value
Cross-sectional analysis			
Pandemic Phase (caseload)	Implementation Rate	0.23	0.002
Pandemic Phase (caseload)*	Implementation Rate*	0.77	0.0000000000000002
Pandemic Phase (caseload)	Hospital to Expert Ratio (center)	0.24	0.001
Hospital to Expert Ratio (center)	Implementation Rate	0.41	0.00000002
Hospital to Expert Ratio (domain)	Implementation Rate	-0.36	0.000001
Resource Dependency (center)	Implementation Rate	0.16	0.03
Resource Dependency (center)	Hospital to Expert Ratio (center)	0.45	0.0000000002
Pandemic Phase (caseload)	Resource Dependency (center)	0.30	0.00003
Resource Dependency (domain)	Hospital to Expert Ratio (domain)	0.47	0.0000000003
Longitudinal analysis			
Implementation rate	Catch-up Implementation	-0.15	0.04
Resource Dependency (center)	Catch-up Implementation	-0.18	0.01
Resource Dependency (domain)	Catch-up Implementation	0.4	0.00000009
Hospital to Expert Ratio (domain)	Catch-up Implementation	0.47	0.0000000003
Influence of Media Attitude and Governmental Strictness			
Media Attitude	Implementation Rate	0.17	0.02
Media Attitude	Hospital to Expert Ratio (center)	-0.31	0.00001
Governmental Strictness	Implementation Rate	0.3	0.00005
Governmental Strictness	Resource Dependency (center)	-0.36	0.0000008

**) after omitting outliers (= high responses despite low caseload or relatively low responses despite highest caseloads)*
EPDWG = European Pediatric Dialysis Working Group; COM = Capability, Opportunity, Motivation, B = Behavior change

LEGENDS TO FIGURES

Legend to Figure 1.

Response rates (calculated as relative frequencies) of implemented counter- measures for each center ('mean center response rate', corresponding to the center columns of Supplemental Figure 1) and for each of the eight defined domains per center, displayed as functions of pandemic phase (expressed as infected cases per million people) on March 20 2020 (T1). Colors depicting center response rates range from lowest (dark-blue) to highest (dark-red). Linear regression lines calculated after outlier exclusion (corresponding to (*) in Table 2) are plotted (black) with 95% CI in grey.

Legend to Figure 2.

Panel A: Center-specific ratios of hospital rules (red) to expert opinion (blue) (H/E-Ratio) driving countermeasure implementation for each of the 13 EPDWG centers as a function of infected patient caseload (LOG2 of infected cases per million people) a measure of pandemic phase on March 20 2020 (T1).

Panel B: Domain response rates (implemented countermeasures per domain as % of total) as a function of countermeasure resource dependency (mean of all estimates from each center for each Individual domain) for each of the eight countermeasure domains and their drivers (red, hospital rules; green, expert opinion) on March 20 2020 (T1). Higher implementation rates of countermeasures with comparable resource dependency often correlated with higher hospital/expert driver ratio (compare 'Testing HCP' to 'Patient Testing' as opposed to comparison of 'Suspension of Routine Care' to 'Remote Work.)

Legend to Figure 3.

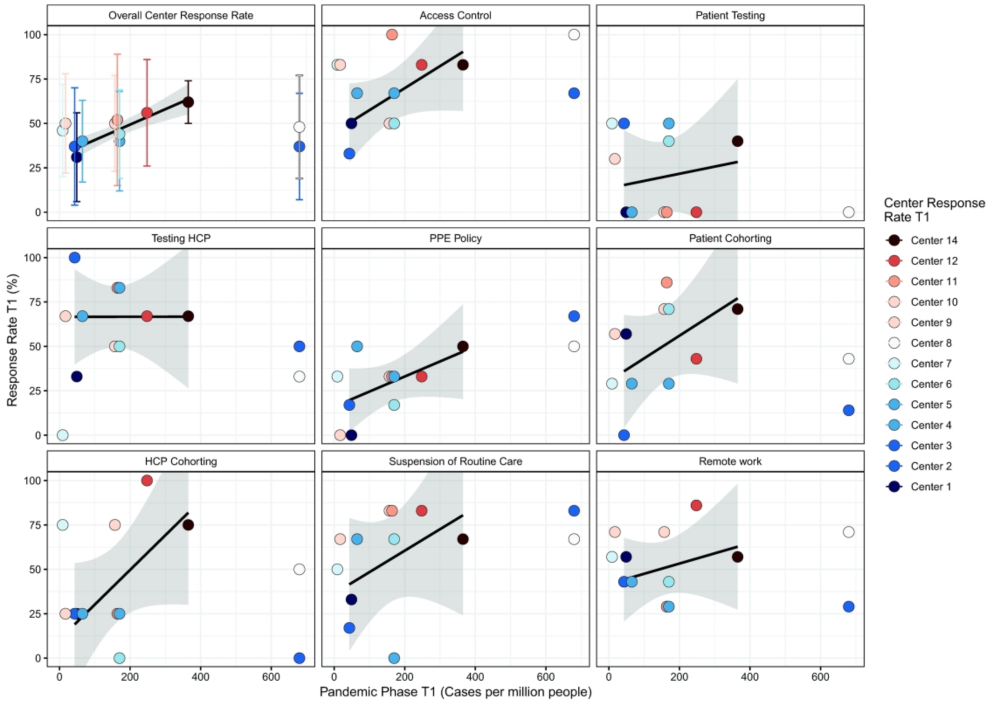
Panel A: Response rate dynamics were plotted for each center vs. dynamics of pandemic phase (log2-transformed cases per million people) during the period of March 20 to April 3, 2020 (DELTA).

Panel B: Changes in response rates during the period of March 20 to April 3, 2020 (DELTA) for each countermeasure domain were plotted against the average domain-specific hospital-to-expert ratio. Drivers for implementation are quantitated as relative domain resource dependency, from low (green) to high (red).

Legend to Figure 4.

Panel A: The conceptual framework of COM-B is based on interaction between Capability, Opportunity, and Motivation to change Behavior. To **implement** countermeasures, **expert opinion** and/or **hospital rules** balance **resource dependency** of a given measure with the pressure to counteract COVID-19 during the progressive **pandemic phases**.

Panel B: Factors relevant in implementing countermeasures and their interactions structured according to COM-B and the Behavior Change Wheel (positively correlated, green arrows; negatively correlated, red drumsticks).



Response rates (calculated as relative frequencies) of implemented counter- measures for each center ('mean center response rate', corresponding to the center columns of Supplemental Figure 1) and for each of the eight defined domains per center, displayed as functions of pandemic phase (expressed as infected cases per million people) on March 20 2020 (T1). Colors depicting center response rates range from lowest (dark-blue) to highest (dark-red). Linear regression lines calculated after outlier exclusion (corresponding to (*) in Table 2) are plotted (black) with 95% CI in grey.

