



COVID goes Cuckoo

How the March-April 2020 COVID-19 surge overwhelmed Dutch hospitals and undermined regular care

AN INDEPENDENT STUDY

Amsterdam, 21 May 2020

Gupta Strategists

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About this study

On March 24, 2020 we signaled an unintended crisis in hospital care¹. The REGULAR medical care was severely impacted by COVID care in hospitals, and across other forms of care. Up to 40% of the REGULAR care was not being delivered. We based this early work on interviews and surveys.

In this study we delve deeper.

In medical terms, the March study may be considered a first anamnesis. In this study we supplement and confirm the early diagnosis based on detailed diagnostics and clinical parameters. We analyze data of hospitals to deduce which patient groups are being impacted. And we follow it up by estimating the impact this had and will continue to have on both the costs (efficiency) as well as life expectancy (efficacy).

The title of the study refers to how the common cuckoo raises its young, by laying its eggs in the nests of other birds, like the crow or warblers. Understandably COVID care had to be delivered in the REGULAR hospitals. But like the cuckoo COVID has brought parasitic damage to the eggs of the host – in this case REGULAR care. Yet like all relationships there might also be long term benefit. This study explores the initial impact and lays the ground for better symbiosis.

We intend follow-up with a third study in this series. In the third study we shall present different solutions to mitigate the costs and loss of life years. In other words, following the detailed diagnosis in this study, we discuss treatment scenarios and implications in the next study.

Acknowledgements

We are highly thankful to the hospitals and their management for their help and cooperation as well as their insightful comments. The willingness and speed with which hospitals have worked with us and others in this difficult period to ensure timely analyses and signaling is unprecedented.

This study has benefited from discussions with Professor Westendorp. He was the first to suggest a route to calculating the efficacy of non-delivery of REGULAR care. Prof. Westendorp wishes to acknowledge grant NNF170C0027812 for his 'Big data Group'.

¹ Read the previous study on our website at <https://gupta-strategists.nl/studies/in-de-slipstream-van-corona-een-secundaire-crisis-in-de-zorg>

Professor Kuipers emphasized, and reinforced early on us, that both COVID and REGULAR care must go together, and we cannot address one without the other. Also Prof. Kuipers referred us to scientific literature on potential impact of delayed oncological care. He showed us that this theme is both difficult and scientifically uncertain. Our sincere gratitude to Prof. Kuipers for sharing his scientific, medical and management knowledge with us.

It goes without saying that the conclusions and remaining mistakes in this study are entirely ours.

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Summary (ENGLISH)

The COVID care response in the Netherlands has led to a gain of 13-21 thousand healthy life years. However, this gain has come at an unacceptable loss in REGULAR care. As COVID care overwhelmed the hospital system, REGULAR care appears to be the unintended victim with disproportional 'collateral damage'. The loss of healthy life years due to the reduction in REGULAR care resulting from the COVID epidemic is estimated to be 100 to 400 thousand in the Netherlands. REGULAR care loss is thus an order of magnitude larger when compared to both the number of healthy life years gained with COVID care and the 10-15 thousand healthy life years lost from COVID.

The financial burden of COVID is equally disproportional. Direct costs of COVID care are EUR 7-23 thousand per healthy life year gained. At the same time COVID has driven up REGULAR hospital unit costs by 40%. Accounting for this effect, the 'true' cost of COVID care per healthy life year gained is estimated to be EUR 100-250 thousand. This is higher, potentially several folds so, than the current upper cost-effectiveness reference norm of EUR 80 thousand used by Dutch authorities. Considering the current and unprecedented economic downturn these costs are even more untenable.

This COVID epidemic is likely to have a protracted course. The way we delivered COVID care so far is unsustainable. Given the size of the problem (order of magnitude higher costs and order of magnitude loss of healthy life years in REGULAR care) and the uncertainty surrounding even the near-term future, it is imperative to thoroughly explore and implement efficient and efficacious solutions.

We should use this period of relative calm to design and implement a well thought out action plan to deliver both COVID and REGULAR care. Such a plan must consider fully novel and hitherto 'unpalatable' choices, like fully specialized and centralized COVID facilities, centralized hospital capacity management, triage based on efficacy and efficiency, accelerated adoption of alternative delivery models (like outreach, telemedicine and home care), or, perhaps, an acceptance of structurally higher per-unit cost of delivery for the foreseeable future.

In our next study, we will estimate the potential impact of the various policy options.

Samenvatting (DUTCH) – Het koekoeksjong dat COVID heet

Ziekenhuiszorg voor COVID-patiënten heeft in Nederland naar schatting 13 duizend tot 21 duizend gezonde levensjaren (QALY's) gered (in maart en april). Echter, deze winst ging gepaard met een onacceptabel verlies in de REGULIERE zorg. Terwijl COVID-zorg de ziekenhuizen overspoelde, liep juist de REGULIERE zorg ongekende, disproportionele schade op. Het stopzetten van de reguliere zorg leidde tot een verlies van naar schatting 100 duizend tot 400 duizend gezonde levensjaren. Daarmee is het verlies in de reguliere zorg ongeveer tien keer zo hoog als zowel het aantal gezonde levensjaren gewonnen met COVID-zorg als het aantal gezonde levensjaren verloren door COVID.

