# Rapid Assessment of Pandemic Indirect impacts and mitigating interventions for Decision-making (RAPID)

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University of California San Francisco

Final Report

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UCSF

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- **Matt Schueller**, Chief of Staff, Office of the California Surgeon General
- **Devika Bhushan, MD,** Chief Health Officer, Office of the California Surgeon General

And

- **Steve Wirtz**, **PhD**, Research Scientist Supervisor, Special Assistant to the Deputy Director of Operations, California Department of Public Health

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## EXECUTIVE SUMMARY

**Background:** The COVID-19 pandemic, now one year old, is unprecedented in our lifetimes in terms of the scale of health and societal harm. California has had more than 56,000 deaths due to the infection itself, with hundreds of thousands more experiencing hospitalizations and long-term health problems. In addition, the indirect pandemic effects have been far-reaching: millions have lost jobs, secure housing, educational opportunities, food supply, and confidence in a stable and comfortable life. Almost every Californian has been negatively affected by elevated chronic worry and stress.

To guide California's unfolding response to the pandemic, state decision makers must be well informed to anticipate, where future harm will likely arise – from not just direct health effects, but rather substantial *indirect* impacts as well. "Indirect burden" encompasses health harms not due to infection with the SARS-CoV-2 virus itself, but rather due to the biological impacts of other stressors caused by the COVID-19 pandemic and necessary mitigating interventions to control the epidemic. These include, to name a few among so many, economic distress related to lost wages, employment and financial assets; mass school closures, and necessary physical distancing, all of which induce stress and stress-related conditions.

California state and federal programs have mobilized to buffer populations from indirect pandemic effects, even in the context of a worsening economy, through direct financial assistance, deferred rental and mortgage payments, extended unemployment benefits and many others. Despite these efforts, populations have by necessity experienced prolonged periods of sheltering-in-place and other economic dislocations. Californians also suffer a growing range of indirect mental and physical health impacts, including an increase in stress-related morbidity and mortality. These indirect effects, as the pandemic itself, fall unevenly across racial and economic groups. Furthermore, Adverse Childhood Experiences (ACEs) and ACE-Associated Health Conditions, including depression, homelessness and alcohol and opioid use, are critical mechanisms, both for increasing current health burden and long-term consequences of these problems.

Scientific evidence on the negative effects of toxic stress and biologic response points to the opportunity that mitigating upstream problems not only can impact downstream health outcomes (e.g., reduced anxiety, depression) and longevity in affected adult, but also offers benefits to their offspring, avoiding toxic-stress related health outcomes that emerge gradually later in life (e.g., hypertension, cardiometabolic disease).

**Project purpose:** The overall purpose of the "Rapid Assessment of Pandemic Indirect Impacts and Mitigating Interventions for Decision-making" (RAPID) project is to:

- Compile and synthesize the best available and relevant scientific evidence on the indirect impact of COVID-19 on health
- Analyze the added burden due the pandemic stressors on leading non-COVID-19 causes of disability and death in adults and their offspring,

- Estimate the disproportionate impact of pandemic stressors on adults with a history of exposure to Adverse Childhood Experiences (ACEs), and
- Provide economic analyses that support California state decision-making on strategies that mitigate the human suffering and high societal costs resulting from current and downstream indirect health harms from the pandemic.

**Approach:** RAPID researchers at the University of California, San Francisco worked in close partnership with the Office of the California Surgeon General (OSG) to develop a flexible, but rigorous analytic approach. This report presents our initial effort, for 6 major health conditions and 7 interventions, including literature reviews, economic modeling, and data needs. We selected six key public health priorities – adult depression, alcohol use and substance use, housing insecurity, intimate partner violence (IPV), and stroke. Our hope is to provide timely and helpful information, as well as to obtain feedback on ways we can further assist the State with further analyses using this platform.

**Literature review:** The focus of our literature reviews was on high-burden, short-term, adverse health conditions that are not the direct health effects of COVID-19 (e.g., death or hospitalization due to the virus or worsening comorbidities). We prioritized studies that provided the most contextually relevant information (e.g., US-based) and had relatively higher-quality data (e.g., reported a reasonable baseline). When no US data was available for key outcome categories or their quality was uncertain, we utilized studies from outside the US. We collected and analyzed data extracted via two different types of literature searches. Review #1 systematically reviewed pre-reviewed literature on the current COVID-19 pandemic with the last update on August 13, 2020. Review #2, up to February 25, 2021, involved targeted and ongoing searches of a variety of data sources to inform the economic modeling and also identify relevant studies to fill gaps from Review #1 for the indirect effects of COVID-19, upstream risk factors, and potential effects of interventions. We extracted key data from relevant studies in structured datasheets, transformed heterogenous outcome data to a common metric of risk ratio, and assessed studies' strength of evidence. We also narratively synthesized data and provided a summary of key findings.

**Economic modeling***:* To estimate the indirect health and financial burdens of COVID-19, we designed a cost-effectiveness analysis framework that could be flexibly applied across conditions. We selected six conditions (adult depression/depressive symptoms, intimate partner violence, homelessness, excessive alcohol use, opioid use disorder, and stroke mortality) in consultation with the OSG based on: high quality evidence of worsening in the pandemic, high burden, and availability of effective and cost-effective interventions. The BRACE (Broad & Rapid Analysis of COVID-19 indirect Effects) model estimates QALYs (Quality-Adjusted Life Years) and direct medical and non-medical costs. We extracted inputs (prevalence, efficacy, and costs) from the scientific literature. We modeled effects

for adults (primarily affected) and their children (secondarily affected) both short- and long-term. We conducted extensive sensitivity analyses to assess the effect of uncertainty in input values.

**Key Findings of the Literature Review:** Our literature reviews cover an ever-expanding range of studies on a wide range of indirect health and social problems resulting from the pandemic.

- Our systematic review of the literature, identified 93 relevant studies in a wide arrange of topics as follow: Mental health (16), Stroke (14), Acute stress, loneliness and burnout (9), Heart disease (9), Intimate partner violence (7), Social determinants of health (7), Substance use (7), Suicide and self-harm (7), Dietary and exercise habits (6), Emergency care (5), Diabetes mellitus (4), Child maltreatment (2), Chronic respiratory illness (2), Communicable disease (2), Organ donation (2), Cancer (1), Musculoskeletal disorders (1), and Risk of violence (1).
- Although limited in quantity, mixed in quality, and not directly measured from Californians, we found that, in the past year, California's people have likely experienced elevated rates of increased depression, anxiety and suicidality, increased alcohol and substance use, increased intimate partner violence (IVP), decreased cancer screening, out-of-hospital acute cardiovascular events, and worsened stroke mortality outcomes.
- Most studies captured by our review of the scientific literature studies were available during the first six months of the COVID-19 pandemic. There is, however, little reason to suppose that indirect health harms discussed here have been abated, given subsequent epidemic surges and the rise of new variants, continued or renewed lockdowns, and initial delays in vaccine rollouts.
- There is in fact every reason to believe that indirect effects have been exacerbated by the continuing societal and economic upheaval, and uncertainties about the pandemic. For some indirect health outcomes, such as heart disease, there is no evidence yet of increased prevalence. This could be an artifact of delays in routine medical care use.
- Furthermore, the pandemic has shed light on the wide-ranging dramatic disparities among racial/ethnic and income groups experiencing the burden of COVID-19 unevenly, reflecting income and social inequities. As yet, however, few studies have reported data relevant to disparities in the rising rates of indirect health effects due to COVID-19.

**Key Findings from the Health and Economic Forecasting Analysis:** Indirect effects are exacting a heavy health and economic toll, but there exist cost-effective mitigation strategies that can be quickly scaled, even during periods of sheltering-in-place that will prevent considerable loss to life while achieving net economic savings to the society.

- Our forecasting models estimate substantial human and economic costs for failing to mitigate six health conditions known to be increasing due to the pandemic: adult depression, intimate

partner violence (IPV), homelessness, excessive alcohol use, opioid use disorders, and stroke mortality.

- Over time, we are likely to learn of many more indirect health harms in addition to these six. Health harms resulting from increased exposure to Adverse Childhood Experiences (ACEs) during the pandemic are likely to be observed over long time horizons.
- Across the six selected health outcomes, we found large prevalence increases due to the pandemic, ranging from an 11% increase in IPV to a nearly 7-fold increase in homelessness.
- Pandemic-related increases in adult IPV, excessive alcohol use, opioid use disorder and adult depression suggest that today's children are being exposed to elevated levels of ACEs. Mitigation of these growing health harms to adults could have far-reaching effects on their offspring.
- The excess burden of Quality-Adjusted Life Years (QALYs) lost due to the pandemic ranged from 1,200 for stroke mortality to 69,000 for depression per million total population. In the offspring of affected adults, QALYs lost ranged from 3,000 for opioid use disorder to 15,000 for homelessness per million population.
- On the whole, adults with a history of childhood exposure to ACEs can be expected to suffer disproportionately high rates of QALYs lost due to indirect effects of the pandemic.
- The costs of inaction are likely to be significant. The medical and non-medical direct costs associated with pandemic increases in adult depression are an estimated $2.3 billion per one million total population. Costs associated with increased homelessness during the pandemic are $2.2 billion per million total population, while increased costs due to excessive drinking are $1090 million for every million people.

- We studied seven mitigation strategies that are evidence-based and cost-effective for mitigating adult depression, intimate partner violence (IPV), homelessness, excessive alcohol use, opioid use disorders, and stroke mortality.
- Six out of seven of these mitigation strategies proved to be cost-saving within 10 years. Some could achieve a net savings within just one year.
    - Increasing access to a cognitive-behavioral therapy combined with anti-depressant medications for adult depression could yield a large net savings fairly quickly. This is in part because there has been such a rapid increase in the population-wide prevalence of depressive symptoms.
- Increasing the availability of Nurse-Family Partnerships for IPV would yield a net savings within 3 year while buffering more children from exposure to adverse childhood experiences.
- These results should be considered in light of practical considerations (e.g., available workforce).

RAPID is able to provide a range of cost-saving interventions to offer a flexible menu of economically attractive alternatives.

## PROJECT PURPOSE, KEY CONCEPTS, AND SCOPE

This report describes results from the "Rapid Assessment of Pandemic Indirect Impacts and Mitigating Interventions for Decision-making" (RAPID) project. RAPID was conducted by a team at the Philip R. Lee Institute for Health Policy Studies (IHPS) at the University of California, San Francisco (UCSF) for the California Office of the Surgeon General. In this section, we answer key questions about RAPID's background, concepts, and scope.

**What is the "indirect burden" of COVID-19?** Indirect burden refers to health harms not due to the SARS-CoV-2 virus itself, but rather to the biological and psychological impacts of the stress response associated with the COVID-19 pandemic. Stressors of the pandemic (e.g., social isolation, anxiety, loss of schooling and employment) produce neurological, hormonal and immune system dysregulations in the human body that lead to long-term physical and psychological disorders. Additionally, the pandemic has decreased access to health-promoting resources and medical care, and has disrupted healthy lifestyle behaviors, such as healthy eating and physical activity.

**What kinds of stressors has COVID-19 caused?** Several stressors and anxiety-inducing conditions have kept Californians in a high level and prolonged state of uncertainty, distress, and anxiety, including; fear of contracting COVID-19, hospitalization and death; the loss of loved ones; and major disruptions in housing, educational and employment. The economic hardships (lost wages, employment, and financial assets), mass school closures, and loneliness resulting from the need to physically distance create prolonged stressful condition and trigger a chronic stress response. If not properly buffered, exposure to toxic stress will have long-term and cascading health consequences over the life course, in particular on children (more in the background) (Bhushan et al., 2020; Shonkoff 2012).

**There are vast inequities in exposure to pandemic stressors and the long-term health consequences:** A key challenge is that indirect effects of the pandemic fall disproportionately on socioeconomically disadvantaged groups. This exacerbates existing structural racial and economic inequities, thus widening already-large gaps in health between the "haves" and the "have nots" (Nomura 2016). Exposure to increased childhood adversities during the pandemic will also have health consequences that span generations. Adults with a history of exposure to ACEs carry hormonal, metabolic and emotional dysregulations from childhood that can adversely impact the in-utero environment of their offspring as well as childrearing practices (Bhushan et al., 2020). California's children should be prioritized to prevent ACEs and because mitigation efforts made earlier in life increase resilience and obviate the need for costly healthcare later on (Bhushan et al., 2020; Bibbins-Domingo 2020). RAPID seeks to identify mitigation strategies that will reduce these impacts now in order to limit inequities in the toll of human suffering and downstream medical costs for years to come.