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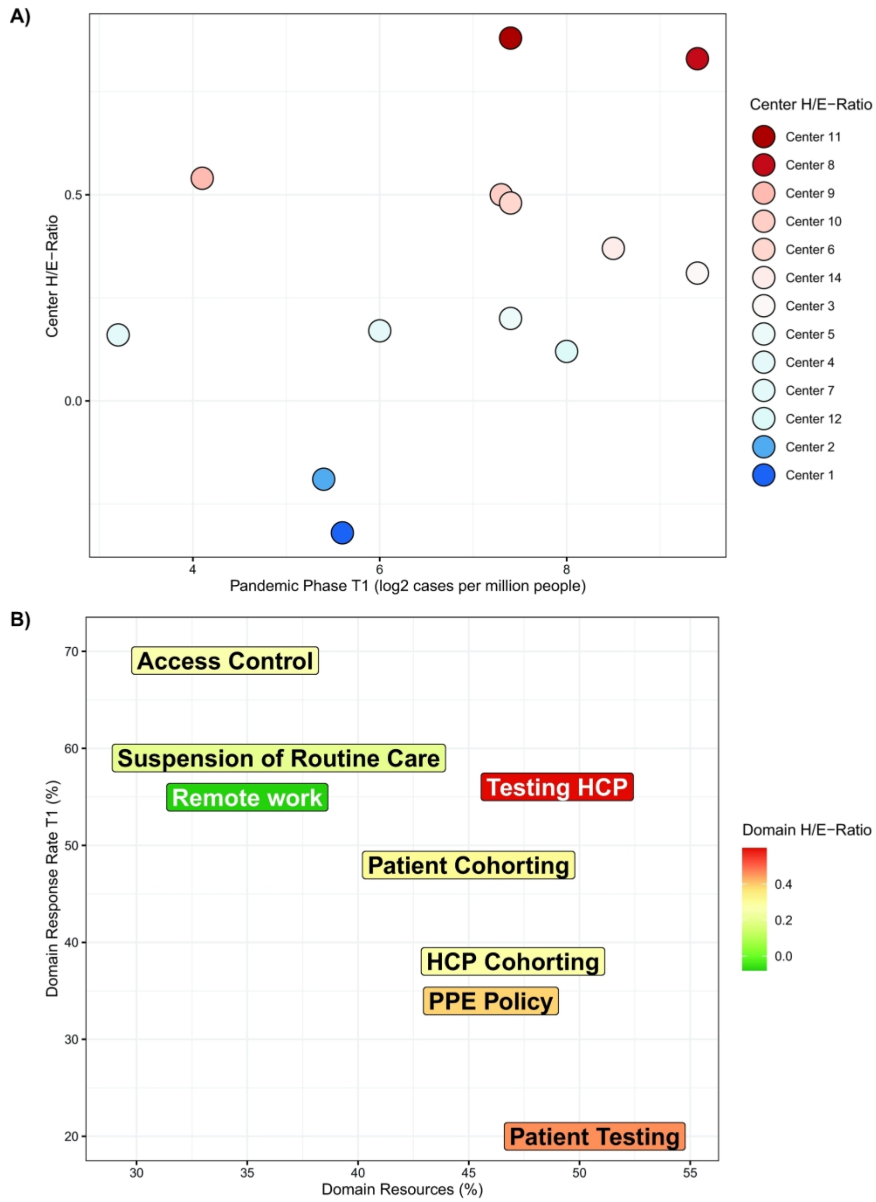
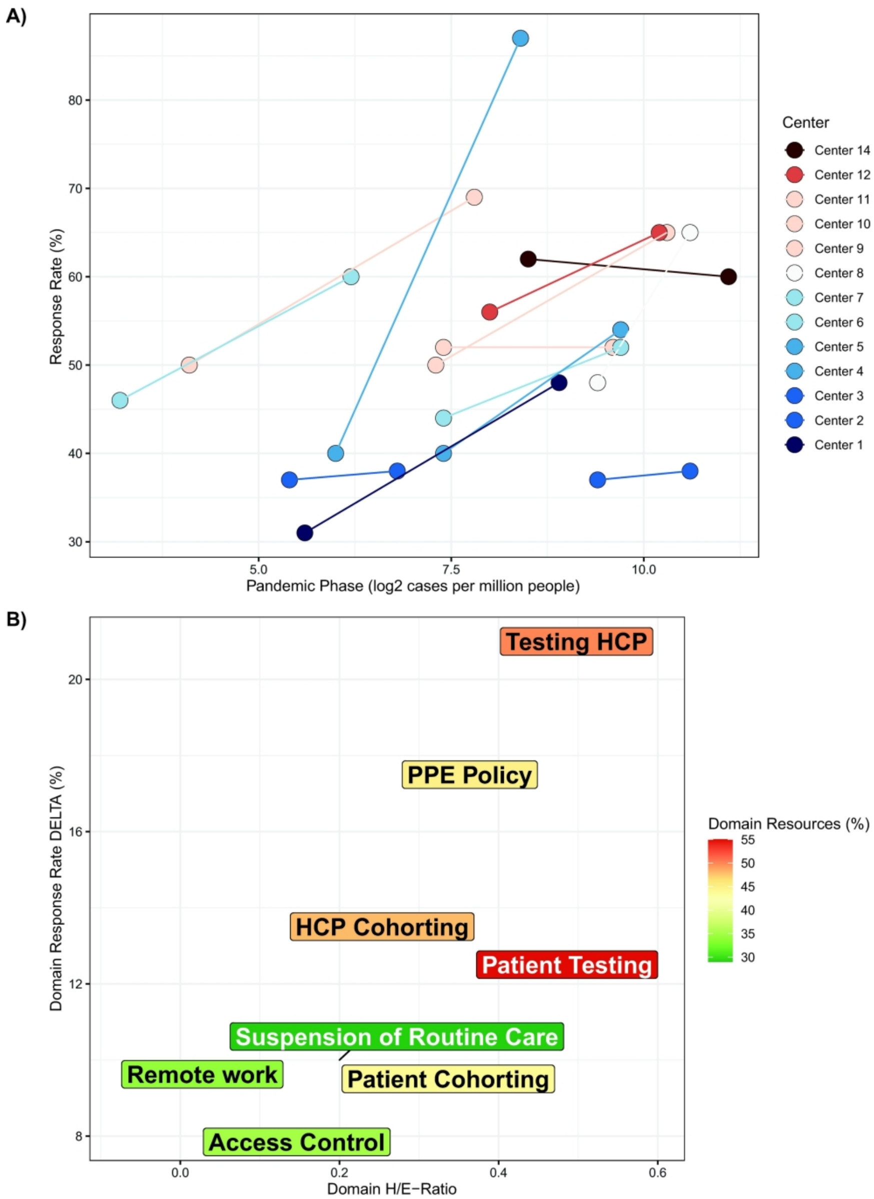


Panel A: Center-specific ratios of hospital rules (red) to expert opinion (blue) (H/E-Ratio) driving countermeasure implementation for each of the 13 EPDWG centers as a function of infected patient caseload (LOG2 of infected cases per million people) a measure of pandemic phase on March 20 2020 (T1). Panel B: Domain response rates (implemented countermeasures per domain as % of total) as a function of countermeasure resource dependency (mean of all estimates from each center for each Individual domain) for each of the eight countermeasure domains and their drivers (red, hospital rules; green, expert opinion) on March 20 2020 (T1). Higher implementation rates of countermeasures with comparable resource dependency often correlated with higher hospital/expert driver ratio (compare 'Testing HCP' to 'Patient Testing' as opposed to comparison of 'Suspension of Routine Care' to 'Remote Work.)

217x297mm (300 x 300 DPI)



Panel A: Response rate dynamics were plotted for each center vs. dynamics of pandemic phase (log2-transformed cases per million people) during the period of March 20 to April 3, 2020 (DELTA).
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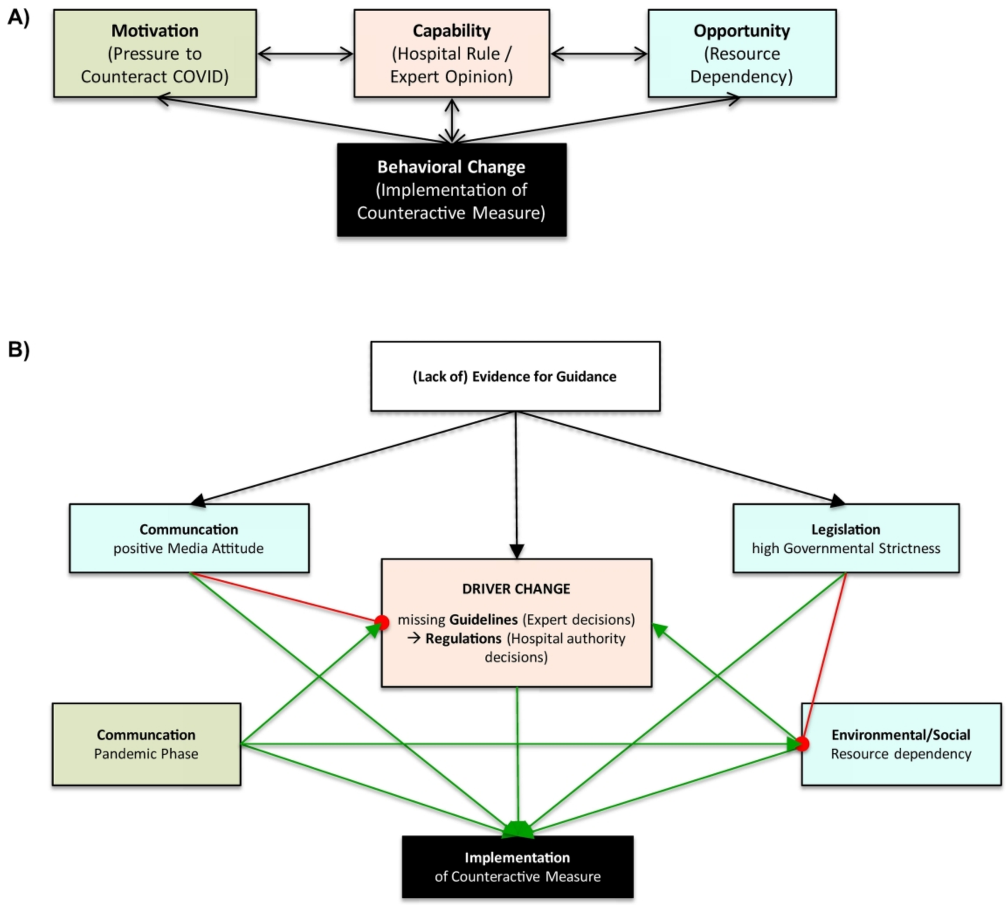
219x298mm (300 x 300 DPI)