De financiële druk van COVID op het zorgstelsel is al even disproportioneel. De directe kosten van COVID-ziekenhuiszorg bedragen ongeveer EUR 7 duizend tot 23 duizend per gewonnen gezond levensjaar. De gemiddelde kosten per patiënt van REGULIERE zorg daarentegen zijn met ruim 40% toegenomen. De 'werkelijke' kosten van COVID-zorg per gewonnen gezond levensjaar zijn daarmee 100 duizend tot 250 duizend euro. Dit is veel hoger dan de referentiewaarde van EUR 80 duizend die Zorginstituut Nederland hanteert voor de kosteneffectiviteit van nieuwe medisch specialistische behandelingen.

Deze COVID-epidemie zal waarschijnlijk nog lang duren. Door het effect op REGULIERE zorg is het onwenselijk om de manier waarop we COVID-zorg tot nu toe leverden nog langer zo door te zetten. Daarom is het nodig om op basis van rationale scenario-analyse efficiënte en effectieve oplossingen te verkennen.

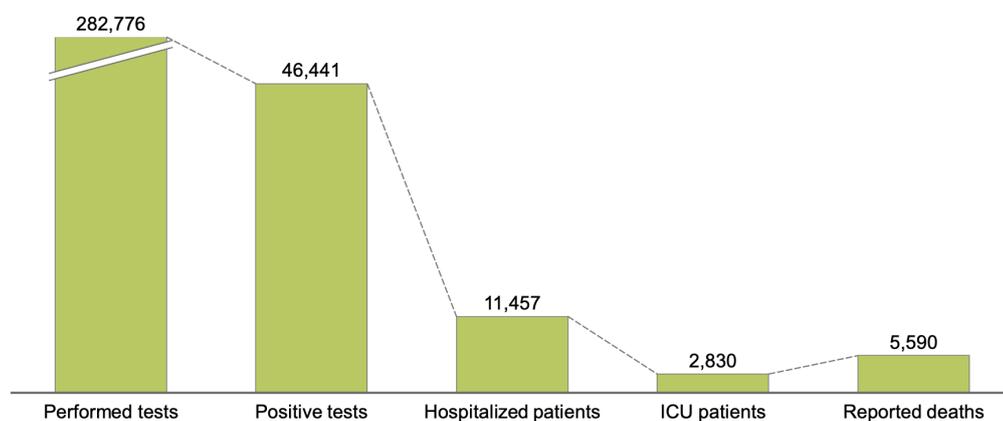
We moeten deze periode van relatieve rust gebruiken om een grondig onderbouwd 'Deltaplan' te ontwikkelen voor zowel COVID-zorg als REGULIERE zorg. Bij de totstandkoming van een dergelijk plan moeten we de afweging van nieuwe en tot voor kort lastig bespreekbare keuzes niet schuwen. Denk daarbij aan centrale gespecialiseerde COVID-faciliteiten, centrale capaciteitsplanning, triage van zorg gebaseerd op effectiviteit en efficiëntie, versnelde adoptie van nieuwe zorgmodellen en acceptatie van structureel hogere zorgkosten. In onze volgende studie zullen we de potentiële impact van deze en andere beleidskeuzes nader verkennen.

Chapter 1: Viewed by itself, COVID hospital care is cost-effective

While situations like in Lombardi or New York City appear to have been avoided, the surge in COVID infections in the Dutch population in the months of March and April overwhelmed the hospital system. Around 45 thousand patients have tested positive for COVID. Of these, around 12 thousand were admitted to hospital and just under 3 thousand were admitted to the ICU (Exhibit 1).

Exhibit 1: In the Netherlands, 46 thousand COVID cases led to 11 thousand hospitalizations and 3 thousand ICU admissions.

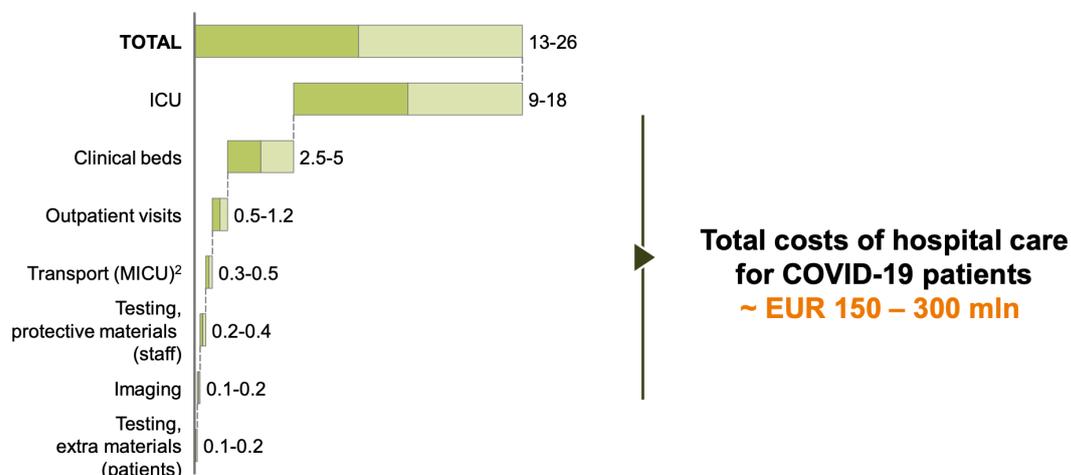
Summary statistics of COVID-19 epidemic in the Netherlands since start of epidemic on March 9th 2020
[figures as of May 14th 2020]



Sources: RIVM (www.rivm.nl), NICE foundation (www.stichting-nice.nl)

Exhibit 2: Total costs of hospital care for COVID in the Netherlands is estimated to be EUR150-300 million, or EUR13-26 thousand per patient.