**Why a RAPID initiative?** Given the dynamic nature of the COVID-19 pandemic and California's unfolding response, state decision makers require the capacity to anticipate which indirect health impacts will prove especially costly over time and which cost-effective interventions could mitigate

adverse health and financial outcomes for Californians. The overall objective of RAPID is to provide timely simulation analyses to support California state decision making on strategies to mitigate the mid- and long-term indirect health burdens of the COVID-19 pandemic.

**What does the RAPID team offer?** Our team is an interdisciplinary, scientific taskforce. Our policy simulations provide a clear, transparent framework for defining what constitutes a set of foreseeable indirect effects of the pandemic. For this report, we conducted comprehensive reviews of the literature on the current pandemic and select past crises (e.g., natural disasters, economic recessions) to project the most likely indirect health outcomes and their magnitude, helping state officials define public health priorities. A combination of systematic reviews and targeted searches of the literature allowed us to identify high priority and trending public health problems that worsened during the pandemic, identify cost-effective mitigation strategies that are within the state's reach, and develop and apply economic models to project the costs and cost offsets of each intervention strategy.

**Scope of this report:** There is considerable complexity and interconnectivity in the underlying mechanisms through which Californians' health is being affected by the pandemic. Isolating the effects of any single stressor or toxic stress mechanism is not plausible. However, the current moment presents a profound opportunity for mitigating the long-term indirect effect of the pandemic on Californians through sound public policies and programs. The encouraging message of the RAPID team's analyses is that cost-effective mitigation strategies can help individuals, while simultaneously preventing ACEs and ACE-Associated Health Conditions for years into the future.

## REPORT OBJECTIVES

The objectives of this report are:

- **To highlight major indirect effects of COVID-19, specifically conditions that research suggests increased during the pandemic**. Our literature review covers a rapidly expanding number of studies on a wide range of indirect health and social problems resulting from the pandemic, ranging from rising rates of mental illnesses, substance use, stress, cardiovascular diseases, stroke, food insecurity, and more. We selected six key public health priorities – adult depression, alcohol use and substance use, housing insecurity, intimate partner violence (IPV), and stroke. We selected these outcomes because reliable evidence suggests that they are worsening during the pandemic and that substantial human suffering and healthcare costs can be prevented by making cost-effective intervention programs available.
- **To offer short- and long-term perspectives on COVID-19 indirect effects.** Where possible, our analyses focused on health outcomes that are proximal to the pandemic and situated upstream in causal chains of cascading health harms. Mitigating upstream problems, such as homelessness or interpersonal violence, can sometimes achieve positive "spillover" for

consequent problems, such as cardiometabolic diseases or asthma. Research shows that preventing ACEs and mitigating their effects on physiology immediately helps children and adults and can even have mitigate health problems emerging gradually later in life (Bucci 2016; Danese 2008; Miller 2016; National Scientific Council on the Developing Child 2014).

- **To use RAPID's analytic approach and capabilities to bridge the gap between scientific evidence and action.** Over the past months, we invested resources to develop a flexible yet rigorous and timely approach. This model is designed to provide decision makers with timely summaries of the evolving scientific evidence and practical recommendations of cost-effective interventions that can alleviate human suffering and avert the medical costs of treating them.
- **To recommend actions going forward.** The final portion of this report discusses ways that we can expand the current RAPID scope and makes recommendations for next steps. While the pandemic has disrupted our lives and affected our well-being in many different ways, this is just the beginning of what is yet to unfold in months and years to come. As we are wrapping up this phase of the project, we are learning that there is growing recognition of indirect health effects of COVID-19 among researchers, policymakers, and the public. Studies currently show very high margins of excess mortality during the pandemic that cannot be fully accounted for by unrecorded COVID-19 deaths (Modi et al.,2020), suggesting that a significant disease burden is resulting from these indirect effects (Bibbins-Domingo 2020; Khatana et al., 2021, Rice et al., 2020).

## BACKGROUND

As the COVID-19 pandemic continues beyond its first dramatic year, most public health efforts have focused on mitigating the direct health impacts to individuals – preventing and clinically managing infection. However, emerging evidence reveals the profound indirect mental and physical health impacts. The California population has experienced a prolonged period of fear, grief and uncertainty resulting from the pandemic, the social isolation from sheltering-in-place, as well as economic dislocation and hardship. These stressors, among others, can activate the biological stress response which can cause short- and long-term health effects. To mitigate the effects of these adversities, governments can use *macro-level economic policies* (e.g., financial stimulus packages, interest rate reductions, rent, eviction, and mortgage moratoria, relax conditions of debt payments and income taxes); *organization-level measures* (e.g., school enhancements, workplace safety protections); and *public health interventions* that target vulnerable populations for short and long-term remediation. A truly effective, comprehensive policy response requires a thorough understanding of the indirect impacts of the pandemic itself, and of existing COVID-19 mitigation policies, and of the experience with other population-level disasters.

Studies of natural and human-caused disasters, as well as severe economic shocks, find that the health impacts unfold over long periods of time and across multiple generations (Raker 2019; Nomura 2016). A key challenge is that the indirect effects fall disproportionately on socioeconomically disadvantaged groups, exacerbating the longstanding racial and economic inequities that drive health disparities (Nomura 2016). A toxic stress model depicted in Figure 1 predicts that traumatic events, and sustained traumas resulting from stressful social conditions during the pandemic, will have cascading health impacts over the life course, as demonstrated by research on the potentially lifelong effects of toxic stress induced by ACEs (Shonkoff 2012) .

This delayed effect occurs because the early years of life comprise a crucial period during which the human body goes through critical physical, physiological, neurological, behavioral, and emotional development. During this stage, not only are children's bodies more vulnerable to biological pathogens and environmental toxins, they are also more susceptible to certain traumatic events, such as physical or emotional neglect; verbal, sexual, or physical abuse; family dysfunction; and other toxic stressors known collectively as adverse childhood experiences (ACEs)(Felitti et al., 1998). Such experiences not only affect the well-being of children during the early years of their lives. but can also have profound, life-long impact (Hughes et al., 2017; Kalmakis et al., 2015).

**Figure 1: Impact of toxic stress and biological response on the life course**


ACEs have been linked to numerous hard-to-treat or expensive diseases during childhood as well as adulthood. There is ample scientific evidence that exposure to ACEs has profound mental health consequences, such as increased likelihood of depression, suicidal behavior, and substance abuse, as well as increased severity of addiction (Dube et al., 2003; Gerra et al., 2014; Heffernan et al., 2000; Stein et al., 2017). ACEs have also been associated with increased risk for communicable diseases, such as sexually transmitted infections and HIV, as well as non-communicable diseases, such as ischemic heart disease, chronic obstructive pulmonary disease and type 2 diabetes in adulthood (Anda et al., 2008; ; Baldwin et al., 2013; Dong et al., 2004; Felitti et al., 1998). Further, evidence suggests a dose-response relationship between the number of ACEs and certain health conditions – for instance, the greater the

number of ACEs that a child has had, the more likely they are to develop hypertension (Felitti et al., 1998; Almuneef et al., 2014).

The pandemic is exposing more children today to ACEs because of rising rates of family violence, substance use, and emotional distress in parents and other caregivers. Moreover, pandemic stressors have particularly detrimental impacts on adults with histories of ACEs, which are childhood exposures to major stressors encounters (Bhushan et al., 2020). Given that approximately 60% of Californian are exposed to at least 1 ACE and roughly 1 out of 5 have a history of 4 or more ACEs (KidsData, 2021) the potential negative impact of additional stressors due to COVID-19 pandemic in our population can be devastating.

These indirect effects, in addition to the pandemic itself, are falling unevenly across racial and economic groups within California. California's children should be prioritized for intervention(s) because mitigation efforts provided earlier in life are effective at increasing resilience against otherwise costly health consequences that result later in life (Bhushan et al., 2020; Bibbins-Domingo 2020). RAPID seeks to identify mitigation strategies that could be deployed to reduce these impacts now, and to mitigate the human suffering and high public costs resulting from their downstream health effects for years to come.

## APPROACH

**Overview:** The RAPID team developed a novel approach to rapidly synthesize and analyze harms and interventions, in order to provide evidence-based guidance for state policymakers seeking to buffer Californians from the indirect effects of COVID-19. Our approach starts with systematic literature reviews that consider a large number of potential indirect effects on health. Where the literature identifies specific public health priorities, we drill down on key outcome to identify cost-effective mitigation strategies. Then, using publicly available data, we estimate the costs of making no changes in current services and also forecast changes in costs should the state deploy each mitigation strategy. In sum, our approach is designed to reduce uncertainty for decision makers with respects to:

- Compile and synthesis the best available and relevant scientific evidence on the indirect impact of COVId-19 on health
- Analyze the added burden of pandemic stressors on some of our state's leading non-COVID-19 causes of disability and death,
- Estimate the added economic and health burden associated with certain adversities (e.g., adult depression) in offspring,
- Estimate the portion of added burden in adults who have a personal history of ACEs, and
- Provide economic analyses that support California state decision-making on strategies that mitigate the human suffering and high societal costs resulting from current and downstream indirect health harms from the pandemic.

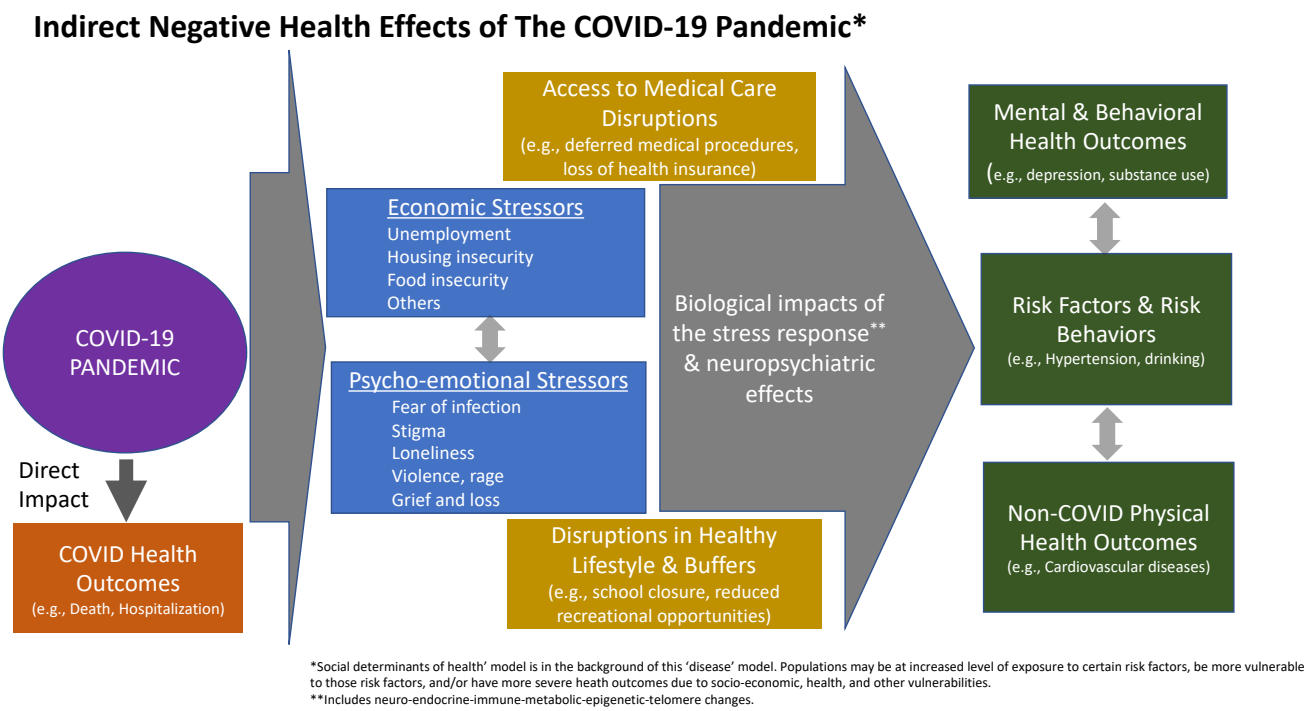
Our approach is intentionally flexible and iterative, allowing the RAPID team to respond to the pandemic's evolving conditions and the state's response. In collaboration with the Office of the California Surgeon General, we build upon the burgeoning literature on COVID-19. This approach will enable California to take advantage of cost-effective mitigation strategies that are guided by the evidence and target specific indirect health outcomes that we know are worsening during the pandemic. Where gaps exist in COVID-19 research in California and the United States, they are filled by targeted reviews of literature from non-US high-income settings (in order to most approximately represent similar social and economic conditions) or prior disasters (e.g., Hurricane Katrina, the 2008 economic recession).