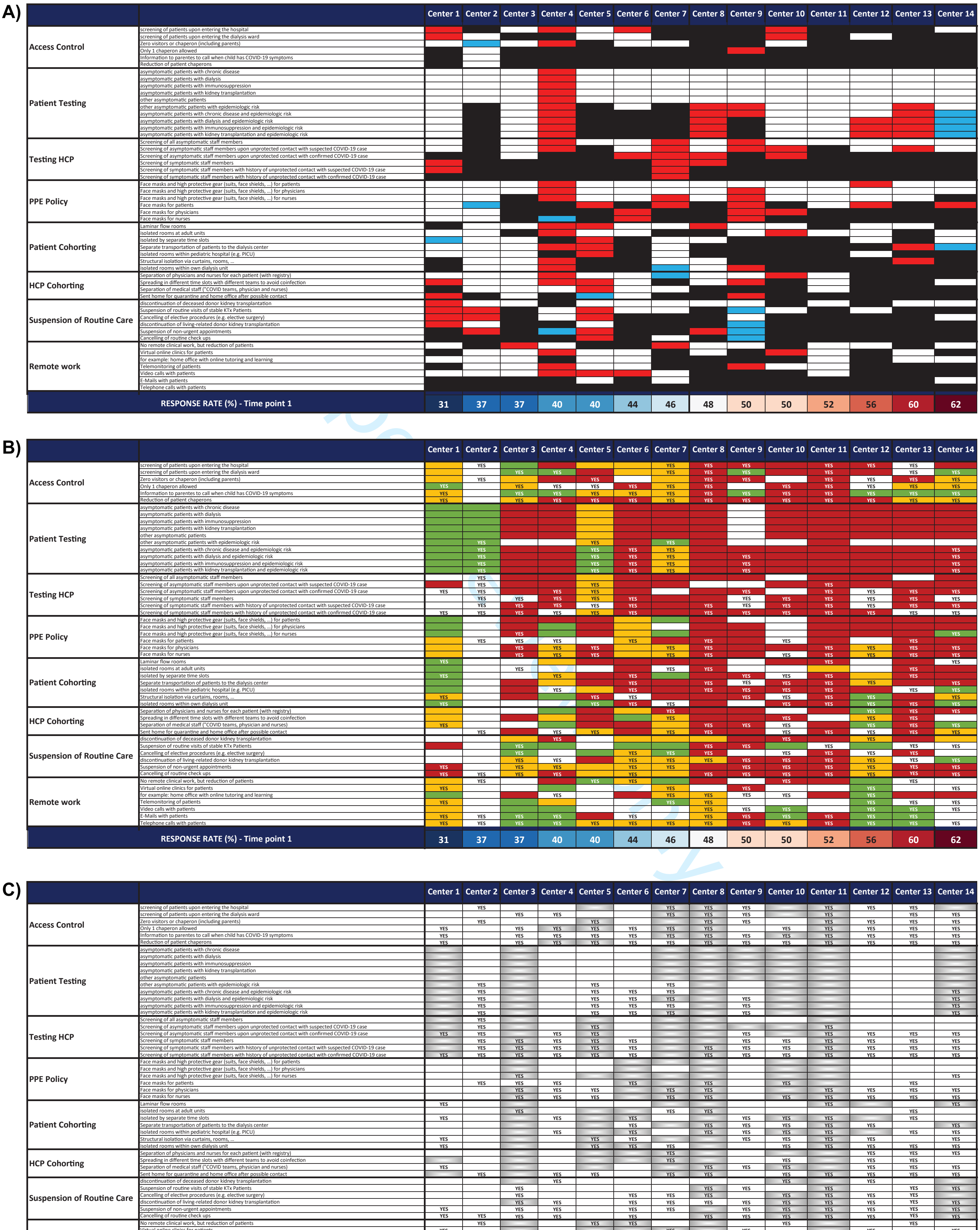
Panel A: The conceptual framework of COM-B is based on interaction between Capability, Opportunity, and Motivation to change Behavior. To implement countermeasures, expert opinion and/or hospital rules balance resource dependency of a given measure with the pressure to counteract COVID-19 during the progressive pandemic phases.

Panel B: Factors relevant in implementing countermeasures and their interactions structured according to COM-B and the Behavior Change Wheel (positively correlated, green arrows; negatively correlated, red drumsticks).

228x205mm (300 x 300 DPI)

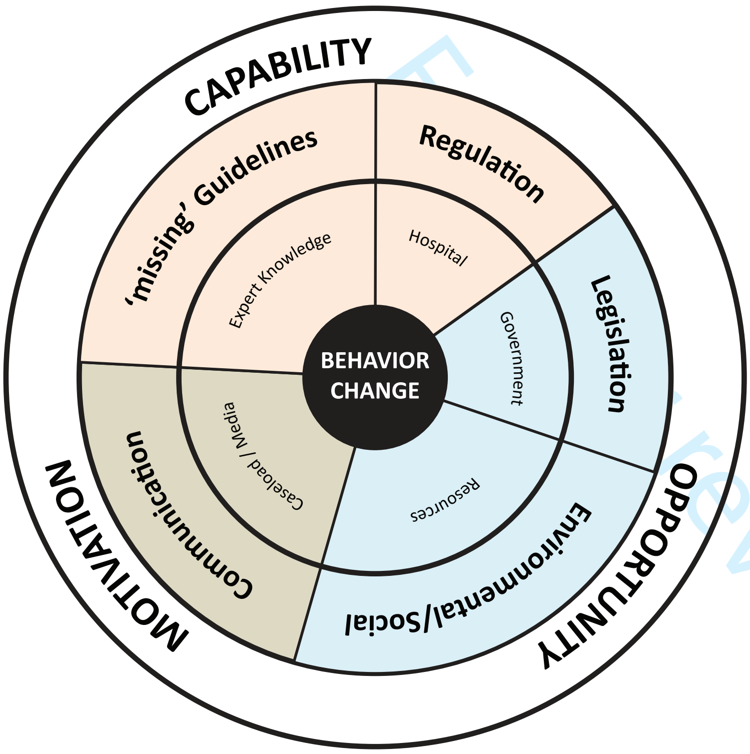
Supplementary Material

Supplemental Figure 1



Legend to Supplemental Figure 1.
Heat map displaying heterogeneity and dynamics of countermeasures implemented against COVID-19 in 14 EPDWG centers in 12 European countries between March 20 (Time point 1) and April 3, 2020, as well as decisive drivers (expert decisions, hospital authority decisions, resource dependency). Columns are sorted by average center response rates at March 20 (calculated as mean relative frequencies of implemented countermeasures), beginning with the lowest, from left to right. Rows are sorted by a logical response domain order, and within domain by response rate for each countermeasure, from top (lowest) to bottom (highest). Response rates are color-coded from dark blue (lowest) to dark red (highest).
Panel A: BLACK = implementation at March 20, RED = additional implementation at April 3, BLUE = implementation reversed at March 20.
Panel B: GREEN = expert decision, YELLOW = expert and hospital authority decision, RED = hospital authority decision, YES = countermeasure was implemented.
Panel C: GREY = resource dependency, YES = countermeasure was implemented.

Supplemental Figure 2



Legend to Supplemental Figure 2.
Behavior Change Wheel within the COM-B model displaying the five policy measures, with their respective concepts, influencing behavior change as implementation of countermeasures according to the EPDWG.

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Countermeasures against COVID-19: How to navigate Medical Practice through a nascent, evolving Evidence Base – a European multi-center mixed methods study

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Countermeasures against COVID-19: How to navigate Medical Practice through a nascent, evolving Evidence Base – a European multi-center mixed methods study

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ABSTRACT (max. 300 words)

Objectives

In a previously published Delphi exercise the European Pediatric Dialysis Working Group reported widely variable counteractive responses to COVID-19 during the first week of statutory public curfews in 11 European countries with caseloads of 4 to 680 infected patients per million. To better understand these wide variations, we assessed different factors affecting countermeasure implementation rates and applied the *capability, opportunity, motivation model of behavior* (COM-B) to describe their determinants.

Design

We undertook this international mixed methods study of increased depth and breadth to obtain more complete data and to better understand the resulting complex evidence.

Setting

This study was conducted in 14 Pediatric Nephrology centers across 12 European countries during the COVID-19 pandemic.

Participants

The 14 participants were pediatric nephrologists and EPDWG members from 14 European centers.

Main outcome measures

52 countermeasures clustered into eight response domains (Access Control, Patient Testing, Personnel Testing, Personal Protective Equipment Policy, Patient Cohorting, Personnel Cohorting, Suspension of Routine Care, Remote Work) were categorized by implementation status, drivers (expert opinion, hospital regulations) and resource dependency. Governmental Strictness and Media Attitude were independently assessed for each country and correlated with relevant countermeasure implementation factors.

Results

Implementation rates varied widely among response domains (median 49.5%, range 20%-71%) and centers (median 46%, range 31%-62%). Caseloads were insufficient to explain response rate variability. Increasing caseloads resulted in shifts from expert opinion-based to hospital regulation-based decisions to implement additional countermeasures despite increased resource dependency. Higher Governmental Strictness and positive Media Attitude toward countermeasure implementation were associated with higher implementation rates.

Conclusions

COVID-19 countermeasure implementation by pediatric tertiary care centers did not reflect caseloads but rather reflected heterogeneity of local rules and of perceived resources. These data highlight the need of ongoing reassessment of current practices, facilitating rapid change in 'institutional behavior' in response to emerging evidence of countermeasure efficacy.

Strengths and limitations of this study

- This is the first study using a mixed methods approach to evaluate and better understand the most important drivers of behaviors conducive to counteracting the COVID-19 pandemic during the first week of public curfews.
- The capability, opportunity, motivation model of behavior (COM-B) to understand the generic mechanisms of our responses to COVID-19 allows for a more critical review and appraisal of current practices than standardized responses usually provided by policy makers and societal guidelines.
- Put into general context, these dynamic domains with manifold factors may provide some of the most important guiding principles but lack general completeness and might be rapidly outdated.
- Interpretation of the results of this study is limited by the small number of participating centers and mixed methods character of this study, wherefore statistical tests and their corresponding p-values should be interpreted with caution.
- Although our results are representative for pediatric dialysis, they may not represent to the same degree other medical responses to the COVID-19 pandemic.

Public and Patient Involvement Statement: This paper was co-produced with members of different medical and non-medical specialties, including experts in information technology and qualitative research, contributing analysis of public realms, including news(papers) and governmental (law) enforcement.

Funding: No funding was secured for this study.

Competing interests: We declare no competing interests.

Ethical approval: No ethical approval was required for the conductance of this study.

Data sharing: No additional data available.

Authors' Contributions: F. Eibensteiner and C. Aufricht conceptualized and designed the study, had full access to all study data and take responsibility for data integrity, accuracy and analysis. They drafted the initial manuscript, analyzed and interpretated the data and reviewed and revised the manuscript. Data collection and critical manuscript revision for important intellectual content was conducted by S. L. Alper, C. P. Schmitt, V. Ritschl, T. Stamm, A. Cetin, G. Ariceta, A. Jankauskiene, G. Klaus, F. Paglialonga, A. Edefonti, B. Ranchin, R. Shroff, C. J. Stefanidis, J. Vande Walle, E. Verrina, K. Vondrak, A. Zurowska, S. Bakkaloğlu. All authors approved the final manuscript as submitted.