Approximate cost per patient seen in hospital¹ for COVID-19 in the Netherlands
[EUR per hospital patient, x 1.000]

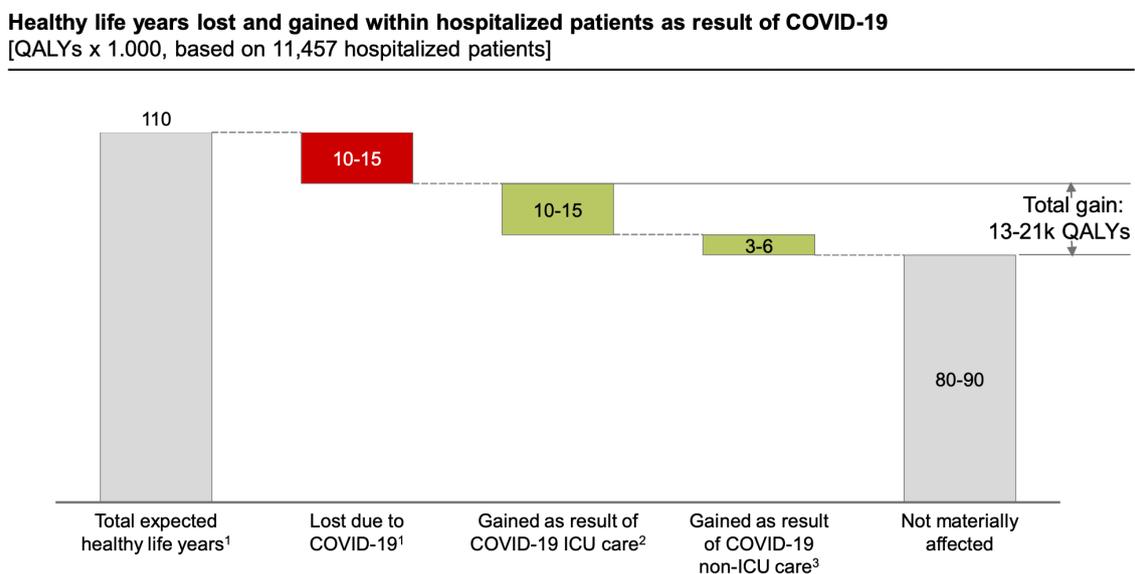


1) Based on ~12.000 hospitalized patients, assuming 50% of patients seen as outpatients are admitted; 2) MICU = mobile intensive care unit; Sources: RIVM, Gupta Strategists hospital database, Gupta Strategists analysis

While detailed cost estimates still need to be undertaken, based on ‘normal’ activity-related costs, we estimate that the costs of COVID care in hospitals so far amount to EUR 150-300 million (Exhibit 2). That translates to average costs of EUR 13-26ⁱ thousand per hospitalized COVID patient.

By applying published mortality and life expectancy tables to published age-group data of COVID hospitalized patients we estimate that COVID hospital care led to a 13-21 thousandⁱⁱ gain in healthy life years (expressed in QALYs, i.e. Quality-Adjusted Life Years; Exhibit 3). The loss of healthy life years due to COVID among Dutch hospital patients is estimated to be 10-15 thousandⁱⁱⁱ.

Exhibit 3: Approximately 13-21 thousand healthy life years were saved in the Netherlands as result of COVID hospital care.



1) adjusted for age-specific cases; 2) assuming 50% mortality rate at ICU, and assuming that all patients who survived an ICU stay did so as a result of the care received – i.e., 100% efficacy. 3) assuming, perhaps optimistically, that the average cost-effectiveness of hospital care of EUR 11.500 applies to hospitalized non-ICU COVID-19 patients. Sources: Stadhouders et al, ‘The marginal benefits of healthcare spending in the Netherlands: Estimating cost-effectiveness thresholds using a translog production function’, Health Economics (2019); RIVM; Gupta Strategists analysis

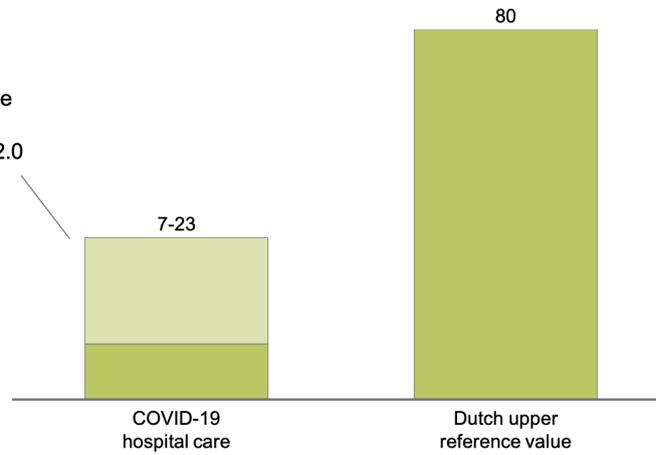
The cost per gained healthy life year for COVID care is then between EUR 10-30 thousand (Exhibit 4). Given that the Dutch National Health Care Institute (*Zorginstituut Nederland*) uses EUR 80 thousand as the upper reference value for financing innovative care, we conclude that delivery of COVID care (not considering its impact on REGULAR care, see more in the next chapter) is within typically used cost-effectiveness norms.