**Conceptual Framework:** For RAPID, we crafted a conceptual framework, shown in Figure 2, that allows us to chart a course through the complexity. It identifies the most prominent causal pathways through which the indirect health effects of the pandemic are likely to unfold. Grandfathered into the framework are pre-pandemic socioeconomic inequities and a longstanding system of structural racism that predisposes many Californians to disproportionately negative health outcomes.

The causal chain starts with the already-visible economic stressors (e.g., unemployment, food insecurity), necessitated by the urgent need to control the direct human toll of COVID-19 via shelter-in-place orders. Also situated upstream are the direct psychological and emotional stressors of the pandemic itself (e.g., loneliness, fear, grief and loss) as well as decreased access to buffering or stress-relieving relationships/environments, lost optimal educational opportunities and social interaction with peers).

These effects of the pandemic itself lead to increased exposure to toxic stress in the population, resulting in biological impacts of the stress response (i.e., neurological, immunological, metabolic, epigenetic, epigenetic, and other changes) which disproportionately affects disadvantaged groups due to predisposing inequities pan. In addition, the pandemic has disrupted access to healthcare, and access to pro-health resources and behaviors that buffer the human organism from stressors (e.g., access to fresh produce, access to nurturing school environment, gyms and playgrounds).This increases the likelihood of risky behaviors (e.g., increased alcohol consumption, stress eating, physical inactivity) and stress-related risk factors (e.g., hypertension, cardiometabolic disorders, increased risk of infection). Distal or downstream outcomes in the causal chain include mental and behavioral outcomes (e.g., depression, substance use disorders) and non-COVID-19 physical health outcomes for all Californians, but especially those subject to predisposing economic and racial inequities.

**Figure 2. RAPID conceptual framework**




# METHODS

We present the methods in two sub-sections: literature review methods and economic forecast modeling using BRACE methods.

## Systematic and Targeted Reviews of the Literature

**Overview:** The focus of our literature reviews was on high-burden, short-term, adverse health conditions that are not the direct health effects of COVID-19 (e.g., death or hospitalization due to the virus or worsening comorbidities). We prioritized studies that provided the most contextually relevant information (e.g., US-based) and had relatively higher-quality data (e.g., reported a reasonable baseline). An additional subset of articles were captured through targeted searches to expand our data on specific

outcomes of interest. When no US data was available for key outcome categories or their quality was uncertain, we utilized studies from outside the US.

We collected and analyzed data extracted via two different types of literature searches. Review #1 systematically reviewed pre-reviewed literature on the current COVID-19 pandemic with the last update on August 13, 2020. Review #2, up to February 25,2021, involved targeted and ongoing searches of a variety of data sources to inform the economic modeling and also identify relevant studies to fill gaps from Review #1 for the effects of COVID-19, upstream risk factors, and effects of interventions (Table 1).

**Table 1. Sources of literature and search strategy**

| | **Systematic Review #1 (COVID-19 era)** | **Targeted Review # 2 (Before & after COVID-19)** |
|---|---|---|
| **Last Updated** | August 13, 2020 | Feb 25, 2021 |
| **Approach** | Systematic | Targeted |
| **Objective** | Identify COVID-19 specific data | Identify relevant studies to fill data gaps |
| **Data type** | Indirect health impacts | Upstream risk factors, effects of other disasters, cost-effective interventions |
| **Publication time frame** | March 2020 forward | 2010 forward |
| **Search platforms** | PubMed, Embase, EconLit, grey literature | PubMed, Embase, EconLit, Cochrane, Google scholar |
| **Study type** | All | All |
| **Settings** | US + select OECD countries* | US + OECD* |

* Organization for Economic Cooperation and Development countries included/excluded based on 2020 membership

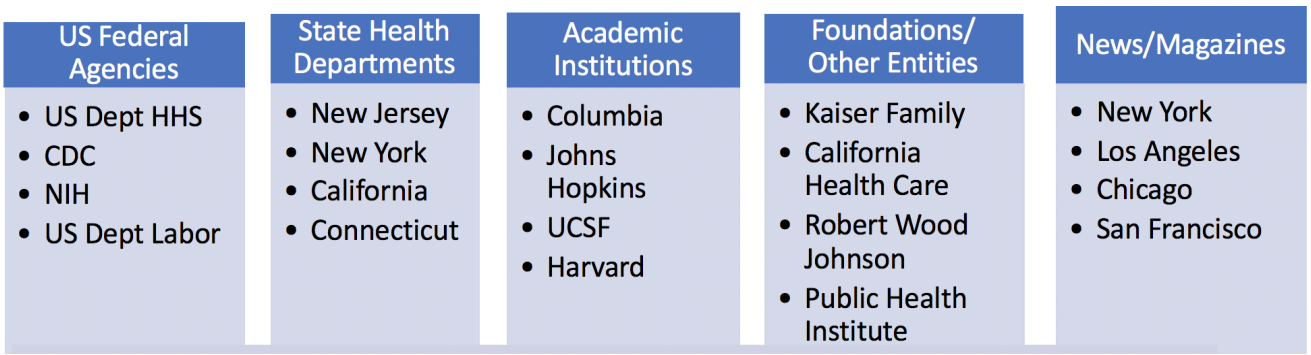
**Database search strategies:** Our search strategies were based on Cochrane guidance, which is the global standard for systematic review methodologies (Higgins 2019). Review #1 (COVID-19 era) involved a comprehensive search of studies on the current pandemic using PubMed, Embase and EconLit. PubMed fully indexes "medRxiv," which is a preprint server that allows us to gather emerging, but not yet peer-reviewed, health sciences articles. Our systematic search was conducted on July 28, 2020 and again on August 13, 2020

to expand the range of search terms (see Appendix A). It captured scientific papers published between March 1, 2020, through December 31, 2021, thus including some with advanced publication dates. We placed no restrictions on language or publication status, pre-print vs. published in peer-reviewed journals. The full list of search terms, as well as number of studies can be found in Appendix A.

**Citation management and study screening:** After conducting these searches, we imported all records into EndNote citation management software and removed duplicate records. We exported all remaining records to an Excel spreadsheet. Pairs of reviewers independently screened titles and abstracts, applying the review's inclusion criteria (see Appendix B), and judged whether to exclude records or advance them to the next level of scrutiny. Reviewers resolved disagreements about study eligibility through discussions. Additional reviewers stood ready to serve as neutral arbiters, if necessary.

**Use of grey literature:** Grey literature on the current pandemic includes scientific and other kinds of documents published outside the mainstream peer-reviewed literature. This search and results were used to supplement rather than become part of the formal data synthesis, in which we consolidated information drawn from high quality peer-reviewed papers. Grey literature is potentially inexhaustible, necessitating prescribed limits on these searches. We used the same outcome keywords listed in Appendix A in combination with advanced Google search syntax for specific sources such as certain US health federal agencies, state health departments, and others. Figure 3 provides an overview of the entities searched for in the grey literature.

**Figure 3. Review #1 grey literature search strategy**

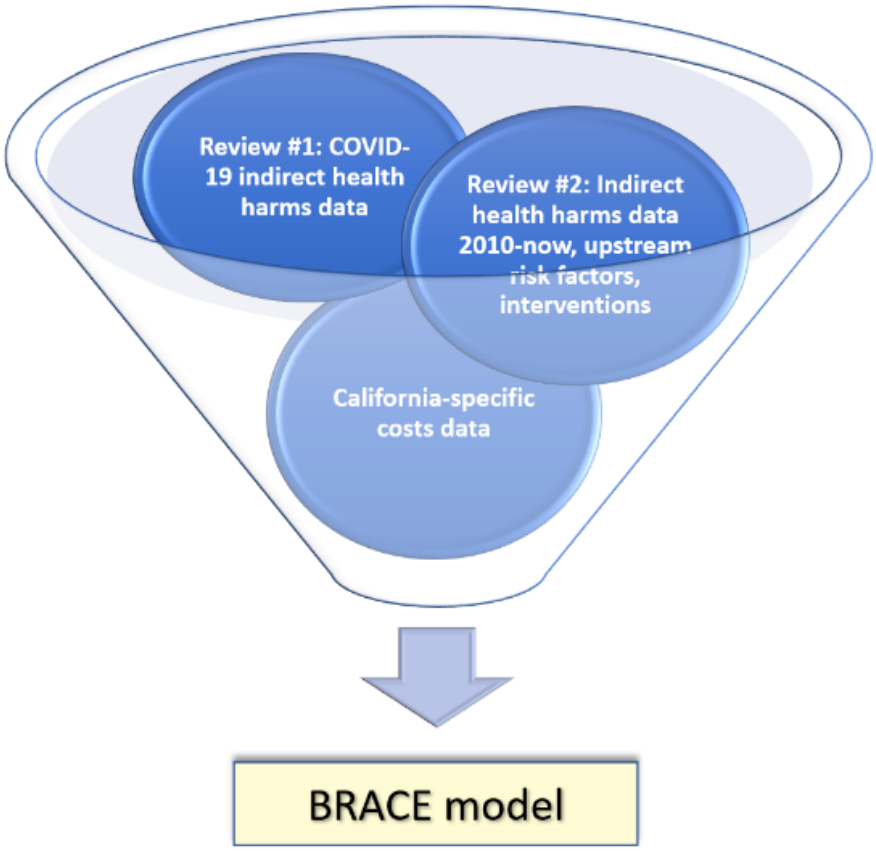



**Data extraction process:** To capture relevant data from the literature, we used a systematic data extraction and synthesis approach. One reviewer extracted data into pre-structured Excel spreadsheets, extracting key information about each study's population, outcomes, methodology, effect size, characteristics of the included population, risk factors, specific outcomes, and data needed to calculate risk ratios (RR) and 95% confidence intervals (CI). This extraction process included data on both risk factors and health conditions (see Appendix A and B for types of conditions) that may indirectly have been affected by COVID-19, and interventions that might ameliorate those effects.

**Data synthesis**: To synthesize and distill extracted data, we followed a multi-step process, starting with "Study Sheets." This is the most granular level of data extraction and includes all potentially relevant information. The process ended with a "consolidated sheet," which includes more simplified and distilled findings from studies and an assessment of the strength of evidence. Where data were available and it was mathematically possible to do so, we **transformed effect size estimates into risk ratios** to allow for comparisons across outcomes and intervention effects, and to provide inputs for our modeling. This might involve, for instance, comparing prevalence between control and treatment groups, or between subgroups, to examine disparities. An electronic supplement is available upon request.

**Strength of evidence assessment**: For each outcome that reached the highest level of data distillation, we conducted a high-level assessment of the strength of evidence. The intention was to assess the trustworthiness of evidence for high-level decision-making in an expedited manner. We considered both the external validity (directness) and internal validity (risk of bias) of the evidence. For outcomes that were further aggregated into single data points for economic modeling, we added measures for the consistency of all available evidence, the precision of the aggregated point estimate (i.e., width of the confidence interval), and the number of data points available for aggregation. Overall strength of evidence was scored on a four-point scale ranging from very low, to low, moderate, and high. A detailed outline of our methodology for our strength of evidence assessment is in Appendix C.