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INTRODUCTION

SARS-CoV-2-related disease (COVID-19) spread throughout Europe when minimal evidence was available to support efficacy of then available countermeasures.[1-4] The European Pediatric Dialysis Working Group (EPDWG) conducted a Delphi exercise over five days during the first week of statutory public curfews in 13 pediatric nephrology centers from 11 European countries[5] using 'crowd intelligence' to define countermeasures in several relevant response domains, and to assess their implementation rates.[5] Whereas some countermeasures (replacement of routine visits by telephone calls) were widely implemented, others (asymptomatic staff member testing) were rarely implemented, and implementation rates varied widely among countermeasures and centers.[5] This heterogeneity may have reflected country-specific infection rates and pandemic stage-dependent measures to decrease infection rates. However, the mechanisms underlying COVID-19 countermeasure implementation by individual centers were not studied.

The *capability, opportunity and motivation model of behavior* (COM-B) [6] describes determinants of behavior [7], including *capability* (physical and psychological capacity to engage in an activity, such as knowledge and skills), *opportunity* (physical and social factors outside the individual that permit or prevent a certain behavior), and *motivation* (brain processes that energize and direct behavior).[6] In 2011 *the Behavior Change Wheel* (BCW) was added to the COM-B to distinguish between *interventions* (activities aimed at changing behavior) and *policies* (actions of responsible authorities or the government that enable interventions, respectively change of behavior).[6]

In this study, in order to explain the huge response variability among these tertiary care centers, we explored factors affecting practice behavior changes for the implementation of countermeasures in each pediatric dialysis center. We therefore used the COM-B and the BCW to map and conceptualize determinants of behavioral change in pediatric tertiary care centers relating to COVID-19 countermeasure implementation rates during the first week of statutory public curfews in Europe. Such insights may permit improved management of impending COVID-19 resurgence(s) and of future pandemic events, especially on how to implement evidence-based changes in practice to optimize management of complex health care interventions.

MATERIALS AND METHODS

The methodology of the Delphi exercise conducted among the EPDWG in March, 2020 was recently described.[5] This follow-up study examines 14 EPDWG centers from 12 countries (Austria, Belgium, Czech Republic, France, Germany, Greece, Italy, Lithuania, Poland, Spain, Turkey and the United Kingdom). Exploration of complex and pluralistic contexts, such as cross-national studies, requires a comprehensive research-approach. The mixed methods design is an ideal means to gain both depth and breadth. It allows the researcher to gain a better understanding of the research-problem by yielding more complete evidence.[8-10] Therefore, individual sets of 52 countermeasures (see[5]) were mailed to each center to validate countermeasure implementation rates on March 20, and to assess altered rates on April 3, 2020. Participants were asked whether implementation decisions concerning individual countermeasures were based on expert opinion and/or hospital regulations and/or resource availability. Country-specific caseloads from the European Centre for Disease Prevention and Control [11] were calculated as case number per million (from Eurostat [12]). Pandemic phase was expressed as binary logarithm of caseloads per million, since exponential case doubling times in the EPDWG countries (~two days at that time) transitioned gradually to a logistic function.

Behavior change determinants

COM-B and BCW components were mapped to concepts derived from anonymized EPDWG experts' initial open email replies to the first Delphi exercise.[5] Mapping was conducted by component definitions and experts' wording, using modified meaning condensation analysis to aggregate experts' statements in terms of underlying concepts (Figure 1). For example, the email statement *'Timely recipient testing should be feasible in our center'* was mapped to *Opportunity (physical)* and to BCW policy *'environmental/social planning'*, whereas the statement *'I read a lot about this, but to my knowledge we cannot draw any firm conclusions'* was assigned to *Capability (psychological)* and to BCW policy *'guidelines'* (Figure 1 Panel C). To ensure accuracy and rigor, initial mapping performed by one researcher (FE) was independently reviewed by a second, senior qualitative researcher (VR). In cases of disagreement, consensus was achieved through discussion.

Governmental Strictness

Country-specific online news agencies and governmental information websites were searched for governmental interventions in response to COVID-19. Relative frequencies of 23 defined governmental interventions to achieve 'social distancing' were combined to yield a Governmental Strictness score (Supplemental Table 1). Interventions included *restriction of free public movement, restriction of hospital access, restriction of prison access, recommended or mandatory teleworking, requirements for adequate mouth and nose coverage in public, closure of parks and playgrounds, closure of governmental facilities (e.g. schools, universities), closure of mass events, recommendation to limit gatherings to five people, prohibition of gatherings exceeding five people, police surveillance, closure of non-essential businesses, closure of restaurants, local quarantine, nationwide quarantine, selective border closure, complete border closure, state of emergency, vacation ban for health care professionals, implementation of tele-medicine, export and sales ban on all FFP3-type respirators and selected medications, ban on minors leaving home unaccompanied by a legal guardian, censorship of medical personnel*.

Media Attitude

Cover page articles during the week of March 20, 2020 from the three widest-circulating newspapers in each EPDWG country and text blocks containing COVID-19-related news and/or opinion pieces were manually classified. Transcribed, translated and anonymized excerpts from the selected articles were rated by participants (n=5) for positivity of reporting attitude on COVID-19 countermeasures on a scale from 1 (lowest) to 5 (highest). Excerpts were uniformly formatted without country identifiers. Mean values yielded a country-specific Media Attitude score (Supplemental Table 1).

Data analysis and Statistics

Data were clustered into eight response domains (*Access Control, Patient Testing, Testing Health Care Personnel [HCP], Personal Protective Equipment [PPE] Policy, Patient Cohorting, HCP Cohorting, Suspension of Routine Care, Remote Work*) and visualized as implementation rates and their rates of change (Supplemental Figure 1). Response rates (%) were calculated as numbers of implemented countermeasures divided by numbers of total identified countermeasures for March 20 and April 3, 2020. Resource dependency (%) for March 20, 2020 was calculated as numbers of decisions for which resources were decisive for implementation, divided by numbers of total identified countermeasures.

Expert decisions and hospital authority decisions were expressed as the Hospital-authority-decisions-to-Expert-decisions (H/E) ratio for March 20, 2020:

$$\frac{H}{E}\,Ratio = \frac{(Hospital\ authority\ decisions\ (n) - Expert\ decisions\ (n))}{total\ countermeasures\ (n)}$$

The H/E-Ratio expresses the degree to which response rates are influenced by hospital authority decisions (resulting in positive values to +1) or by expert decisions (resulting in negative values to -1), with the balanced H/E-Ratio of zero reflecting equivalent contributions of hospital authority and experts' decisions.

Each of these variables was calculated (I) on the domain level, as mean for each domain across all centers, and (II) on the center level, as mean for each center across all domains. Data was analyzed with descriptive statistics utilizing scatter plot matrices, bar plots, histograms and heat maps. Kendall's tau correlation analysis was conducted within a correlation matrix for each dependent and independent variable on each level. Correction for multiple testing was not performed, reflecting the exploratory character of this analysis. For Kendall's tau, correlation analysis between Response Rates and Pandemic Phase outliers was omitted post-hoc (high response despite low caseload, or relatively low responses despite highest caseloads).

RESULTS

Implementation of individual counteractive measures varied widely among response domains and centers in the March 20, 2020 cross-sectional analysis. Domain response rates ranged from 20%

(28/140) to 71% (59/84); median 49.5%. Center response rates ranged from 31% (16/52) to 62% (32/52); median 46%. Re-assessment of response rates on April 3 demonstrated increased countermeasure implementation, particularly in centers with lower initial response rates ('catch-up implementation').

'Snapshot' of implemented COVID-19 countermeasures (March 20): Center response rates or individual countermeasure response rates correlated weakly with center caseloads. Figure 2 demonstrates that centers at both ends of the pandemic phase spectrum markedly deviated from the assumption of correlation. Although overall correlations between center responses and pandemic phase were statistically significant, country/center-specific caseloads correlated with implemented countermeasures only after outlier exclusion (Table 1).

Policy measures influencing implementation of countermeasures per BCW: Five of seven BCW-defined policy measures [6] were reported as reasons for behavior change in the clinical setting (Figure 1 Panel C). As expected, 'regulation' by employers (establishing rules of principles of behavior) and/or governmental 'legislation' were important reasons for behavioral changes at the centers. However, information from mass media ('communication'), missing 'guidelines' and 'environmental/social'-related restrictions were equally often determinative for change in behavioral patterns. 'Fiscal measures' and 'service provision' were not mentioned as influencing behavioral changes. Mass media information indicated increasing pressure from growing caseloads in the EPDWG centers ('communication'), corresponding to correlation of pandemic phase with average countermeasure implementation rates (Table 1). Respondents often noted that recommendations ('guidelines') for clinical decision-making remained lacking, likely explaining why rules and principles established by hospital management ('regulation') contributed more as important drivers for implementation than did 'guidelines' (Table 1). Growing mass media pressure ('communication') in most centers resulted in a pandemic phase-dependent shift from expert opinion (missing 'guidelines') to hospital-based 'regulations' (Table 1).

Resource dependency was a major inhibitor of countermeasure implementation ('environmental/social' restrictions). Estimated resource dependency of eight individual measures correlated negatively with their implementation rates at the domain level (Figure 3, Table 1). Increasing resource dependency associated with an increasing ratio of hospital rules ('regulations') over expert opinion (missing 'guidelines') as a driver of countermeasure implementation (Table 1). Interestingly, implementation rates for countermeasures of comparable resource dependency ('environmental/social' restrictions) increased in direct proportion to the H/E ratio ('regulations'; compare, for example, 'Suspension of Routine Care/Remote Work" with comparably low resource dependency and 'Testing HCP/Patients" with comparably high resource dependency; Figure 3 Panel B, Figure 4).