Exhibit 4: Cost of COVID care is, by itself, within cost-effectiveness reference values used in the Netherlands.

Cost per gained healthy life year– COVID-19 hospital care vs. Dutch upper reference value
[EUR x 1.000 per QALY]

Assumptions:

- Costs of COVID-19 hospital care per patient: EUR 13-26k
- QALYs gained per patient: 1.1-2.0

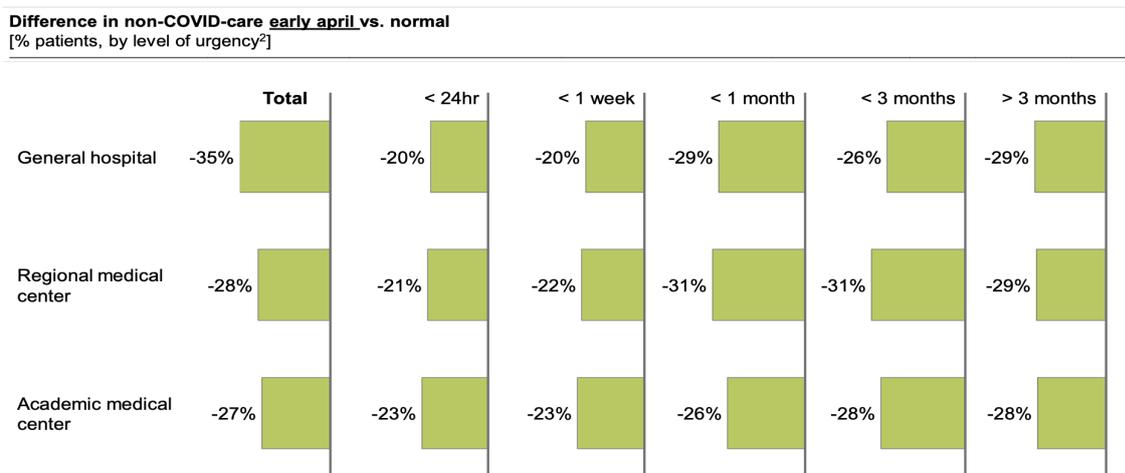


Sources: Stadhouders et al, 'The marginal benefits of healthcare spending in the Netherlands: Estimating cost-effectiveness thresholds using a translog production function', *Health Economics* (2019); Gupta Strategists analysis

Chapter 2: Accounting for reduction in REGULAR care, COVID care well exceeds cost-effectiveness limits

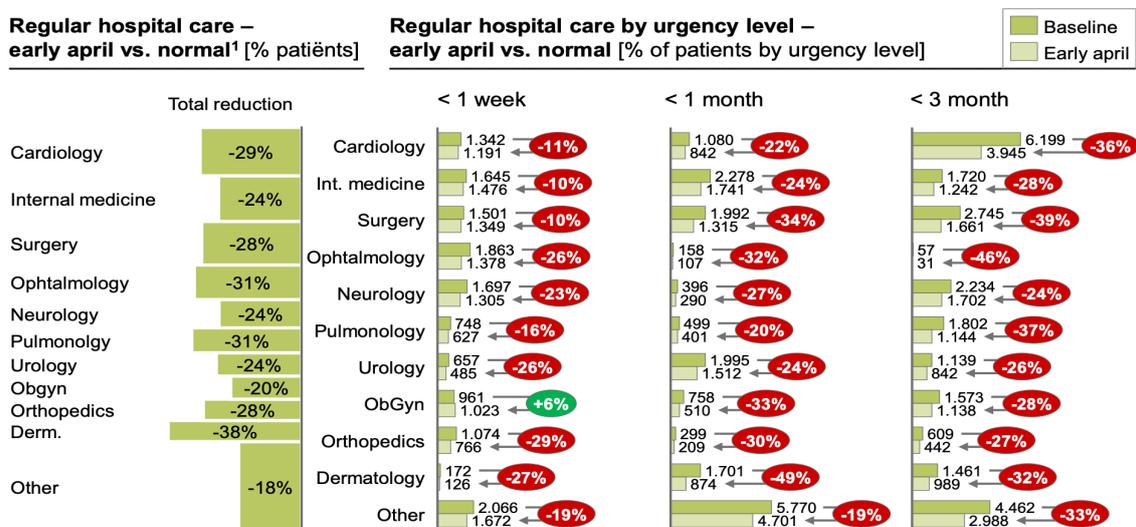
To understand the true impact of COVID care we also analyzed the implications for REGULAR care in Dutch hospitals. Based on a detailed analysis of patient data from several Dutch hospitals we estimated that 30% of the patients that required urgent and acute care did not get the treatment (Exhibit 5).

Exhibit 5: Overall, we see a ~30% decline in hospital production, varying but marginally by type of hospital and urgency of care.