**Figure 4: BRACE model inputs**




**Collection and synthesis of other data to inform economic models:** Our general methods for Review #2was similar to Review #1 with the main objective of identifying relevant epidemiologic and intervention effect input data for the economic models. The interventions that we extracted data on and included in our modeling were identified through a combination of input from

content area experts and a review of relevant public organization recommendations (e.g., SAMHSA website, US Surgeon General reports, US Veterans Administration/Department of Defense treatment guidelines). We then examined the relevant literature on each intervention, prioritizing systematic reviews and meta-analyses, ultimately extracting data on at least one intervention per condition. In choosing interventions, we identified either a prevention intervention and/or one treatment intervention for each selected condition, taking into consideration the built-in constraints on rolling out programs in the context of the pandemic

## Health and Economic Forecast Modeling Methods: BRACE

We developed a health and cost simulation modeling tool designed specifically to portray COVID indirect effects, called BRACE (Broad & Rapid Analysis of COVID-19 Indirect Effects). The BRACE model uses a cost-effectiveness framework then can portray any condition exacerbated by the pandemic (e.g., depression, opioid use disorder), including short and long-term effects in adults and offspring, as well as the cost and health impacts of interventions (e.g., rent support or counseling). It produces estimates of costs (direct medical and non-medical) and health outcomes (e.g., deaths, quality-adjusted life years) for specified interventions. The model can specify the extent of mitigation interventions. Sensitivity analyses are used to estimate how inputs uncertainties affect results. Components of BRACE analyses are divided into three major categories:

- **effects of pandemic on selected indirect health outcomes and their costs on affected adults and their offspring**
- **health and cost savings of deploying recommended mitigating interventions, and**
- **health and cost burden in adults with a history of ACEs.**

**How the pandemic affects selected indirect health outcomes and their costs**: The following models include the prevalence of the condition before the COVID-19 era ("pre-COVID-19"), derived from epidemiologic studies, and estimates of the effect of COVID-19 on the condition ("post-COVID-19"), based on the risk ratio derived from the literature review. Health effects are standardized into quality-adjusted life years [QALYs], which combine morbidity (decreased health state utility for specified durations) and mortality (likelihood and associated QALY loss), yielding life expectancy estimates weighted for the burden of disease. QALYs allows for comparison across different diseases and interventions, making this standardization especially useful in analyzing the diverse impacts of the COVID-19 pandemic on society.

Costs are considered from a societal economic perspective, rather than costs to specific actors (e.g., the State or insurers). The costs are categorized into short-and long-term medical and non-medical direct.

- ***Short-term Costs:*** For all six priority public health conditions, condition-specific cost estimates included the short-term medical costs (e.g., ambulance, emergency room visits, medicine) and non-medical costs (e.g., police intervention, prison) for individuals

experiencing each of the six conditions. These costs are expected to be incurred in the first year and is not discounted.

- ***Long-term Costs:*** We estimated the percentage of individuals who will experience long-effects from each of the conditions and calculated long-term medical costs and non-medical costs (electronic supplement can be provided upon request). These long-term costs are assumed to be incurred after a mean of 10 years, discounted at a 3% discount rate, and adjusted to net present value.
- ***Future Cost of ACEs:*** To estimate the cost incurred by children who experience ACEs due to the spillover effect of adult depression, alcohol use and substance use, housing insecurity, and IPV, we estimated the percentage of individuals who will experience the spillover effect and the long-term medical and non-medical costs. The costs resulting from spillover effects are assumed to be incurred 25 years in the future, discounted using a 3% discount rate, and adjusted to net present value.
- ***Contribution of past ACEs:*** We also estimate the portion of short-term disease burden that can be attributed to past exposure to ACEs (i.e., during the childhood of current adults, increasing the current risk of various ACEs-affected conditions such as depression).
- ***Productivity Loss:*** Economic cost of productivity loss was noted when relevant, although not included in sums, due to overlap with QALYs.

Application of various U.S. cost estimates to our modeling allowed us to link a wide range of data sources to our California perspective.

The primary sources for measuring medical and non-medical costs of depression, alcohol use and substance use, housing insecurity, IPV, and stroke mortality to society were peer-reviewed publications and grey literature studies, which often provided California-specific cost information described above. For most of the conditions, only documented economic burdens of conditions and diseases between 2008 and 2020 were included; the only exception is the cost estimates for alcohol consumption. This inclusion criterion ensured that the cost estimates were time-relevant and applicable during the COVID-19 pandemic. Concomitantly, this inclusion criterion allowed us to capture the impact of the 2008 “Great Recession.” Cost estimates for alcohol consumption were derived from as early as 1996 as more recent data were not measured by individual cost and cannot be accurately incorporated into the models in this study.

In cases where no published cost information was available for medical costs, Medi-Cal payment rates from the Medi-Cal fee schedule, which is published and updated monthly by the California Department of Health Care Services, were used. For each condition, the relevant medical treatments that are commonly required and utilized were identified. For these treatments, we then determined the associated Current Procedural Terminology (CPT) codes, a medical code set that is used to report medical, surgical and diagnostic procedures and services, and the related unit cost(s) and basic rate(s). For treatments that can be billed with multiple CPT codes, the full range of possible costs were documented, and the mean costs were employed to estimate cost per individual.

National and, if necessary, selected international data, were utilized to calculate individual costs when no California-specific data is available. If available in the future, confidential cost data from the government of the State of California can be used to enhance the calculations. All cost estimates were adjusted for inflation, converted to US dollars (if necessary), and presented in 2020 US dollars.

Estimated outcomes pre-COVID-19 are calculated by applying these cost and health outcomes data to the pre-COVID-19 prevalence. Estimated outcomes post-COVID-19 are calculated by applying the cost and health outcomes to the post-COVID-19 estimates.

**Health and Cost Savings of Deploying Recommended Mitigating Interventions:** The intervention effect measures the changes in outcomes that may result from implementation of specific mitigating interventions, including lowered prevalence and the cost per person of the intervention. For all but one intervention, we consider the effects of partial implementation (e.g., 20% of the impacted population served). The approach to estimating intervention costs follows the same approach as condition costs. Peer-reviewed publications and studies in the grey literature were used. CPT codes and related Medi-Cal unit cost(s) and basic rate(s) were used to calculate intervention costs when no existing calculations are available. The cost of interventions (e.g., cognitive behavioral therapy, housing) are estimated and assumed to be incurred in year one and are thus not discounted.

Interventions can result both in financial savings (due to reduced medical and social service expenditures when the prevalence is lowered, for example) and in better health outcomes (e.g., improvement in QALYs). If the **intervention cost exceeds savings**, we calculate a cost-effectiveness ratio: net cost per QALY gained. If the **intervention cost is less than the savings**, the intervention is described as "dominant," meaning that it is both: 1) less expensive than doing nothing and also 2) produces better health outcomes. Finally, the model scales up the per-person estimates to calculate the anticipated costs, savings, and QALYs gained per population size (e.g., 1 million).

**Health and cost burden in adults with a history of ACEs:** The BRACE model accounts for health and cost burden that can be attributed to ACEs. The model uses the prevalence distribution of ACE scores in the population and associated relative risks for a specific health condition in adulthood to calculate the portion of prevalence of the condition due to ACEs (compared to 0 ACEs). The number is applied to the overall added prevalence of the condition due to COVID to calculate the absolute risk due to ACEs exposure.

# RESULTS

We present study results in two sub-sections of findings: Literature review and economic forecast modeling using BRACE results.

## Literature Review Findings

Database searches for both reviews yielded 15,803 records. After removing duplicates, we reviewed the titles and abstracts of 11,662 records. We applied the aforementioned inclusion criteria, excluded 11,128 records and reviewed the full texts of 534 articles. Of these, 93 articles were eligible for data synthesis as they reported a range of significantly worsened mental and physical health outcomes, as well as significantly worsened social determinants of health. (Table 2 depicts our screening process).

In these studies, we discerned three broad pathways through which indirect health harms could be explained, and categorized studies accordingly: 1) Psychological and emotional stressors (46 studies); 2) disruption in access to healthcare (38 studies); and 3) disruption in healthy lifestyle (9 studies). Appendix D provides frequency of these categories by geographical setting.

**Table 2. Review process leading to extracted studies for the effect of COVID-19 on health**

| | Initial search (March1, 2020 - July 28, 2020) | Expanded search (August 13, 2020) | Targeted search (as-needed from July - February 2021) | Total |
|---|---|---|---|---|
| Initial records identified | 13,203 | 2,600 | -- | 15,803 |
| Duplicates removed | 3,013 | 1,128 | -- | 4,141 |
| Titles & abstracts reviewed | 10,190 | 1,472 | -- | 11,662 |
| Full text reviewed | 454 | 80 | -- | 534 |
| Provisionally included for data extraction | 109 | 12 | 17 | 138 |
| Included for data synthesis | 72 | 4 | 17 | 93 |

**Key take-aways from the literature review:** Although limited in quantity, mixed in quality, and not directly measured among Californians, we found that a variety of disease control efforts that were implemented to mitigate the COVID-19 pandemic, as well as other stressors, likely resulted in serious and wide-ranging indirect health harms. At a time of great uncertainty and crisis as the country and as

policymakers were coming to terms with what public health measures to pursue, including school and business closures, mandatory shelter-in-place orders, and other government efforts, there was wide-ranging fear and stress that many people developed in reaction to inconsistent public health messaging about the pandemic. Additionally, mass media and social media misinformation also contributed to these harms. In the past year, California's people have likely experienced elevated rates of out-of-hospital acute cardiovascular events; worsened stroke outcomes; decreased cancer screening; increased depression, anxiety and suicidality; increased substance use; increased intimate partner violence; and many other kinds of indirect health harms arising from pandemic control efforts. Table 3 briefly summarizes key findings in regard to specific health conditions that have likely worsened during the pandemic, as well as our level of confidence (strength of evidence) in the validity and contextual relevance of these findings. Following this table, we provide a bulleted narrative synthesis of health conditions that have likely worsened, as well as conditions within six health domains (mental health; acute stress; heart disease; diet and exercise; diabetes; communicable disease) where there is mixed evidence. A detailed summary of key findings from each included study can be found in Appendix C.

**Relevance of our key findings in the context of the literature review timing and buffering programs:** It must be acknowledged that most of our included studies were published relatively early in the COVID-19 era and are therefore limited to the first stage of the pandemic response. Even so, there is little reason to suppose that the indirect health harms facing Californians would have abated, with continued or renewed lockdowns and other restrictions in response to multiple epidemic surges and new virus variants, as well as with the initial delays in vaccine rollouts. Indeed, there is every reason to believe that they have likely been exacerbated by the continuing societal and economic upheaval, and uncertainties about the pandemic. We should also acknowledge that these indirect effects are taking place in the context of some important buffering effects of different waves of State and Federal programs, including direct financial assistance, deferred rental and mortgage payments, extended unemployment benefits and many others. However, there are many who continue to experience great societal upheaval.

**Note about health disparity:** Few studies reported data relevant to health disparities. Of six studies with any such data, four made passing mention to indicate that they did not find disparities (Bhatt 2020; Boyarsky 2020; Hamm 2020; Luchetti 2020). Two additional studies did not explicitly consider disparities in health status or outcomes among groups but did report relevant data. For these studies, our analysis included a visual inspection of reported differences in estimates rather than a formal analysis. (See Appendix F).

| Table 3. Brief key findings from the literature review for health conditions worsened during the COVID-19 pandemic | | |
|---|---|---|
| | **Key findings** | **Confidence** |
| **Mental health (16)** | Large increase in rates and severity of depression and anxiety as well as pediatric behavioral complaints | **HIGH** |
| **Stroke (14)** | Large decrease in presentation of patients with stroke and large increase in worsened discharge outcomes, including stroke mortality | **HIGH** |
| **Acute stress, loneliness and burnout (9)** | Large increase in acute stress, fear, loneliness and burnout | **HIGH** |
| **Heart disease (9)** | Large decrease in presentation of patients with heart disease and large increase in out-of-hospital cardiac events | **HIGH** |
| **Intimate partner violence (7)** | Large increase in reports of intimate partner violence | **HIGH** |
| **Social determinants of health (7)** | Increased food insecurity, job loss | **HIGH** (food insecurity) to **VERY LOW** (homelessness, job loss) |
| **Substance use (7)** | Increased substance use and opioid-related emergency response | **MODERATE** |
| **Suicide and self-harm (7)** | Increased suicidal ideation and suicide risk | **LOW** |
| **Dietary and exercise habits (6)** | Decreased physical activity | **MODERATE** |
| **Emergency care (5)** | Large decrease in emergency department encounters | **HIGH** |
| **Diabetes mellitus (4)** | Increased severe diabetic ketoacidosis in children | **MODERATE** |
| **Child maltreatment (2)** | Increased child maltreatment, increased case severity | **HIGH** |
| **Chronic respiratory illness (2)** | Decreased pediatric asthma-related emergency visits | **LOW** |
| **Communicable disease (2)** | Decreased routine childhood immunizations | **HIGH** |
| **Organ donation (2)** | Increased wait times for those on organ donation list | **HIGH** |
| **Cancer (1)** | Delay in treatment, visits, testing for women with ovarian cancer. | **MODERATE** |
| **Musculoskeletal disorders (1)** | Decreased elective orthopedic surgeries | **MODERATE** |
| **Risk of violence (1)** | Large increase in firearm purchases | **LOW** |

## Narrative synthesis of the literature on the indirect harms of the COVID-19 pandemic

Below we provide a brief summary of the key findings from the 93 included studies. Expanded narrative summaries for each can be found in Appendix E.