Longitudinal assessment of 'catch-up' implementation of COVID-19 countermeasures: The above cross-sectional assessment describes associations between individual factors and countermeasure implementation rates in different centers/countries at different pandemic phases. Longitudinal changes in countermeasure implementation rates were assessed by another survey on April 3, 2020 and plotted as a function of pandemic phase. Panel A of Figure 3 and Figure 4 show that pandemic progression resulted in globally increased rates of countermeasure implementation from March 20 to April 3 in almost all centers (Table 1). At the center level, mean changes of response rates were negatively influenced by cumulative local perception of resource dependency on March 20 (= 'resource awareness', perceived 'costs'; Table 1). However, 'catch-up implementation' of counteractive measures from March 20 to April 3 positively correlated with higher H/E ratio (between hospital rule and expert opinion as drivers), and with resource dependency of particular measures (Table 1). Thus, growing pressures of increased country-specific caseloads increased local implementation of hospital rules, thereby overcoming the initially inhibitory effects of locally perceived resource dependency for these measures in a center-specific way.

Role of country-specific, non-medical influencers on countermeasure implementation: Center-specific patterns of longitudinal changes suggest that local countermeasure implementation rates represent a balance of local influences only poorly modulated by global medical evidence, allowing study of the influence of non-medical drivers such as Media and Government. Media Attitude (Supplemental Table 1) shows scores for implementation of COVID-19 countermeasures in the 11 EPDWG countries. Cover page articles from the three widest-circulation newspapers during the week of March 20 each contained >75% of COVID-19-related text. Media Attitude was only weakly associated with center response rates (Table 1). However, centers in countries with higher Media Attitude scores demonstrated significantly lower ratios of hospital rules over expert opinion (Table 1), in turn associated with higher implementation rates and catch-up (Table 1). Indeed, the two centers with the highest Media Attitude Scores demonstrated the highest response rates. Supplemental Table 1 also shows Governmental Strictness Scores of the 11 EPDWG countries. As for Media Attitude, Governmental Strictness associated only weakly with response rates (Table 1). However, centers in countries with higher Governmental Strictness scores demonstrated lower perceptions of resource dependency regarding countermeasure implementation (Table 1), in turn associated with higher implementation rates and catch-up implementation (Table 1). Interestingly, positive Media Attitude (potentially enhancing motivation) paired with high Governmental Strictness (potentially reducing resource dependency) was found in the two countries with the highest response rates (at intermediate caseload).

DISCUSSION

During the COVID-19 pandemic, the most important motivational driver of behaviors conducive to counteracting the pandemic has been the magnitude of pandemic growth. In the absence of prior evidence, many interventions were rapidly executed on local, national and international levels with different degrees of coordination.[1 4 13] The recent Delphi study from the European Pediatric Dialysis Working Group (EPDWG) confirmed marked heterogeneity of COVID-19 countermeasure implementation as of March 20, 2020, across 13 Pediatric Nephrology centers in 11 European countries,[5] with caseloads ranging from 4 to 680 infected patients per million (median 161 per million). This variability led us to hypothesize that growing pressures from increasing, country-specific caseloads were the main drivers for countermeasure implementation in our centers, and that differing numbers of infected patients might explain the heterogeneity in response rates among centers, consistent with general international trends amidst the COVID-19 pandemic.[5 14]

However, the present study's comparisons of center caseloads with mean center responses or with mean response rates of individual measures found no close correlation. Thus, pandemic phase alone cannot explain the observed heterogeneity of COVID-19 countermeasure implementation rates across European centers. We therefore treated countermeasure implementation as a complex process with multiple influencers. [6 15] In the conceptual framework of COM-B, countermeasure implementation rates likely represent the 'capability' (as 'regulation' and/or 'guideline' policies) of their drivers (experts and/or hospital authorities) to allocate resources by opinion or rules, balancing pressure of the pandemic phase ('motivation' as 'communication' policies) and availability of resources ('opportunity' as 'environmental/social' policies).

Complex interactions between these factors in the BCW (Figure 1) might better explain observed heterogeneities of implementation rates among different centers and measures. In this context, increased pressure from pandemic progression shifted expert opinion-based decisions towards more formal hospital rules, likely to overcome growing barriers to additional countermeasure implementation that in part reflected increasing awareness of growth in resource dependency. This might further reflect transfer of decisions from a personal individual level to systemic levels with increasing moral injury and mental health issues due to constrictions in provision of care caused by inadequate resources.[16] From the perspective of children requiring long-term kidney replacement therapy (dialysis or kidney transplantation), examples of resource dependency include increased difficulties in accessing medical care and traveling to hospitals for regular kidney function tests, drug concentration monitoring at specialized clinics, and acquisition of medical supplies such as peritoneal dialysis fluids and equipment. [17] In a February, 2020 Chinese survey of caretakers of children requiring long-term kidney replacement therapy in the midst of the pandemic, these resource-dependent factors were thought by nearly 80% of participants to negatively affect their children's treatment, with one third perceiving the effect as severe or extremely severe.[17] EPDWG center implementation rates of COVID-19 countermeasures, when regarded as changes of 'institutional behavior,' thus reflected the ability of drivers at each center to overcome local resource dependency. These changes motivated by local perception of growing global medical need led to diverse local rules and heterogeneous responses. Longitudinal assessment of countermeasure implementation from March 20 to April 3 supported the hypothesis that pressure from growing country-specific caseloads increased local implementation of hospital rules, overcoming the initially inhibitory effects of locally perceived resource dependency of these measures, particularly measures with lower initial response rates. Initial inhibitory effects of locally perceived resource dependency might have diminished with the passage of time as medical supply deliveries and medical resource mobilization has accelerated. These supplies are essential to carry out measures for pandemic control, protection of health care workers and mitigation of the severity of patient outcomes.[18] Ordinarily, a shared body of scientific evidence ('what is right') underlies consensus procedures to harmonize 'institutional behavior' in response to medical challenges. Evidence-based medicine utilizes the best available evidence to help provide an optimal basis for decision-making according to individual circumstances and values.[19] However, whereas COVID-19 countermeasure implementation rates increased at almost all EPDWG centers, overall response patterns among centers with similar caseloads or at similar pandemic phase did not converge. Despite the pressure of pandemic progression, individual within-center drivers appeared influenced by different perceptions of this pressure, and by different local resource dependencies (and/or awareness of those dependencies). This suggests other center- and/or country-specific factors, beyond pandemic phase progression, that significantly influence countermeasure implementation. The COM-B and BCW model also allows systematic analysis of drivers for different behaviors and interventions on all levels, from individuals to national governments and civil societies.

Our analysis identified the non-medical influencers, Media Attitude and Government Strictness, as important determinants of EPDWG center responses to COVID-19 which might foster effective implementation of other medically relevant measures.[20] Governmental interventions, in particular those aimed at social distancing, were recognized early in China as the most effective non-medical tool to 'flatten the curve' of the pandemic, in several observations.[1,13,21] Similar interventions, ranging from banning large events to strict curfews, were implemented to varying degrees in European countries during the week of March 20. Our study quantified these interventions and found that higher 'Governmental Strictness' correlated with increased center responses, associated with reduced perception of resource dependency ('resource/cost awareness') of countermeasure implementation. Media dissemination of information can be incorporated in the COM-B and BCW model as a motivational driver for behavior and decision making on all social levels.[20] This pertains especially to

European countries attempting to contain the pandemic to the degree achieved in China, but in settings where Governmental Strictness effects on social distancing depend more on individual decisions and actions.[1] Furthermore, important obstacles opposing a comprehensive European response to COVID-19 are being exposed, despite high level political commitment.[22] During the week of March 20, the three widest-circulation newspapers in each participating European country covered COVID-19 with >75% of front page text. Centers in countries with more positive Media Attitude towards Governmental Strictness (based on front page articles) also demonstrated higher response rates, associated with higher perception of importance of expert opinion as driver for countermeasure implementation. This is in line with a Chinese study exploring new and traditional media use amidst the beginnings of the COVID-19 outbreak.[23] Chao et al. found that, new media use with heavier engagement was associated with negative psychological outcomes, whereas viewings of heroic acts, speeches from experts, and knowledge of the disease and prevention were associated with positive psychological impact. They conclude that timely public health communication from official sources might be beneficial in terms of general psychological health.[23] The rapidly evolving shared knowledge base and emerging 'best practices' for counteracting COVID-19 in the European context allowed our study on EPDWG center practice patterns, utilizing COM-B and BCW models to describe behavioral drivers, to serve as a case study of institutional 'behavioral changes' under high pressure with insufficient available information. Under such conditions, we might expect that skills (but not knowledge) and tactics (but not strategy) will guide an individual's decisions and (measurable) actions. The same held true at the institutional level where, for example, varied initial policies on PPE and testing material led to nationwide export bans, prioritizing local demand and production.[3] Furthermore, differences in testing strategy inherent to differences in commercially available laboratory tests, especially those failing to detect low-level immune responses to SARS-CoV-2 in asymptomatic or mildly affected subjects, as well as those indicating false-positive results [24], might complicate decision guidance through other factors. Such mechanisms and interdependencies detected by our targeted statistical approach might increase understanding of still heterogeneous response patterns among countries with similar infection rates. This is in line with most countries having responded to this acute crisis with different tactics, often borrowed from non-medical sectors, in order to reduce transmission, increase local resources and contain medical, economical and other public threats accompanying this pandemic - whether being successful or not.[25 26]

As COVID-19 countermeasure implementation in the European context was not based on 'hard' scientific evidence, none of the implemented local policies can be objectively judged from a medical viewpoint as 'right' or 'wrong'. At time of submission six months after the initial Delphi exercise, there remains no strong evidence on efficacy of individual COVID-19 countermeasures pertaining to the European pediatric dialysis population. Recent Chinese consensus guidelines [27] mentioned neither suspension of routine care nor testing strategies (for HCP and patients), although these measures were advocated as important to COVID-19 control.[28] The COVID-19 outbreak in a German pediatric dialysis center [29] also highlights the importance of adequate testing, tracing and monitoring strategies for successful outbreak containment and prevention in the hospital setting. However, in the meantime at least one comprehensive systematic review has been published. This meta-analysis supporting physical distancing and face mask use provides the best evidence yet available, given the body of literature generally lacking robust randomized trials.[30]

This exploratory work provides a framework containing the most important domains that emerged during the lockdown phase in Pediatric Dialysis Centers across Europe. Put into general context, these domains may provide some of the most important guiding principles but lack general completeness and might be rapidly outdated. However, put into perspective of the Behavior Change Wheel and the COM-B model, these domain sets present an important framework for regular and multi-layered re-assessment by policy makers and clinicians to provide a basis for further decision-making and evolving awareness of possible limitations and subliminal influential factors.