1) For this analysis, all combinations of care products by specialism by diagnosis were categorized into urgency levels by doctors. Sources: production data of 3 Dutch hospitals, Gupta Strategists analysis

Exhibit 6: Example of analysis by specialty of reduction in regular hospital care; only Obgyn is unaffected.

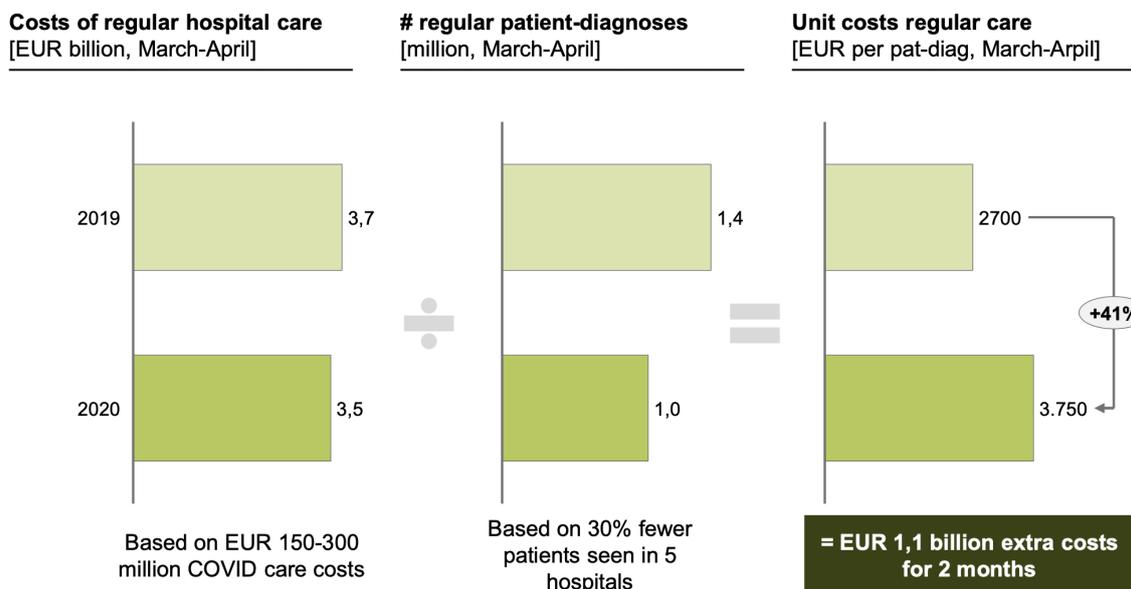


1) Based on analysis of one hospital in the Netherlands; 3 similar analyses for other hospitals showed similar impact; Sources: production data of one Dutch hospital, Gupta Strategists analysis

Aside from childbirths, hospital care for all other REGULAR patient groups was reduced as a result of the COVID epidemic. This includes, but is not limited to, treatments that have proven benefits, like heart care, oncology, dialyses etc. (Exhibit 6).

The costs of REGULAR care per patient increased by 40% compared to 2019 in March-April (Exhibit 7). Normally, average costs amount to EUR 2,700 per hospital patient. In March and April, costs per patient increased to nearly EUR 4,000. In absolute terms, the extra costs for just these two months studied add up to over EUR 1 billion - nearly 10 times as much as the direct costs of COVID care estimated in the previous chapter^{iv}.

Exhibit 7: The unit cost of regular care increased by 40% due to fixed ongoing costs for the ‘missing’ patients.



1) These numbers do not consider the potentially higher costs due to change in hospital delivery processes. Presumably the excessive capacity given lack of patients is sufficient to adjust for these; Sources: production data of 3 Dutch hospitals, Dutch Society of Hospitals (NVZ) sector report, Gupta Strategists analysis

The loss of healthy life years due to the REGULAR care not delivered, estimated in the range of 100-400 thousand, is also alarming. This, again, is an order of magnitude higher than the loss of healthy life years amongst patients hospitalized for COVID (Exhibit 8)^v. We estimate that the price per healthy life year gained by REGULAR care in this period has gone up by ~40% - from the normal EUR 11 thousand to EUR 15 thousand.

Clearly, the collateral damage of COVID is substantial. If we account for the increase in costs of REGULAR care costs and the resulting loss in healthy life years, the costs of COVID are much higher: we estimate the ‘true’ cost per

healthy life year gained due to COVID care can EUR 100-250 thousand. This well exceeds the current upper norm for cost-effectiveness (Exhibit 9).

Exhibit 8: Based on 2 different approaches, we estimate ~100-400 thousand healthy life years lost due to discontinuity in regular care.

Approach 1 – based on cost per QALY **Approach 2 – based on study of burden of disease**

Assumptions:
 a) Total hospital spend: EUR 22 bln²
 b) Average EUR per QALY of hospital care in the Netherlands: EUR 11.5k³
 → QALYs attributable to hospital care in the Netherlands = a / b = ~ 2 mln QALYs

Assumptions:
 Total burden of disease in NL: 2.9mln DALYs⁴
 Estimated impact of hospital care on burden of disease: 1.4 mln DALYs gained (based on analysis of 40 countries, see appendix)

→ 2 scenario's for speed of recovery in 2020¹

- Fast: 5% reduction in delivered care												
Urgency level	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
< 1 week	100%	100%	95%	95%	100%	100%	100%	100%	100%	100%	100%	100%
< 1 month	100%	100%	50%	50%	100%	100%	100%	100%	100%	100%	100%	100%
> 3 months	100%	100%	10%	10%	100%	100%	100%	100%	100%	100%	100%	100%