**Mental health (13 US studies, three non-US studies):**

- Five studies found significantly increased anxiety or depressive symptoms in general populations (Almandoz 2020; Czeisler 2020; Farewell 2020; Kaparounaki 2020; Liu 2020).
- Eight studies found elevated anxiety or depressive symptoms in subpopulations of women, young adults, healthcare workers in COVID-19 wards, people with pre-existing mental health conditions, people who identify as transgender or non-binary, and other subgroups (Alonzi 2020; Asmundson 2020; Di Tella 2020; Fitzpatrick 2020; Flentje 2020; Huckins 2020; Kaparounaki 2020; Pierce 2020).
- A US Census Bureau study found that respondents were three times as likely to screen positive for anxiety or depressive disorders in the pandemic era, compared to the same period in 2019 (Twenge 2020).
- One nationally representative US survey found worsened parental mental health and child behavioral health co-occurring in nearly 10% of families (Patrick 2020).
- CDC surveillance data showed a sharp rise in pediatric mental health-related visits, compared to the same period in 2019 (Leeb 2020).
- In a cohort of older adults with known depression, one study found no change in depression scores, compared to the previous year (Hamm 2020).

**Stroke (thirteen US studies, one non-US study):**

- Aside from one single center which saw a slight increase in stroke presentation, investigators in all studies found an overall decline in emergency room presentation and admission rates for patients with acute stroke, with rates dropping by approximately 15%-45% in the COVID era study populations (de Havenon 2020; Desai 2020; Esenwa 2020; Friedlich 2021; Ghanchi 2020; Hsiao 2020; Jasne 2020; Nagamine 2020; Nguyen-Huynh 2020; Siegler 2020; Uchino 2020).
- Several studies found that among those presenting for the treatment of acute stroke, mortality rates were increased, discharge outcomes were significantly worse, and time to definitive treatment was delayed (Agarwal 2020; Friedlich 2021; Kerleroux 2020; Nagamine 2020; Siegler 2021).

**Acute stress, fear, loneliness (nine US studies):**

- Eight studies found increased self-reported stress, anxiety symptoms and loneliness in adults, including healthcare providers (Civantos 2020; Emerson 2020; Fitzpatrick 2020; Killgore 2020a; Killgore 2020b; Park 2020; Schechter 2020; Tull 2020). Lockdowns were associated with greater self-reported health anxiety, financial worry, and loneliness (Tull 2020).
- Significantly more fear of COVID-19 was reported in participants who were younger, female, Asian-American, Hispanic, foreign-born, in families with children, or who were caregivers (Fitzpatrick 2020; Park 2020).

- One study found no significant mean change in loneliness in adults over age 65 by the third week of lockdown (Luchetti 2020).

**Heart disease (seven US studies, two non-US studies):**

- Five studies found significant decreases in emergency room presentation and hospital admission rates for acute ischemic heart disease or acute coronary syndrome, with an average decline of 33% observed (Bhatt 2020; Braiteh 2020; de Havenon 2020; Kessler 2020; Legutko 2020).
- Two studies found increased rates of delayed presentation to care and a three-fold increase in out-of-hospital cardiac arrests, with fatality rates exceeding 90 percent (Braiteh 2020; Lai 2020).
- One study found that patients with stress cardiomyopathy during the COVID-19 pandemic had a longer median hospital length of stay compared with those hospitalized in the pre-pandemic period (Jabri 2020).
- One study found worsened prognostic indicators among patients with heart failure (AlMufleh 2020).
- One article found an increase in sleep duration, thought to correlate with improved cardiac health (Advani 2020).

**Intimate partner violence (five US studies, two non-US studies):**

- Specific trends differed, but five studies found increases in arrests, police reports, and/or calls to crisis centers in regard to intimate partner violence (Boserup 2020; Buttell 2020; Leslie 2020; Piquero 2020; Usher 2020).
- One study estimated that nearly 1,000 cases of intimate partner violence went unreported in Chicago, Illinois in March and April 2020 (Bullinger 2020).
- In the United Kingdom, one study found that in the first six weeks of that country's lockdown, sexual assault referral centers saw a 50% decrease in referrals (Johnson 2020).

**Social determinants of health (seven US studies):**

- Two studies had mixed findings in regard to crime rates in US cities, ranging from a 54% decline in Nashville, Tennessee to a 40% increase in Louisville, Kentucky; and finding no significant change in the volume of police calls for petty crime (Ashby MPJ 2020; Mohler 2020).
- One study found that San Francisco Bay Area residents after the first lockdown were significantly more likely than residents of other US states to report increased difficulty in obtaining groceries. This study also found that Bay Area respondents were less likely to report job losses or wage decreases (Elser 2020).
- Using Google Trends data, researchers in one study found that searches for terms related to job loss and unemployment were up very sharply (Halford 2020).

- In one study, households with children reported increases in moderate to severe food insecurity and decreases in employer-sponsored healthcare for children, with nearly one-quarter reporting a loss of regular child-care (Patrick 2020).
- In one study, households with new food insecurity were significantly less likely to accept food or money from friends or family, sign up for government programs, or get food from a food pantry (Niles 2020).

**Substance use (six US studies, one non-US study):**

- Five studies found increased self-reported substance use or increased proportion of emergency department visits for alcohol-related problems (Czeisler 2020; Dumas 2020; Lechner 2020; Pollard 2020; Smalley 2020).
- Two studies found an increased percentage of ambulance calls for adverse outcomes of substance use, such as overdose-related cardiac arrests and calls where naloxone was administered. Both studies found a temporal relationship of increased fatal overdoses to implementation of lockdowns (Friedman 2020; Glover 2020).

**Suicide and self-harm (six US studies, one non-US study):**

- Three studies found elevated proportions of participants with recent suicidal ideation or high suicide risk scores (Czeisler 2020; Fitzpatrick 2020; Gratz 2020).
- Increased suicidal ideation was more likely to be reported among racial minorities, young adults, essential workers, those with self-reported confrontations with their partners, those with serious legal problems, and those concerned about life-threatening illness in their family or friends (Bryan 2020; Czeisler 2020; Fitzpatrick 2020).
- Compared to the year before, one study found sharp increases in internet searches using terms relevant to suicide prevention services (Halford 2020).
- Investigators in one study found that as a percentage of all emergency department encounters, suicidal ideation encounters decreased during the pandemic era. They theorized that this was related to fear of the pandemic and delayed care-seeking, rather than a decrease in actual suicidal ideation (Smalley 2020).
- Using historical findings from the Great Recession, investigators in Canada found a one percent increase in suicide rates for every one percent increase in unemployment and estimated that there may be more than 2,000 excess suicides in that country as an indirect harm of the COVID-19 pandemic (McIntyre 2020).

**Dietary and exercise habits (four US studies, two non-US studies):**

- Four studies found through self-reports and tracking data that across study populations, there was an overall increase in sedentary lifestyles during lockdowns (Almandoz 2020; Di Stefano 2020; Gallo 2020; Huckins 2020).

- One study analyzing Google Trends data found an increased interest in physical activity that peaked within two weeks of the pandemic and remained above pre-pandemic levels (Ding 2020).
- One study analyzing positional tracking data found a small decrease in patronage of unhealthy eating establishments (Ashby NJS 2020).

**Emergency care (three US studies, two non-US studies):**

- A CDC report from early in the pandemic highlighted significant reductions in the presentation of heart attacks (down 23%), stroke (down 20%), and uncontrolled high blood sugar (down 10%) (Lange 2020).
- One study found an estimated 42% overall decline in emergency department visits at the peak of the initial lockdown periods across the nation (Hartnett 2020).
- Investigators in Italy, early in the pandemic, found a 37% decrease in emergency department patient volume (Franchini 2020).
- A study in Australia found a 47% decrease in emergency department presentations among pediatric patients in the months following lockdowns (Cheek 2020).
- One study found that admissions for pediatric fractures were down by more than 50% at one large East Coast hospital (Bram 2020).

**Diabetes mellitus (four non-US studies):**

- A German study found an 82% increase in the incidence of diabetic ketoacidosis in children, a severe complication of uncontrolled Type 1 diabetes mellitus that can result in death (Kamrath 2020).
- Investigators in Spain and Italy found improved blood glucose levels or glycemic control in their subset of adult patients with Type 1 diabetes during the initial lockdown (Fernandez 2020; Bonora 2020). Investigators in Greece studying a sample of children found no significant difference in these measures (Christoforidis 2020).

**Child maltreatment (one US study, one non-US study):**

- CDC investigators found that despite an apparent significant drop in pediatric emergency department visits related to child abuse and neglect during the pandemic, the proportion of these visits (among all ED visits) increased above the 2019 baseline in all age groups. Notwithstanding the drop in all pediatric emergency admissions related to child abuse and neglect, hospitalizations for child abuse and neglect did not decrease in 2020, suggesting that injury severity did not decrease during the pandemic. Indeed, the proportion of ED visits related to child abuse and neglect resulting in hospitalization increased significantly among children and adolescents under age 18 (Swedo 2020).
- Investigators in the UK found an increased incidence of pediatric abusive head trauma in the month that country entered its initial lockdown (Sidpra 2020).

**Chronic respiratory illness (two US studies):**

- One study found a significant increase in daily controller inhaler use during the early months of the pandemic (Kaye 2020).
- One study found a nearly 85% decrease in pediatric asthma-related emergency department visits. Investigators theorize that the decline was likely related to fear of seeking care during the early months of the pandemic, combined with a decrease in community spread of viral illnesses known to trigger asthma exacerbations (Oreskovic 2020).

**Communicable disease (two US studies):**

- One study found a significant decline in vaccine administration and lower rates of up-to-date immunization status among children, with disparate impacts on children with public insurance (Bramer 2020).
- One study commented on the delay in care and services seen among a subset of patients with HIV. Notwithstanding this delay, the same study found improved adherence to antiretroviral therapy (Kalichman 2020).

**Organ donation (two US studies):**

- Two studies found that the US organ donation system has been negatively impacted by the pandemic, with the potential for significant downstream effects, due to the lack of viable organs for donation and increased wait times for those on the organ donation list (Ahmed 2020; Boyarsky 2020).

**Cancer (one US study)**

- One study found that one-third of ovarian cancer patients experienced delays in some component of their cancer care, including delays in physician appointments, lab testing, and required imaging (Frey 2020).

**Musculoskeletal disorders (one US study):**

- One study found that patients from six surgical centers reported hospital- or surgeon-initiated cancellation or postponement (86%) of elective orthopedic procedures, such as hip and knee replacements. Only 14% of patients reported having initiated the cancellation or postponement (Brown 2020).

**Risk of violence (one US study):**

- One study found that firearm purchases had increased 63% over the expected volume (Schleimer 2020).

**Prioritizing Specific Health Outcomes for Economic Forecasting:** We used a systematic approach to identify six high-priority indirect public health outcomes that are increasing in prevalence due the

pandemic: adult depressive symptoms, excessive alcohol use, opioid use disorder, homelessness, intimate partner violence, and stroke mortality. We confined our economic forecasting analyses to estimate the health and cost impacts of these in six health outcomes although many others are likely to be affected by the pandemic. See Appendix G for detailed data on the increased risk and associated strength of evidence.

Table 4 provides a summary of inclusion criteria used to make decisions about which health conditions to subject to the economic forecast modeling. Rows in the table represent a broad range of indirect health outcomes that could theoretically be affected by the pandemic. Along the rows, we show a combination of criteria used to narrow down the list of possible indirect health outcomes to a feasible number.