As the results of this work reflect, the issues encountered in the course of providing the best possible care for our patients during a pandemic are multi-layered and dependent on internal and external factors that vary across different cultural, legislative, economical geographical area. Moreover, these influences are likely to be subject to changing directives of changing degrees of influence over time. Standardized responses as usually provided by policy makers and societal guidelines do not consider these manifold factors and their dynamics in order to provide the best possible evidence-based medical care during a pandemic.[31]

In such deleterious scenarios where not only single patient groups, but countries and continents are affected, the current gold-standards for guidelines and policies as proposed by evidence-based medicine might not be applicable, and even cause negative effects on specific sub-groups. Carefully graded stages considering legislative, economic and cultural differences need to set the framework for guiding patient care in accordance with increasing knowledge of an emerging evidence base. Policy makers and healthcare provides must maintain awareness of newly emerging influence factors, especially if readily fit into the subcategories Communication, Legislation, Environmental/Social, while sustaining flexibility to respond to the capability, opportunity and/or motivation for change. These graded stages should be selected in accordance with current events, individually applied in different geographical, economic and cultural sub-spaces and continuously re-evaluated with progression of time and events. Therefore, continuous and regular multi-layered re-assessment of the most meaningful domains is necessary.[31]

The major strength of this study lies in its being the first to evaluate the most important drivers of behaviors conducive to counteracting the COVID-19 pandemic during the first week of public curfews. During this time, we applied an accepted model of behavioral change (the COM-B model and BCW) to explore a unique snapshot of 14 pediatric dialysis centers in 12 European countries with caseloads ranging from 4 to 680 infected patients per million. The strength of our novel study approach may also inherently limit the interpretation of our results, due to the absence of comparable studies with which to compare. The interpretation of this study's results is further limited by a small number of participating centers representative of pediatric dialysis, but perhaps not equally representative of other medical responses to the COVID-19 pandemic. In addition, the number of participants per center was limited to one clinician only, in order to facilitate rapid communication and data acquisition. However, given the small number of participants and exploratory mixed-methods character of this study, statistical tests and their corresponding p-values should be interpreted with caution. Moreover, local caseloads of the surveyed centers may not reflect overall disease burdens of the respective countries and/or other medical specialties, with higher numbers of infections and/or patients at risk.

Countermeasures evaluated in this study most likely reflect similar countermeasures in other medical specialties, as current mitigating approaches to COVID-19 all rely on the same measures, such as physical distancing, personal protective equipment and testing capacities.

This study may also serve as a basic framework for research and awareness of factors influencing exit strategies for the implemented countermeasures, providing clinicians and policy makers with guidelines for early and structured adaptation to changing or fluctuating conditions. Ruktanonchai et al.[32] underline the importance of such guidelines in their modeling study which shows that relaxation of countermeasures by one country before others do so could lead to disease resurgence across Europe about five weeks earlier than otherwise. Their study also highlights the importance of key countries, such as France, Germany, Italy and Poland in continental resurgence of disease due to heterogeneous approaches to mobility restriction. [32]

Nevertheless, heterogeneity of countermeasure implementation can be expected to continue among European centers until ongoing 'catch-up implementation' saturates response rates, as limited by local availability and resources. Although our study provides no solutions to that problem, our 'mechanistic' work does provide a mirror for the weak evidence basis underlying current practice patterns.[1] Understanding limitations of current approaches to selection and implementation of COVID-19 countermeasures might help re-assess those practices with open minds, allowing rapid 'institutional behavior changes' in response to emerging evidence on efficacy from controlled clinical trials. These will also provide evidence-based knowledge to optimize non-medical interventions during the COVID-19 pandemic.

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TABLES

Table 1. Statistical analysis of the COM-B model as applied to the EPDWGs decisions

COM – Variable	Variable (B or COM)	Kendall's tau	p-value
Cross-sectional analysis			
Pandemic Phase (caseload)	Implementation Rate	0.23	< 0.01
Pandemic Phase (caseload)*	Implementation Rate*	0.77	< 0.01
Pandemic Phase (caseload)	Hospital to Expert Ratio (center)	0.24	< 0.01
Hospital to Expert Ratio (center)	Implementation Rate	0.41	< 0.01
Hospital to Expert Ratio (domain)	Implementation Rate	-0.36	< 0.01
Resource Dependency (center)	Implementation Rate	0.16	0.03
Resource Dependency (center)	Hospital to Expert Ratio (center)	0.45	< 0.01
Pandemic Phase (caseload)	Resource Dependency (center)	0.30	< 0.01
Resource Dependency (domain)	Hospital to Expert Ratio (domain)	0.47	< 0.01
Longitudinal analysis			
Implementation rate	Catch-up Implementation	-0.15	0.04
Resource Dependency (center)	Catch-up Implementation	-0.18	0.01
Resource Dependency (domain)	Catch-up Implementation	0.4	< 0.01
Hospital to Expert Ratio (domain)	Catch-up Implementation	0.47	< 0.01
Influence of Media Attitude and Governmental Strictness			
Media Attitude	Implementation Rate	0.17	0.02
Media Attitude	Hospital to Expert Ratio (center)	-0.31	< 0.01
Governmental Strictness	Implementation Rate	0.3	< 0.01
Governmental Strictness	Resource Dependency (center)	-0.36	< 0.01

**) after omitting outliers (= high responses despite low caseload or relatively low responses despite highest caseloads)*
EPDWG = European Pediatric Dialysis Working Group; COM = Capability, Opportunity, Motivation, B = Behavior change

LEGENDS TO FIGURES

Legend to Figure 1.

Panel A: The conceptual framework of COM-B is based on interaction between Capability, Opportunity, and Motivation to change Behavior. To **implement** countermeasures, **expert opinion** and/or **hospital rules** balance **resource dependency** of a given measure with the pressure to counteract COVID-19 during the progressive **pandemic phases**.

Panel B: Factors relevant in implementing countermeasures and their interactions structured according to COM-B and the Behavior Change Wheel (positively correlated, green arrows; negatively correlated, red drumsticks).

Panel C: Behavior Change Wheel within the COM-B model displaying the five policy measures, with their respective concepts, influencing behavior change as implementation of countermeasures according to the EPDWG.

Legend to Figure 2.

Response rates (calculated as relative frequencies) of implemented counter- measures for each center ('mean center response rate', corresponding to the center columns of Supplemental Figure 1) and for each of the eight defined domains per center, displayed as functions of pandemic phase (expressed as infected cases per million people) on March 20 2020 (T1). Colors depicting center response rates range from lowest (dark-blue) to highest (dark-red). Linear regression lines calculated after outlier exclusion (corresponding to [(*)] in Table 1) are plotted (black) with 95% CI in grey.

Legend to Figure 3.

Panel A: Center-specific ratios of hospital rules (red) to expert opinion (blue) (H/E-Ratio) driving countermeasure implementation for each of the 13 EPDWG centers as a function of infected patient caseload (LOG2 of infected cases per million people) a measure of pandemic phase on March 20 2020 (T1).

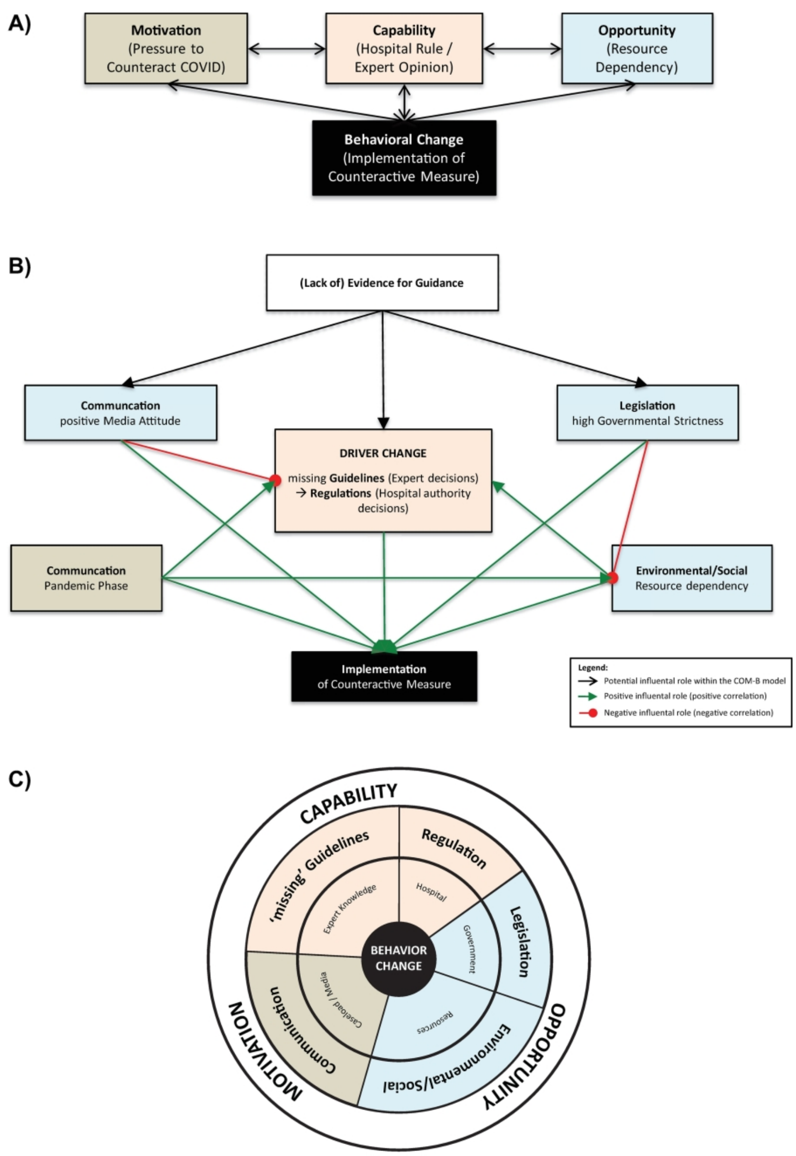
Panel B: Domain response rates (implemented countermeasures per domain as % of total) as a function of countermeasure resource dependency (mean of all estimates from each center for each Individual domain) for each of the eight countermeasure domains and their drivers (red, hospital rules; green, expert opinion) on March 20 2020 (T1). Higher implementation rates of countermeasures with comparable resource dependency often correlated with higher hospital/expert driver ratio (compare