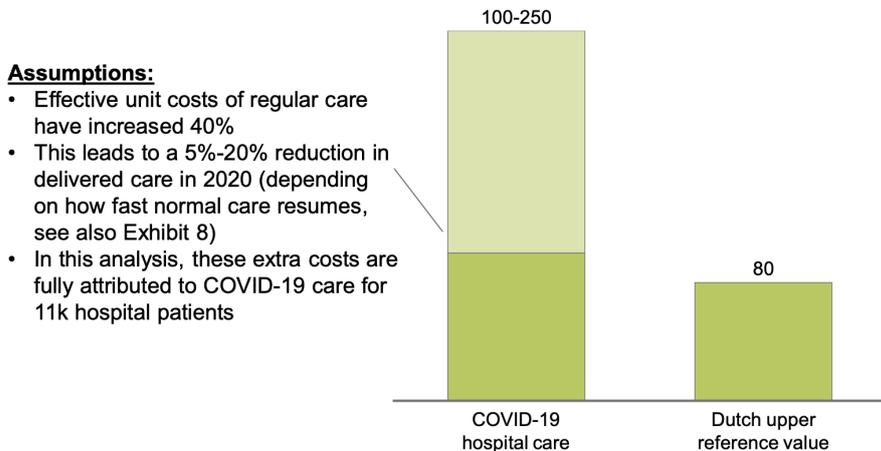
- Slow: 20% reduction in delivered care												
Urgency level	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
< 1 week	100%	100%	95%	95%	100%	100%	100%	100%	100%	100%	100%	100%
< 1 month	100%	100%	50%	50%	60%	70%	70%	70%	70%	70%	70%	70%
> 3 months	100%	100%	10%	10%	20%	30%	40%	40%	40%	40%	40%	40%

→ 5-20% reduction = ~100-400k healthy life years → 5-20% reduction = ~70-300k healthy life years

1) Estimated reduction for 2020, weighted based on approximate hospital costs per urgency level 2) Source: 'branche rapport NVZ' 2018; only 'Zorgverzekeringswet' revenues counted in this figure 3) Source: Stadhouders et al, 'The marginal benefits of healthcare spending in the Netherlands: Estimating cost-effectiveness thresholds using a translog production function', Health Economics (2019) 4) DALYs: disability-adjusted life years, a measure for burden of disease. Source: global burden of disease

Exhibit 9: If effects of reduction in regular care are attributed to COVID care, cost effectiveness well exceeds reference values.

Cost per gained healthy life year – COVID-19 hospital care vs. Dutch upper reference value
 [EUR x 1.000 per QALY]



Sources: Gupta Strategists analysis

Chapter 3: We should use this period of relative calm to devise a new 'delta plan' for both COVID and REGULAR care

We conclude that reduced delivery of REGULAR care is a very real and avoidable loss, which needs to be urgently addressed.

Before moving ahead, it is important to internalize the following learnings from the first wave of COVID infections:

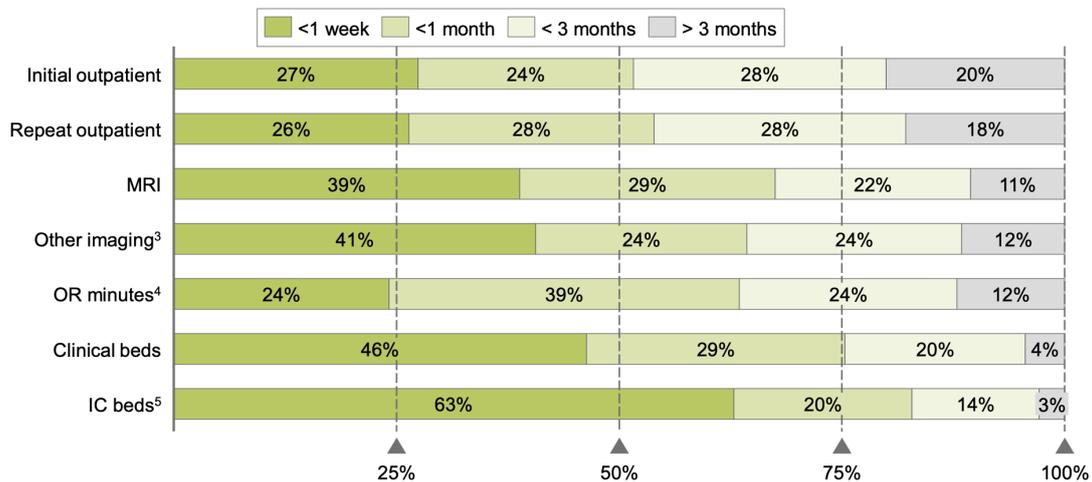
- 1) For every loss due to COVID there are many, many more loved ones whose REGULAR care has been delayed in ways that has already resulted in, and will further result in, deteriorating healthcare and loss of healthy life years
- 2) In terms of EUR per healthy life year gained, COVID care by itself is expensive but cost-effective - but only if it does not impact REGULAR care delivery significantly
- 3) The current COVID infection rates are still in single digits, and we must prepare for scenarios in which COVID will continue to grow further at an unknown pace. In each of these scenarios, COVID care needs to have a 'structural delivery design' model that is both cost effective by itself and, most importantly, is cost effective and efficacious for REGULAR care

The best way forward, then, is to ensure that REGULAR care is delivered in a timely manner, and to ensure that the loss in healthy life years from REGULAR care that we saw in this first wave will not take place in the future. It is fully avoidable. These are proven treatments with proven cost-effectiveness and must be continued in any scenario in the future.