**Table 4: RAPID priority- setting decision matrix**
***conditions selected for BRACE modeling**

| | # of Studies | Change in Prevalence Due to COVID | Life Years Lost due to the Condition | Disability-Adjusted Life Years Lost due to Condition (DALYs) | Association with 4+ ACEs |
|---|---|---|---|---|---|
| | | **Relative Risk** | **YLL** | **DALYs per 100,000, Both Sexes, All Ages** | **Odds Ratio for Adults** |
| **PUBLIC HEALTH CONDITION** | | | | | |
| ***Mental health problems (e.g., mood or anxiety disorders)** | 17 | Increased | 6.4 | 701.8 [depressive disorders]<br>583.6 [anxiety disorders] | 3.7 [anxiety]<br>4.7 [depression] |
| **Heart disease** | 9 | Presentations decreased, severity increased | 121.9 [hypertensive]<br>347.9 [Ischemic] | 2,061 [Ischemic heart disease] | 2.1 [cardiovascular disease] |
| ***Stroke** | 9 | Presentations decreased, severity increased | 138.4 | 935.3 | 2.1 [cardiovascular disease] |
| **Acute stress, fear, and loneliness** | 8 | Increased | _ | _ | 3.7 [stress] |
| ***Intimate Partner (IPV)** | 7 | Increased | 1.5 per episode | 369.5 [IPV] | 7.5 [violence victimization]<br>8.1 [violence perpetration] |
| ***Alcohol and drug consumption** | 7 | Increased | 655 [alcohol]<br>1232 tobacco]<br>110 [illicit drugs] | 1,278.5 [drug use disorders]<br>405.7 [alcohol use disorders] | 6.8 [problematic alcohol use]<br>10.2 [problematic drug use] |
| **Suicide/self-harm** | 7 | Increase in suicidal ideation, suicide prevalence not yet clear | 304.5 | 463.8 [self-harm] | 37.5 [suicide attempt]<br>10.5 [suicidal ideation] |
| **Dietary and exercise habits** | 6 | Decreased | _ | _ | 1.1 [physical inactivity] |

| | | | | | |
|---|---|---|---|---|---|
| **Emergency care use** | 5 | Decreased | _ | _ | 2.8 [high ER use] |
| **Homicide/Crime** | 4 | Reduction in calls for service, projected increase in gun injuries | 190.4 | – | 630.1 [road injuries]<br>540.2 [falls] |
| **Diabetes mellitus** | 4 | Unknown | 105.4 | 1,099.1 [diabetes] | 1.4 |
| **Child maltreatment** | 2 | Increase in rate in UK and severity in US (one study each) | **–** | **–** | **–** |
| **Organ and blood donation** | 2 | Decreased | _ | _ | _ |
| **Communicable diseases** | 2 | Vaccinations decreased | 49.4 [other infectious diseases, excluding TB] | – | – |
| **Chronic respiratory disease** | 2 | Presentations decreased | 474.1 | 1,083.9 [COPD]<br>413.4 [asthma] | 3.1 (2.5 - 3.8) |
| **Musculoskeletal disorders** | 1 | Presentations decreased | 41.9 | 1,040.6 [other musculoskeletal disorders] | _ |
| **Food insecurity** | 1 | Increased | _ | _ | _ |
| **Cancer** | 1 | Access to / use of care decreased | 920.2 [all cancers] | 774.5 [lung cancer] | 2.3 |
| **Hypertension** | 0 | Unknown | _ | _ | _ |
| **Neurological disorders** | 0 | Unknown | 364.7 | 727.0 [headache disorders]<br>525.1 [Alzheimer's diseases and other dementias] | _ |
| **Digestive diseases** | 0 | Unknown | 64.8 | | 2.8 |
| **Substance use disorders** | 0 | Unknown | 624.4 | 1,278.5 [drug use disorders] | – |
| ***Housing insecurity** | 0 | Unknown but projected to increase | 345 PYLLs per 1000 person-years of observation | – | 3.9 |
| **Unintentional injuries** | 0 | Unknown | 245.3 | 630.1 [road injuries]<br>540.2 [falls] | 2.6 |
| **Maternal/neonatal diseases** | 0 | Unknown | 395.6 | 362.7 [neonatal disorders]<br>16.2 [maternal disorders | – |
| **Skin and subcutaneous disorders** | 0 | Unknown | 15.7 | 191.1 [dermatitis]<br>116.7 [viral skin diseases]<br>77.9 [other skin and subcutaneous diseases] | – |

| | | | | | |
|---|---|---|---|---|---|
| **Nutritional diseases** | 0 | Unknown | 7.4 | 51.0 [dietary iron deficiency]<br>34.5 [protein-energy malnutrition]<br>10.5 [other nutritional deficiencies] | – |
| **GUIDE:**<br>-indicates there was not enough information to fill in cell.<br>* indicates the public health conditions that were selected for the BRACE model.<br>**# STUDIES**: The number of COVID-era studies published and gray-literature studies showing changes in rates of the condition during the pandemic.<br>**INCREASE UNDER COVID (RR)**: If available in the literature, the relative risk of the condition after the pandemic as compared to pre-COVID.<br>**RANKED CAUSE OF DEATH IN CA**: Rank in causes of death for Californians as estimated by IMHE, 2017.<br>**YEARS OF LIFE LOST PER 100K**: Years of life lost due to the condition as estimated by California Community Burden of Disease and Cost Engine.<br>**ASSOCIATION WITH ACE**: Degree of correlation between condition and adverse childhood experiences based on reviews of the literature.<br>**DALYs:** Disability adjusted life-years | | | | | |
| Sources for YLL: IHME Data, California Community Burden of Disease and Cost Engine, Hibbs 1994, Single 1999<br>Sources for OR for 4+ ACEs: Hughes 2017, Miller 2020, Chartier 2010<br>Sources for DALYs: IHME Global burden of disease | | | | | |

As Table 4 suggests, decisions about which conditions to pursue were constrained by the availability of rigorous and robust studies conducted during the pandemic that showed significant increases in the prevalence of a given health outcome. We want to underscore that the prevalence of many health outcomes in Table 4 are likely to be increasing during the pandemic. It may simply be too early for studies to document this. There is ample anecdotal evidence, for example, that food insecurity has substantially increased over the course of the pandemic. However, there were no available studies properly quantifying this phenomenon at the time that we completed our first review of the literature (July 2020) that would allow inclusion in the economic forecasting effort. Chronic conditions that may take years to manifest as diagnosable illness, such as heart disease, could take years before the primary impacts of the pandemic are observable in data showing an increased prevalence. For now, given sheltering-in-place and population-wide fears of contracting COVID-19 in hospitals, all that can be observed are reductions in cases presenting to clinical care and an uptick in their severity.

Once we established that there was research evidence showing that a given health outcome is increasing due to the pandemic, we privileged health conditions with a larger overall footprint of harm to population health, using a combination of life years lost and disability-adjusted life years lost as metrics. Finally, we considered the association between childhood exposure to ACEs and each health outcome manifesting in adulthood. ACEs exposure serves as a key indicator of population vulnerability to stressors of the pandemic. People with high levels of ACEs exposure (4 or more during childhood) are also likely to belong to groups that entered the pandemic with greater susceptibility to prolonged stress, including low socioeconomic status and racial minority status (Jones 2020; Baldwin 2021).

## Economic Forecast Modeling Using Brace Results

We applied the BRACE model to the six priority public health outcomes as indicated above. In this section, we summarize the degree to which the prevalence of these conditions are increasing, the

associated costs, the costs and benefits of mitigating interventions, and the special vulnerabilities of individuals exposed to ACEs. Please see Appendix H for detailed interventions included in BRACE model.

**Increased Indirect Health Harms and Medical/Non-Medical Costs of COVID-19:** The human toll of the pandemic in California due to indirect health effects appears to be profound when characterized in terms of rising prevalence (based on the relative risk during COVID vs. pre-pandemic) and QALYs lost. Table 5 depicts the short- and long-term health burden associated with the six priority health conditions with increasing prevalence during the pandemic. The largest relative change in prevalence is in homelessness. As a rough estimate, as many as 700 thousand Californians have or will fall into homelessness due the pandemic (our calculation, based on the reported absolute 2.2% rise in homelessness prevalence applied to the California population). Increasing prevalence rates are next followed by relative changes in opioid use disorder (OUD), stroke mortality, and depressive symptoms.

There are increases of 11% (IPV) to nearly sevenfold (homelessness) in these important problems. Leveraging simulation techniques to circumvent data limitations, our models suggest that there are broad indirect health consequences of the pandemic: across these six conditions, total QALYs lost is more than 250 thousand per million population.

**Table 5. The human toll: increased indirect health harms due to the COVID-19 Pandemic**

| Priority Public Health Condition Indirectly Affected by COVID | Relative Risk: Change Under COVID | Change in Proportion of Population Under COVID | Excess Quality-Adjusted Life Years (QALYs) Lost Due to COVID (Per Million Population)* | |
|---|---|---|---|---|
| | | | QALYs Lost in Affected Adults | QALYs Lost in the Offspring of Affected Adults |
| Depressive symptoms | 1.37 | 0.0685 | 69,000 | 10,000 |
| Intimate partner violence | 1.11 | 0.0061 | 52,000 | 5,000 |
| Homelessness | 6.67 | 0.0215 | 17,000 | 15,000 |
| Excessive alcohol use | 1.19 | 0.0116 | 26,000 | 4,000 |
| Opioid use disorder | 1.63 | 0.0069 | 28,000 | 3,000 |
| Stroke mortality | 1.53 | 0.0001 | 1,200 | n/a |

*Values in each column are the sum of 1-2 years and longer-term outcomes

While the risk ratio for homelessness (RR=6.67) is increasing dramatically, it is estimated that more QALYs are lost due to depression (69,000 QALYS lost) and IPV (52,000 QALYs lost) (Table 5). The number of QALYs lost due to depression and IPV in affected adults is followed by 15 thousand QALYs lost on the offspring of homeless adults, and 10 thousand of the offspring of depressed people (see Appendix I for details). Change in stroke mortality during COVID-19 is also high in relative terms, however the overall increase in QALY burden is not as pronounced as other public health conditions considered.

Our analysis suggests that the medical and non-medical direct costs of *not* acting now to scale up evidenced-based mitigation strategies could be substantial (recall that productivity losses were not assessed). Table 6 summarizes our projections of the long- and short-term costs associated with each of the six priority public health conditions, assuming no additional steps are deployed to address rising rates. The most pronounced estimated costs could result from failing to mitigate rising rates of depressive symptoms in the adult population. While the cost-per-episode of depressive symptoms from an individual, patient perspective may look small, when taking into account the medical and non-medical, short- and long-term costs incurred, including long-term for children of depressed adults, the costs significantly stand out. Overall, medical and non-medical direct costs for adults due to increases under COVID-19 is approximately $2.3 billion per one-million population. Note that this refers to the total population, not just those affected by depression. The magnitude of these costs are largely due to the sheer magnitude of the excess prevalence of depressive symptoms due to the pandemic. Estimated rates of adults reporting one or more depressive symptom have increased by nearly 7% during the pandemic (from 18% pre-pandemic to 25%). Because increased depressive symptomology is a common problem in the general population (about one in six people suffer from it), the increase in societal costs due its rising prevalence under COVID-19 are very high.

Still, other public health problems, such as homelessness, are also likely to incur significant medical and non-medical costs if mitigation strategies are not deployed. Even though homelessness has a lower QALY burden than some other conditions, it could impose a large economic burden if not fully addressed. Increased rates of adult excess drinking during the pandemic are also projected to $1090 million per one million total population, with children exposed to these adults during the pandemic incurring $74 million per million population of adults.

**Table 6. Costs of doing nothing: estimated societal costs from indirect health harms of the COVID-19 pandemic**

| Priority Public Health Condition Indirectly Affected by COVID | Cost per Episode | Excess Societal Costs Due to COVID (Per Million Total Population)* | |
|---|---|---|---|
| | | Societal Costs Incurred by Affected Adults | Societal Costs Incurred by the Offspring of Affected Adults |
| Depressive symptoms | $34,160 | $2,231M | $107M |
| Intimate partner violence | $123,340 | $699M | $47M |
| Homelessness | $102,360 | $2,154M | $51M |
| Excessive alcohol use | $100,420 | $1,090M | $74M |
| Opioid use disorder | $83,000 | $551M | $24M |
| Stroke mortality | $16,770 | $1M | n/a |

*Values in each column are the sum of 1-2 years and longer-term outcomes

**The Health and Economic Impacts of Acting Now to Scale Up Mitigation Strategies:** For each of the six public health conditions, there is at least one strategy to reduce the expected increases in societal costs, achieve a net savings to society, and minimize the number of QALYs lost due to these conditions. While it is true that some of these health and cost burdens have already been incurred, the sooner mitigation occurs, the more suffering and long-term costs can be averted. Moreover, intervening now on any of these conditions will not only benefit individuals who have newly acquired these conditions during the pandemic, but also people who were affected before the start of the pandemic, hopefully arresting increases in severity. The BRACE model included prevalence estimates for both individuals who acquired the condition during the pandemic and individuals who suffer from the condition regardless of COVID-19. The interventions described will lead to health improvements for both of these groups, and therefore would be beneficial even in the absence of a pandemic.

Our economic forecast models examined the impact of a range of evidence-based and cost-effective interventions which are possible to scale up even if sheltering-in-place orders remain in place. Furthermore, where appropriate, we opted for secondary prevention approaches that would be helpful in arresting the progression of pandemic-acquired new cases towards chronic, high-severity problems. In general, our analysis found while some interventions are much more expensive per case than others, all of the recommended interventions will not only reduce human suffering but also will yield significant net savings in medical and non-medical costs. These estimates could be conservative because productivity losses were not assessed.