'Testing HCP' to 'Patient Testing' as opposed to comparison of 'Suspension of Routine Care' to 'Remote Work.)

Legend to Figure 4.

Panel A: Response rate dynamics were plotted for each center vs. dynamics of pandemic phase (log2-transformed cases per million people) during the period of March 20 to April 3, 2020 (DELTA).

Panel B: Changes in response rates during the period of March 20 to April 3, 2020 (DELTA) for each countermeasure domain were plotted against the average domain-specific hospital-to-expert ratio. Drivers for implementation are quantitated as relative domain resource dependency, from low (green) to high (red).



Panel A: The conceptual framework of COM-B is based on interaction between Capability, Opportunity, and Motivation to change Behavior. To implement countermeasures, expert opinion and/or hospital rules balance resource dependency of a given measure with the pressure to counteract COVID-19 during the progressive pandemic phases.

Panel B: Factors relevant in implementing countermeasures and their interactions structured according to COM-B and the Behavior Change Wheel (positively correlated, green arrows; negatively correlated, red drumsticks).

Panel C: Behavior Change Wheel within the COM-B model displaying the five policy measures, with their respective concepts, influencing behavior change as implementation of countermeasures according to the EPDWG.

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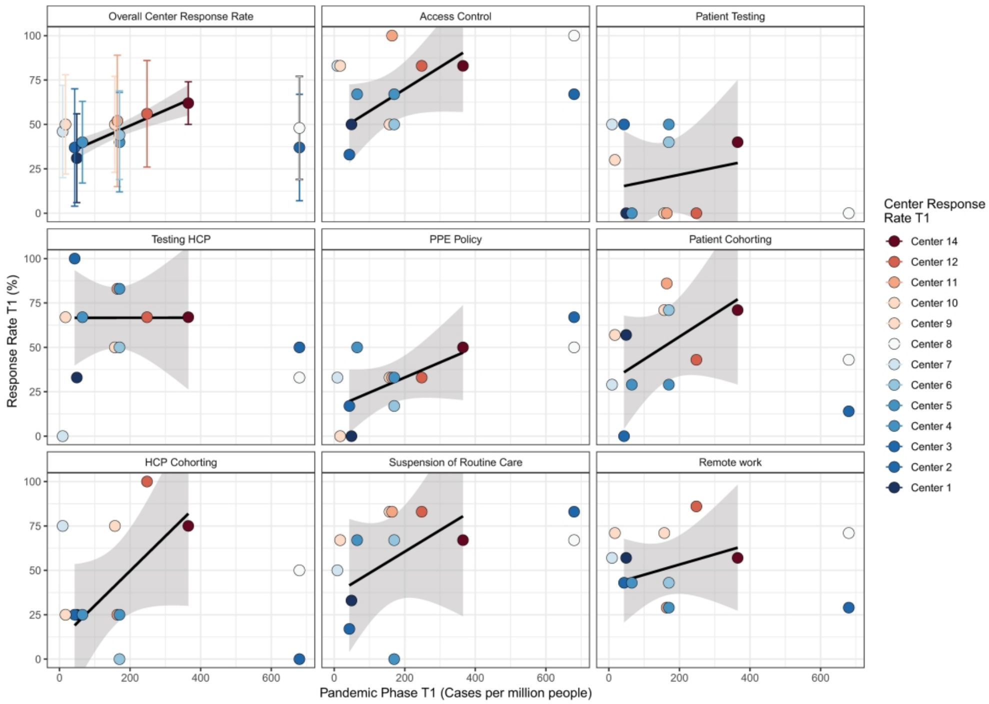
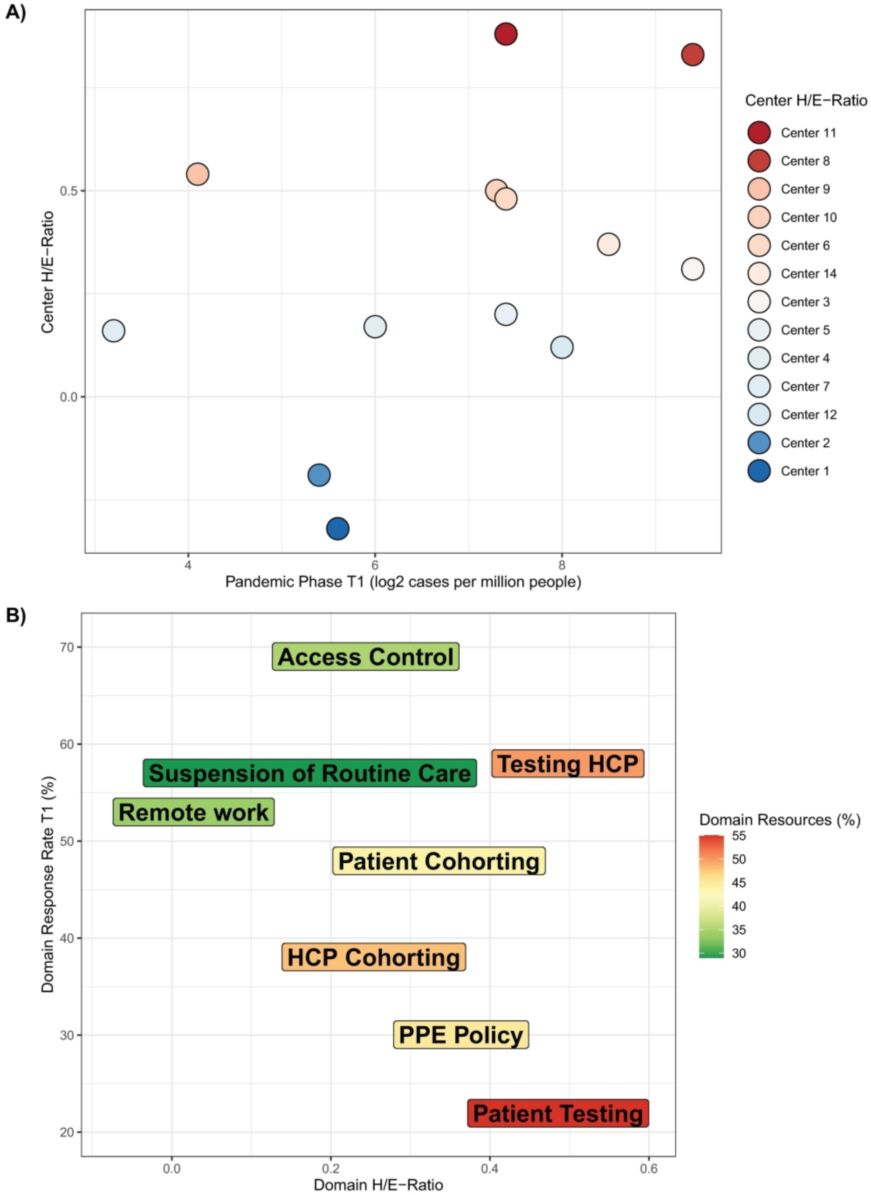