While the goals are clear, the path to achieve them is far from obvious. Hospitals indicate that capacity is unlikely to reach normal levels for a prolonged period. We calculated that at least 75% clinical and ICU capacity is needed for care that must be delivered within 1 month of presenting itself at the hospital (Exhibit 10). This implies that the backlog of REGULAR care is unlikely to be addressed this year.

Exhibit 10: 75% of all hospital capacity is required to facilitate care that should normally be delivered within 3 months

% of regularly used¹ capacity in the pre-COVID-19 situation in a Dutch academic medical center
[2019 data, by capacity and level of urgency²]



1) Note that this analysis reflects used capacity, not available capacity; 2) For this analysis, all combinations of care products by specialism by diagnosis were categorized into urgency levels by doctors. The analysis was supported by the Dutch Federation of Medical Specialists; Sources: production data of 3 Dutch hospitals, Dutch Federation of Medical Specialists, analysis Gupta Strategists

Worryingly, we can expect the backlog to grow further. Patient and community perception and psychology, as well as constraints on ways of working in hospitals, pose real challenges to resuming REGULAR care. A broad and innovative ‘delta plan’ is urgently needed for both COVID and REGULAR care. We now have a short time window to design and deliver such a plan.

Such a plan must consider fully novel and hitherto ‘unpalatable’ choices. Given the size of the problem (order of magnitude higher costs and order of magnitude loss of healthy life years in REGULAR care) and the uncertainty surrounding even the near-term future, it is imperative to use this period to thoroughly explore and implement efficient and efficacious solutions. This exploration should include design options like^{vi}:

- a. Fully separated and centralized COVID facilities that are equipped primarily for future COVID surges and for treating COVID and COVID related co-morbidities only (ICU and clinical care). REGULAR care patients who come to hospitals may of course also have COVID as well as COVID risks. This patient group, REGULAR patients who have COVID need REGULAR treatment and in some cases also COVID treatment. Therefore,

hospitals will continue to treat REGULAR patients who have COVID. The distinction that needs to be investigated is which treatment is the priority for healthy life years and where is the best place to undertake it.

- b. COVID treatment protocols to be evidence-based medical care that contribute to quality of life^{vii}
- c. Enhanced ICU capacity – both material and professionals
- d. Designated REGULAR care only facilities (COVID controlled)
- e. Centralized capacity management for COVID and REGULAR care
- f. Further specialization and concentration of REGULAR medical care in specific facilities
- g. Medically led leadership on REGULAR care prioritization: which REGULAR care must always get the priority, which REGULAR care can safely be postponed or not delivered at all
- h. Accelerating the cessation of REGULAR care that is generally considered ineffective, to free up resources elsewhere
- i. Accelerating delivery models that ensure safety and efficacy of care – like care at home, telemedicine
- j. Integrated delivery systems including medical information sharing across disciplines and with patients
- k. Outreach programs. Access of care in The Netherlands is one of the best in the world. Such is the impact of COVID however, that even the Netherlands must consider outreach programs
- l. Financing choices that may require higher insurance premiums or special earmarked funds for the coming period. Even if human resources to deliver care are limited, cost of delivery may stay higher than we are used to till we are COVID adapted. We need to urgently implement innovative delivery solutions, which in turn may require additional costs.

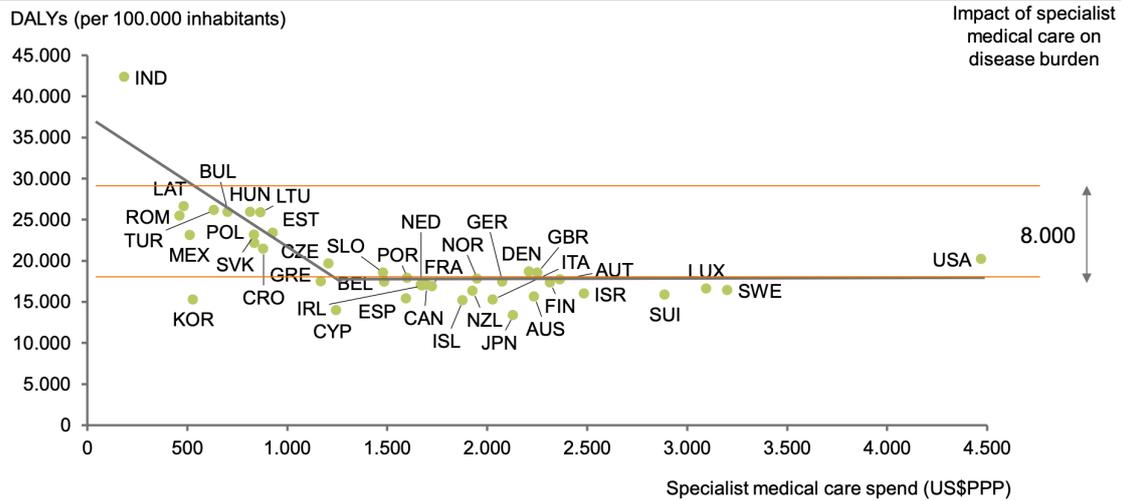
In the third study in this series we intend to analyze the impact of these design choices on both the efficiency and efficacy of COVID and REGULAR care. We shall do this based on different COVID growth scenarios in the Netherlands – the amplitude, and frequency of the COVID infection rates.