Table 7 provides a high-level summary of our economic forecasting results. Note that all intervention outcomes shown, except for the public awareness campaign for reducing stroke mortality, assume that the intervention's reach is confined to 20% of adults affected by each condition, scaled to a total population of one million adults (which includes people with and without the condition). Since it is difficult, if at all possible, to limit the reach of a public awareness ad campaign to only individuals affected by the condition, for this we assumed 100% reach and adjusted the cost of intervention to reflect the cost per person at risk for stroke. The 20% target for intervention penetration of the affected adult population is a somewhat arbitrary number intended to be ambitious but realistic. (Note that the 20% reach assumption can be easily modified upon request and BRACE results can be recalculated.) For example, for one million adults, if the prevalence of a condition is 2% (i.e., 20 thousand affected adults), we assume the intervention reaches 20% of them (i.e., 4 thousand adults).

**Table 7. Mitigation strategies: health and economic losses averted by scaling up evidence-based intervention programs**

| Priority Public Health Condition Indirectly Affected by COVID | Intervention Cost Per Affected Adult | Outcomes from Intervention Programs That Reach 20% of Affected Adults (Per Million Total Population)* | | |
|---|---|---|---|---|
| | | **QALYs Gained** | **Intervention Costs** | **Cost-Effectiveness v. Doing Nothing** |
| **Depressive symptoms** | | | | |
| Cognitive-Behavioral Therapy + Antidepressants | $878 | 14,481 | $44.5M | Cheaper and better |
| Mindfulness Meditation | $200 | 1,207 | $10.1M | Cheaper and better |
| **Intimate partner violence** | | | | |
| Nurse-Family Partnership | $13,489** | 24,208 | $164.7M | Cheaper and better |
| **Homelessness** | | | | |
| Rent subsidies | $9,282 | 3,171 | $47.1M | Cheaper and better |
| **Excessive alcohol use** | | | | |
| Screening and brief intervention | $452 | 5,625 | $6.6M | Cheaper and better |
| **Opioid use disorder** | | | | |
| Medication-Assisted Treatment | $15,669 | 6,284 | $56.2M | Cheaper and better |
| **Stroke mortality** | | | | |
| Public Awareness Campaign | $98*** | 388 | $14,350 | Cheaper and better |

*Except for stroke, which assumes 100% coverage of those at risk for stroke

**Cost per family

***Cost per person at-risk of stroke

As Table 7 shows, the largest health gains are likely to result from intervening in IPV, followed by treating depressive symptoms. Gains from intervention to prevent stroke mortality are more modest due to the rarity of the condition assessed and the modest effects of intervening through a public awareness campaign; however, the intervention is still a dominant strategy. Notably, all of the interventions appear to save money while improving health, in part because models accounted for both short- and long-term medical and non-medical direct costs in adults and their offspring.

Table 8 shows the magnitude of savings associated with reaching 20% of the affected adults in a total population of one million adults affected or not. Note the exception for the stroke intervention which, as a public awareness campaign, targets all of the adults at risk. The first column of Table 8 shows the costs of scaling up the intervention to 20% of affected adults per million population. Intervention costs for IPV are substantially greater than for other interventions, while the costs of an awareness campaign for stroke prevention are fairly low. The next three columns show net savings over one, three

and ten years. The "net" savings represent the intervention costs (from column one) and dollars saved due to averted medical and non-medical services. A positive value means net savings (not costs).

We recognize that decisions about public investments in health interventions reflect a variety of considerations both practical (e.g., available workforce) and political. The range of cost-saving interventions thus offers a flexible menu of economically attractive alternatives.

All of the interventions appear to save money while improving health, mainly because models included both short- and long-term medical and non-medical direct costs in adults and their offspring. For all six conditions, the magnitude of net savings accrue over time. All but two interventions will yield net cost savings within three years. Once again, the largest savings from are associated with providing CBT and antidepressants to people experiencing depressive symptoms. By ten years, all but one intervention (mindfulness) provides net cost savings—mindfulness also saves money, eventually, after ten years. The greatest savings come from providing a combination of CBT and antidepressants to 20% of people suffering from depressive symptoms. Within one year, $61.5 million could be saved by providing this intervention. Alternatively, within one year, $9 million could be saved by providing SBIRT to individuals experiencing increased alcohol use.

**Table 8. Projected economic savings from scaling up evidence-based interventions in three tme periods**

| Priority Public Health Condition Indirectly Affected by COVID | Economic Outcomes from Intervention Programs that Reach 20% of Affected Adults (Per Million Total Population)* | | | |
|---|---|---|---|---|
| | Intervention Costs | Net Savings Over 1 Year | Net Savings Over 3 Years | Net Savings Over 10 Years |
| **Depressive symptoms** | | | | |
| Cognitive-Behavioral Therapy + Antidepressants | $44.5M | $61.5M | $163.7M | $246.5M |
| Mindfulness Meditation | $10.1M | *- $10.1M* | *- $7.5M* | *- $3.4M* |
| **Intimate partner violence** | | | | |
| Nurse-Family Partnership | $164.7M | *- $69.8M* | $5.3M | $59.6M |
| **Homelessness** | | | | |
| Rent Subsidies | $47.1M | *- $4.2M* | $47.0M | $95.3M |
| **Excessive alcohol use** | | | | |
| Screening and Brief Intervention | $6.6M | $9.0M | $53.9M | $110.9M |
| **Opioid use disorder** | | | | |
| Medication-Assisted Treatment | $56.2M | *- $36.0M* | *- $10M* | $15.7M |
| **Stroke mortality** | | | | |
| Public Awareness Campaign | $14,350 | $147,500 | $228,500 | $242,000 |

*Except for stroke, which assumes 100% coverage of those at risk for stroke

**COVID-19 and Adverse Childhood Experiences (ACEs):** The final analyses consider health and dollar costs attributable to ACEs. Table 9 shows the anticipated lifelong burdens attributable to the current exposure of today's children to adult conditions that have increased due to the pandemic. Far and away, children today exposed to IPV in their adult caregivers will experience the largest health losses, and well into their futures. QALYs lost are 0.77 per adult episode of adult IPV. Most of this QALY burden results from increased morbidity (0.72 QALYs). Homelessness and excessive alcohol use also result in significant health losses, ~1/3 QALYs lost. The last two columns of Table 9 shows these same costs in a different metric that takes into account increases in the population prevalence of each condition due to COVID-19. Since increases in depressive symptoms are very common during the pandemic, the excess health and economic costs associated with them are the largest.

**Table 9. Life-long health and economic burdens due to ACEs in the offspring of adults suffering health harms due to the COVID-19 pandemic**

| Priority Public Health Condition Indirectly Affected by COVID | Lifelong Costs and QALYs* Lost for the Offspring of Adults Due to ACEs Exposure (Per Adult Episode of Each Condition) | | Excess Burdens for the Offspring of Adults Due to Increased ACEs Experienced During COVID (Per Capita) | |
|---|---|---|---|---|
| | QALYs Lost | Costs Incurred | QALYs Lost | Costs Incurred |
| Depressive symptoms | 0.12 | $1,558 | 0.009 | $107 |
| Intimate partner violence | 0.77 | $7,774 | 0.005 | $47 |
| Homelessness | 0.29 | $2,390 | 0.006 | $51 |
| Excessive alcohol use | 0.27 | $6,417 | 0.003 | $74 |
| Opioid use disorder | 0.34 | $3,455 | 0.002 | $24 |
| Stroke mortality | n/a | n/a | n/a | n/a |

*Quality-adjusted life years

Table 10 depicts pandemic costs and health burdens attributable to adults with a history of one or more ACEs. Current adults who carry from childhood a history of exposure to ACEs are uniquely vulnerable to the stressors and indirect health effects of the pandemic. A history of ACEs represents a form of "host susceptibility" to stress-related conditions. Adults with a history of ACEs therefore constitute a vulnerable population during the pandemic.

For each of the six conditions, the proportion attributable to a history of ACEs is relatively large, near or above 50%, except for stroke (second column). The third column shows the absolute increase in adult prevalence for each condition that may be attributable to having a history of one or more ACEs. The added prevalence of depressive symptoms is the greatest due to its large increase during the pandemic as well as its strong association with adverse events during childhood.

The final two columns represent the excess health and economic costs due to the pandemic for the adult population carrying a history of ACEs. Under COVID-19, an additional 41,250 QALYs per million

total population will be lost due to the proportion of depressive symptoms associated with a history of ACEs; the associated costs incurred will be $1.2 billion dollars.

**Table 10. Disproportionate harms of the COVID-19 pandemic on vulnerable populations: adults with a history of ACEs**

| Priority Public Health Condition Indirectly Affected by COVID | Proportion of Overall Prevalence Attributable to Adults with a History of ACEs | Increase in Prevalence Under COVID Attributable to Adults with a History of ACEs | Excess Burden Under COVID Attributable to Adults with a History of ACEs (Per Million Population) | |
|---|---|---|---|---|
| | | | Quality-Adjusted Life Years Lost | Costs Incurred |
| Depressive symptoms | 53% | 0.036 | 41,250 | $1,236M |
| Intimate partner violence | 51% | 0.003 | 29,160 | $382M |
| Homelessness | 46% | 0.010 | 14,280 | $1,015M |
| Excessive alcohol use | 53% | 0.006 | 16,020 | $622M |
| Opioid use disorder | 41% | 0.003 | 12,860 | $239M |
| Stroke mortality | 12% | 0.00002 | 241 | $845K |

**Sensitivity analyses:** Economic forecasting models, by design, make a variety of assumptions to achieve estimates and projections that can help decision makers anticipate the consequences of their policy decisions by weigh the costs and benefits of various courses of action. Sensitivity analysis is used to understand how assumptions made in economic forecasting models could be influencing the estimates produced. Because no one can accurately predict the future, it is worthwhile to provide metrics that capture the degree of uncertainty surrounding the estimates above.

The sensitivity analyses that we conducted on the BRACE model results involved computer simulations of the of error surrounding results from each analysis. In one-way sensitivity analyses, each input was varied individually while all others were kept constant. The values included in the sensitivity analyses were obtained through a robust review of the literature; in cases where a reliable value could not be identified, expert opinion was used to inform input values. For example, a one-way sensitivity analysis on the efficacy of a public awareness campaign for stroke showed that even when the benefits are one tenth as much, the intervention still saves both QALYs and costs. A detailed report, including the workbook where we collected all of the BRACE inputs and their sources, as well as all sensitivity analyses conducted, is available as a technical supplement upon request.

Figure 5a represents the possible QALYs gained compared to the overall net savings for each of the interventions using multivariate sensitivity analysis that simultaneously vary all input variables based on probability distributions. This allows a comparison of health benefits and economic savings of

alternative mitigation strategy, while also reflecting the uncertainty associated with estimates of each. Each cloud of points is comprised of 5000 rounds of computer simulation of the intervention model, thus reflecting all estimated uncertainties. Larger clouds suggest a greater absolute degree of uncertainty in estimates for each intervention, which compared with the midpoint values indicates relative uncertainty.

The orange cloud, for example, shows results for the nurse family home visiting intervention for IPV. It indicates a rough midpoint of 20,000 QALYS gained and $150M in savings per one million population; the range in QALYs is 3,000-40,000 with a range between $100M in added costs and $300M in net savings. CBT for depression has a similarly wide dispersion in the results cloud, but with greater overall net savings.