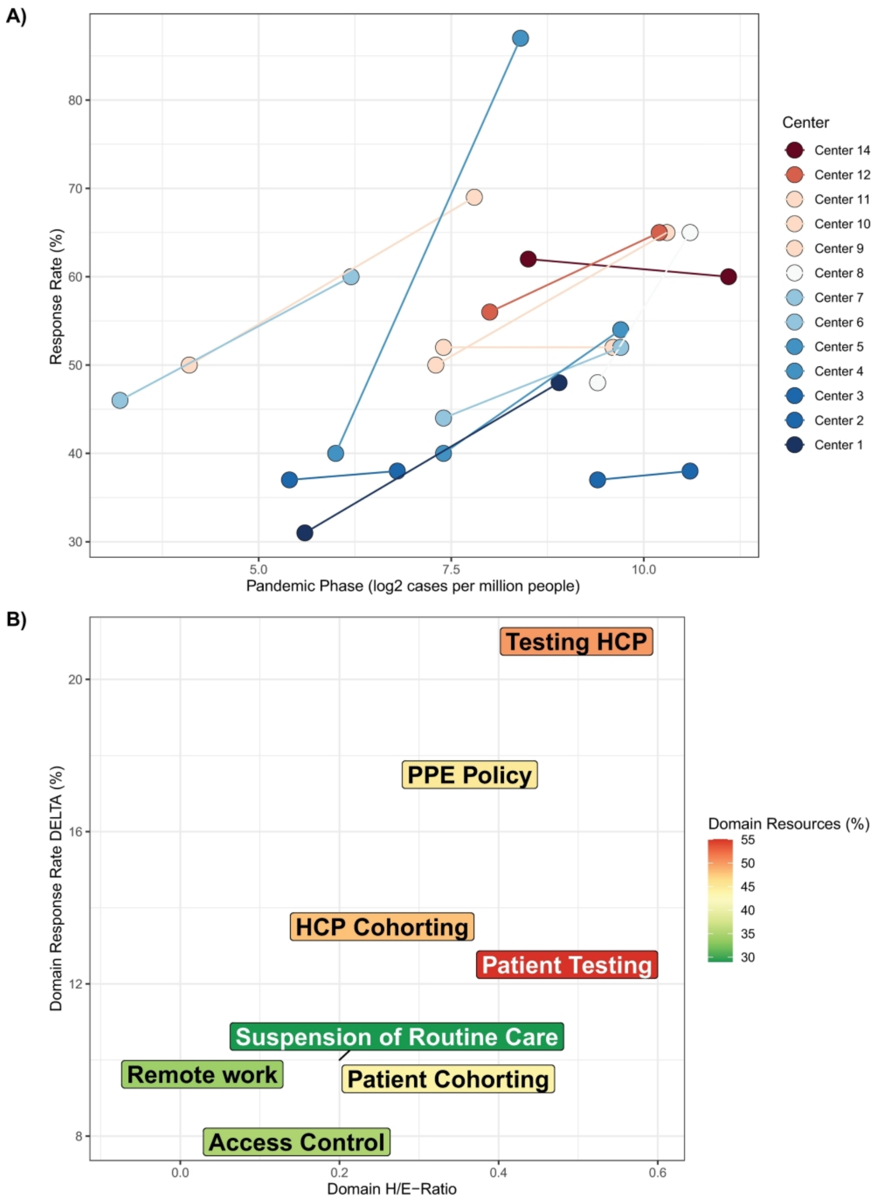
Response rates (calculated as relative frequencies) of implemented counter- measures for each center ('mean center response rate', corresponding to the center columns of Supplemental Figure 1) and for each of the eight defined domains per center, displayed as functions of pandemic phase (expressed as infected cases per million people) on March 20 2020 (T1). Colors depicting center response rates range from lowest (dark-blue) to highest (dark-red). Linear regression lines calculated after outlier exclusion (corresponding to (*) in Table 1) are plotted (black) with 95% CI in grey.

297x210mm (300 x 300 DPI)



Panel A: Center-specific ratios of hospital rules (red) to expert opinion (blue) (H/E-Ratio) driving countermeasure implementation for each of the 13 EPDWG centers as a function of infected patient caseload (LOG2 of infected cases per million people) a measure of pandemic phase on March 20 2020 (T1). Panel B: Domain response rates (implemented countermeasures per domain as % of total) as a function of countermeasure resource dependency (mean of all estimates from each center for each Individual domain) for each of the eight countermeasure domains and their drivers (red, hospital rules; green, expert opinion) on March 20 2020 (T1). Higher implementation rates of countermeasures with comparable resource dependency often correlated with higher hospital/expert driver ratio (compare 'Testing HCP' to 'Patient Testing' as opposed to comparison of 'Suspension of Routine Care' to 'Remote Work.)

217x298mm (300 x 300 DPI)

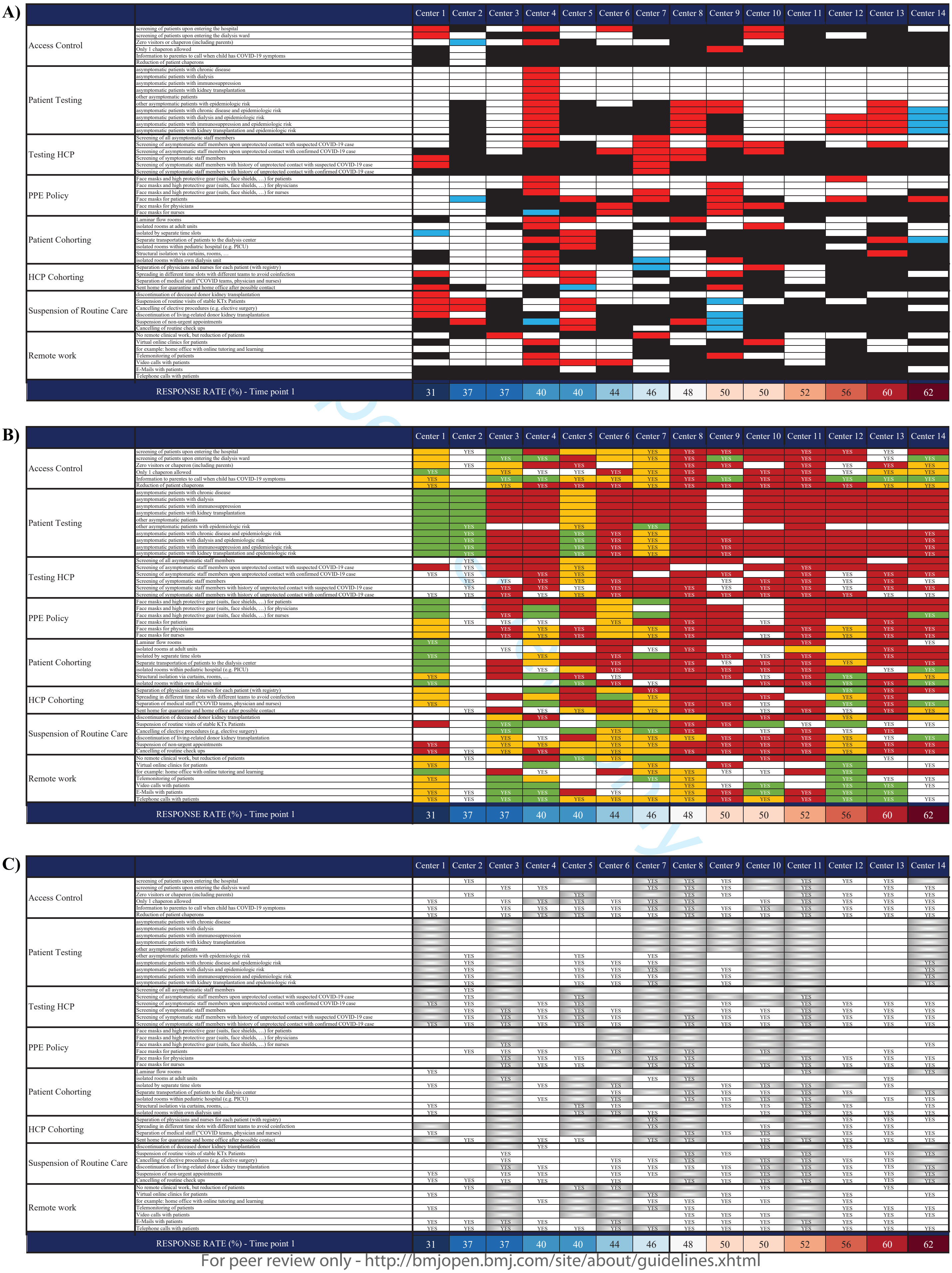


Panel A: Response rate dynamics were plotted for each center vs. dynamics of pandemic phase (log2-transformed cases per million people) during the period of March 20 to April 3, 2020 (DELTA).
Panel B: Changes in response rates during the period of March 20 to April 3, 2020 (DELTA) for each countermeasure domain were plotted against the average domain-specific hospital-to-expert ratio. Drivers for implementation are quantitated as relative domain resource dependency, from low (green) to high (red).

219x298mm (300 x 300 DPI)

Supplementary Material

Supplemental Figure 1



Legend to Supplemental Figure 1.

Heat map displaying heterogeneity and dynamics of countermeasures implemented against COVID-19 in 14 EPDWG centers in 12 European countries between March 20 (Time point 1) and April 3, 2020, as well as decisive drivers (expert decisions, hospital authority decisions, resource dependency). Columns are sorted by average center response rates at March 20 (calculated as mean relative frequencies of implemented countermeasures), beginning with the lowest, from left to right. Rows are sorted by a logical response domain order, and within domain by response rate for each countermeasure, from top (lowest) to bottom (highest). Response rates are color-coded from dark blue (lowest) to dark red (highest).

Panel A: BLACK = implementation at March 20, RED = additional implementation at April 3, BLUE = implementation reversed at March 20.

Panel B: GREEN = expert decision, YELLOW = expert and hospital authority decision, RED = hospital authority decision, YES = countermeasure was implemented.

Panel C: GREY = resource dependency, YES = countermeasure was implemented.

Supplemental Table 1

Media Attitude scores and Governmental Strictness scores in the countries of the EPDWG

Country	Media Attitude score (rank)		Governmental Strictness score (rank)	
Austria	***3.38**	***1**	***52**	***1**
Belgium	2.64	8	***43**	***3**
Czech Republic	2.8	4	***48**	***2**
France	2.73	5	17	7
Germany	2.65	7	26	6
Greece	2.56	10	39	4
Italy	2.62	9	35	5
Lithuania	2.2	11	***43**	***3**
Poland	2.67	6	17	7
Spain	***3.13**	***3**	***43**	***3**
United Kingdom	***3.17**	***2**	4	8

**) top three highest ranking countries for Media Attitude score and Governmental Strictness score*
EPDWG = European Pediatric Dialysis Working Group