Appendix

Exhibit 11: specialist medical care helps to reduce disease burden by ~8 thousand (per 100.000 inhabitants)

Impact of specialist medical care on burden of disease

[US\$PPP; DALYs = disability adjusted life years, a measure for disease burden]



Note: details shown for 40 countries for which spend data by function was available. Sources: OECD, Eurostat, US CDC, India Manual on Health Statistics, Gupta Strategists analysis

Footnotes

Photo credit: www.IStockPhoto.com, ID: 1164403473

ⁱ We assume that hospitals saw twice as many patients in out-patient setting as admitted (based on a recent US study in Health Affairs as well analyses published by the NYU Langone healthcare system). The upper range is based in doubling the activity-based costs per activity. The actual costs could turn out to be higher. Since the regular care impact is magnitude of order higher on both costs and QALYs, this uncertainty is unlikely to have a material impact on the conclusions of this study.

ⁱⁱ We have assumed that the ICU (as WHO guidelines also indicate) is the hospital-based treatment which contributes materially to life expectancy. However, we have included an average QALY based on hospital admissions in general. Such are the uncertainties with COVID-19 that even the efficacy of ICU interventions is not fully evidence based at this stage. Therefore, the range we report here could be broader, being even lower or higher at the upper end if we can find a suitable therapy. Thousands of publications on MedRxiv and BioRxiv in the short span of few months is not a proper indication of our knowledge. It will likely take years and much more laborious research before these uncertainties are settled

ⁱⁱⁱ We use CBS life expectancy and RIVM and NICE reported age distribution of COVID patients. We have corrected for CBS reported excessive mortality

^{iv} Even without any COVID care in hospitals the unit costs of hospital shall be higher than normal due to COVID interventions required to reduce infection risks. The higher costs reported here cannot be seen as resulting only from delivering COVID care in REGULAR hospitals.

^v Estimating the loss of QALY from regular care is difficult for many reasons. There is little direct published evidence available on the impact of not getting regular care. The little evidence available seems to point in both directions: every month is critical (retrospective study of colorectal cancer screening in Taiwan) or there could be a significant period of low impact (In a California study, also on colorectal screening, Odds Ratio changed only after 8 months significantly. Our thanks to Prof. Kuipers for sending these studies to us). Furthermore, the impact is likely to vary from disease to disease and patient to patient. A bottom-up estimation is not possible at this stage. We use two approaches that are similar – both in their benefits as well as their limitations. The first approach was first proposed to us by Prof. Westendorp (our thanks to him for his elegant approach – Prof. Westendorp called it ‘slick and brutal’). It utilizes the estimated EUR per QALY as well as the value of regular care not delivered in this period to estimate the lost QALYs. The second comparison is based on the observation that different countries in the world have different spend on hospital care and have different life expectancies (as well as across classes of population within a country with different access to hospital care). We used the regression curve of hospital spend to estimate the QALY gain for all countries. This then provides an approach to estimate the lost QALYs if there is less care. A similar approach was recently published for cardiological care in The Netherlands. Historically we know that providing best practice hospital cardiology care (above other life-style interventions which have provided substantial additional benefit) has helped gain 3 years of quality of life. Thus, by the reverse logic lack of this care is likely to result in loss of these life years in some proportion. The uncertainty in this estimate is largely due to the unknown impact period in question: 2-3 months. Is 2-3 months large enough to cause an irreversible loss? We cannot answer this question unequivocally. For some cases - both disease areas as well as specific patient pathology, the loss may be inconsequential. For others it may be much worse – since later stage cancers, heart problems or organ deterioration are increasingly difficult to treat. Thus, even a shorter period may result in worse prognoses in some patients. While we remain unsure, we think our conclusions are robust enough. This lack of care delivered problem is unlikely to be just the previous 2-3 months and then resolved quickly. If that was the case than perhaps the uncertainties were more relevant. However, most hospitals indicate that full regular care is unlikely to happen soon. Some have indicated that 50% capacity is perhaps the maximum possible for now. Given the backlog of care means that the period over which regular care is not delivered is likely to be much longer and the effects reported here could also get worse. In which case these uncertainties emphasize the need for rapid and full recovery of regular care.

^{vi} We are not stating a preference or indicating that any of these options are better than current. We are making a case to investigate them further for their costs and benefits

^{vii} Most countries use strict decision-making protocols, delegated to professional healthcare expert organization (in The Netherlands: the Dutch Health Care Institute) based on peer reviewed clinical trials to ensure that the treatments paid for provide proven benefit. This needs to be undertaken urgently for COVID care. While understandable that in the early phases we needed to do whatever we could, benefits of medical different interventions for COVID care are far from obvious and evidence based. So far, these benefits are assumed to be mainly limited to ICU interventions. There is plenty of circumstantial evidence (the popular media), but little evidence that meets normal scientific standards.