**Figure 5a. Multivariate sensitivity analyses on QALYs gained and net savings gained from possible state investments by type of intervention**

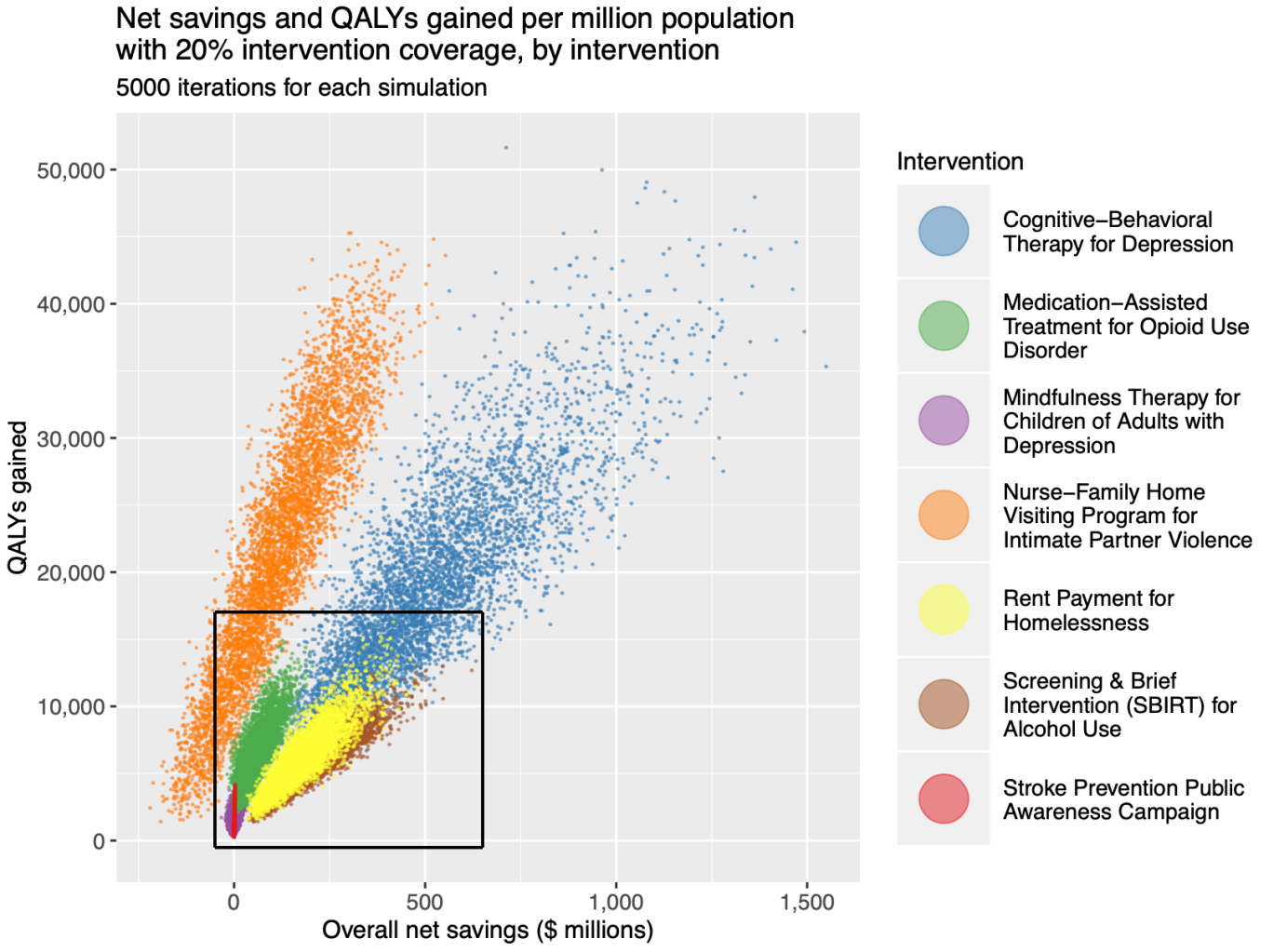
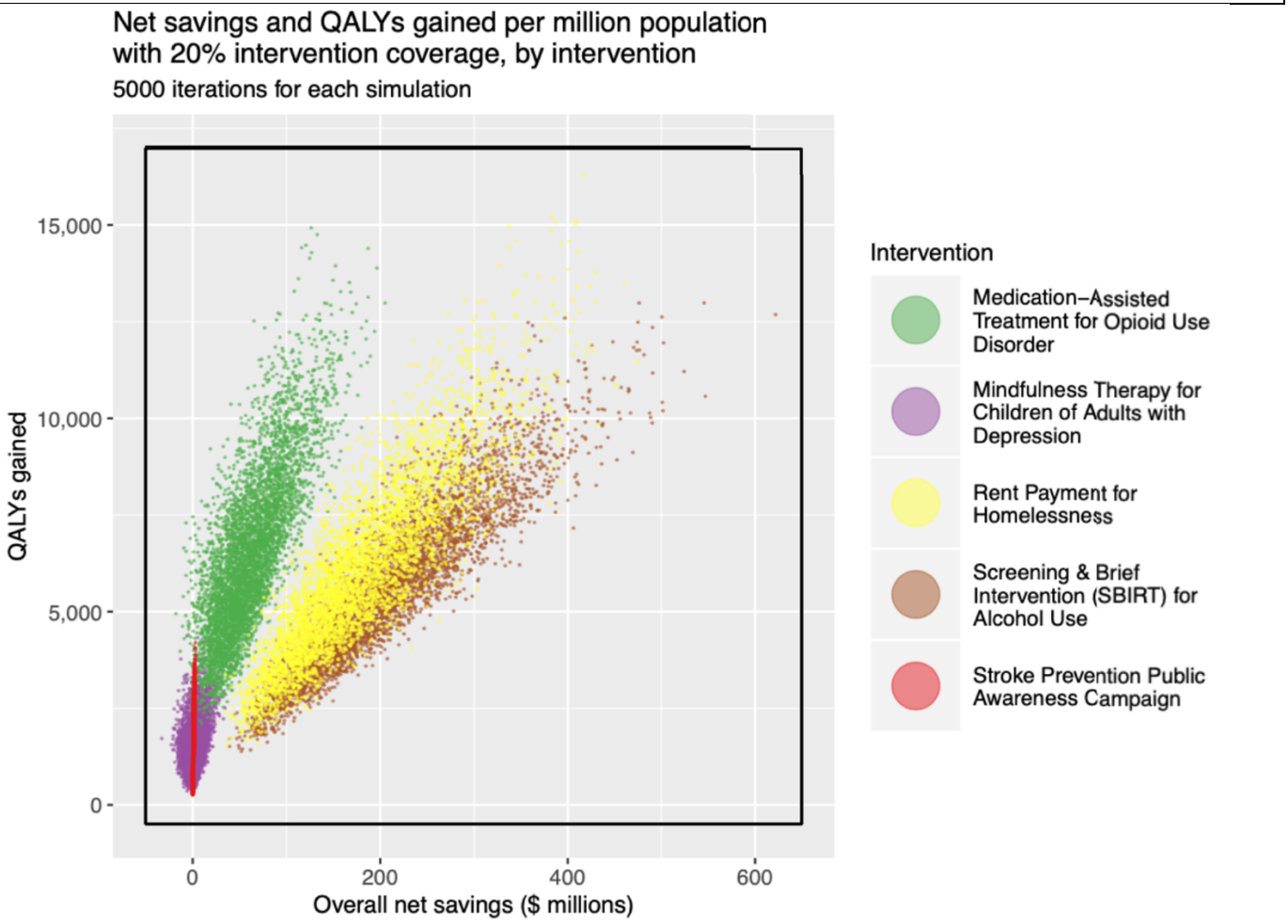


Figure 5b is a closer look at the box in Figure 5a, to reveal differences between smaller clouds of points. It appears that SBIRT for alcohol may yield comparatively greater dollar savings than the other interventions in this subset. The dispersion of the clouds again reflects the degree of uncertainty in estimates. Medication-assisted treatment for OUD has a rough midpoint of 7,000 QALYs gained (with a range of 3,000 to 11,000) and $75M in net savings (with a range of $0-120M)

Overall, results from the multivariate sensitivity analyses indicate that interventions reliably save both QALYs and medical and non-medical costs. This suggests that the State of California has a variety of options for excellent mitigation strategies. Considerations of program feasibility and priority may be especially important, since all interventions are life-improving and cost-saving.

Importantly, this set of results assumes equal coverage (20%) of the interventions across all relevant target populations, except for stroke, since a public information campaign would not be limited to a percentage of the population. This may or may not be realistic, given constraints on human resources and scale-up processes. Please see Appendix I for detailed analysis of BRACE model results.

**Figure 5b. Multivariate sensitivity analyses on QALYs gained and net savings gained for a subset of five State investments**



# SUMMARY

The objective of RAPID is to assess wide-ranging indirect effects of the COVID-19 pandemic in California to support policymakers in making evidence-based decisions within an ever-changing and increasingly urgent environment. While the immediate concerns with preventing COVID-19 infection and saving lives will continue to have high priority and vaccinations holding some welcoming relief, our state's needs will increasingly shift towards timely responses to the indirect health effects of the pandemic, given their magnitude and the racial and socioeconomic disparities being exacerbated. It is imperative that as new evidence about these indirect effects becomes available, California decision makers have access to scientific evidence in forms that are useful for guiding both short- and long-term policy responses. Simply put: we are at the beginning of a long period of challenges for Californians and citizens will continue to look to the government for solutions.

We conceptualized and applied a comprehensive methodological and analytic model to major public health problems that are increasing as indirect effects of the pandemic: adult depression, intimate partner violence (IPV), housing insecurity (homelessness), alcohol use, opioid use disorders, and stroke mortality. We selected the six health-related outcomes in consultation with the OSG because reliable current evidence suggests that they are worsening as a result of the pandemic and have had wide-ranging impact upon those living in California. These were also selected based upon criteria of their burden, their immediacy, quality of evidence, and availability/feasibility of near-term action. We also opted for outcomes that are proximal outcomes of the pandemic, situated upstream in the causal chain of cascading health harms.

In this report, we provide summaries of the quality of existing evidence related to each problem, identify the accumulated costs associated with the condition due to COVID-19, and the potential for investing in evidence-driven interventions that could mitigate further harms, and their long-term cost-effectiveness. We also identified data, research, and intervention study gaps that will be important to track as new information emerges. Uncertainty, which is inherent in all forms of economic modeling and forecasting analysis, was recognized and incorporated in our estimates given the evolving nature of the pandemic, as well as risk of bias and heterogeneity in model inputs. Each of these components will benefit from continuing dialogue and feedback on ways to refine and maximize the utility of RAPID's research for California decision-makers.

Our preliminary economic analyses of six conditions project that the health and cost burdens of these conditions are increasing, both in the short-term and long-term, due to the COVID-19 pandemic. The human toll of the pandemic in California due to indirect health effects appears to be profound when characterized in terms of increases during COVID vs. pre-

pandemic (ranging from an 11% increase for IPV to a nearly 7-fold increase for homelessness) and Quality-Adjusted Life Years (QALYs) lost in affected adults (ranging from 1,200 for stroke mortality to 69,000 for depressive disorders) and in the offspring of affected adults (ranging from 3,000 for Opioid disorder to 15,000 for homelessness). Overall, medical and non-medical direct costs for adults due to increases under COVID-19 is approximately $2.3 billion per one-million population (the total population, not just those affected by depression). Other public health problems, such as homelessness, are also likely to incur significant medical and non-medical costs if mitigation strategies are not deployed: homelessness ($2.2 Billion), adult excess drinking ($1090 million), IPV ($699M), Opioid Use Disorder ($551M), and stroke mortality ($1M) per one-million population.

While it is too early to find concrete measurements of the extent to which pre-existing racial/ethnic and socioeconomic disparities in these conditions are being exacerbated during the pandemic in California, there is good reason to suspect that these gaps are widening due to the disproportionate degree that the economic dislocations associated with the pandemic are affecting already vulnerable groups. Fortunately, there are cost-effective mitigation strategies that can reduce both human suffering and total costs to the state. Our broad review of the literature suggests that there have been significant increases in risk of a wide range of additional physical and behavioral health conditions that we have not yet subjected to complete analysis (Chronic obstructive pulmonary disease (COPD), loneliness, and anxiety), many of which will contribute to the further accumulation of health and cost burdens to California in coming years. For conditions with substantial health and economic burdens, mitigating interventions that serve only even a portion of the population might still yield substantial health benefits and savings greater than costs.

When analyzing these interventions, wherever there exist available data, the model takes into consideration the intergenerational effects of adult conditions on children in their care and estimates the long-term economic and health burdens that could be averted. For example, for adult depression, the BRACE model incorporates the burden of a caretaker's depression on a child exposed and highlights how an intervention not only improves the health condition of the caretaker suffering from depression but also leads to ACE(s) averted in the child. Similarly, for IPV, the cost of healthcare for IPV-associated toxic stress was considered.

The encouraging message of these analyses is that cost-effective mitigation strategies can treat patients while preventing ACEs and ACE-Associated Health Conditions in the children for many years into the future. Results from these first analyses underscore the critical importance of monitoring such intergenerational effects on economic and health burdens, as evidence on additional indirect health impacts of the pandemic become available. Our analysis also suggests that the medical and non-medical direct costs of not acting now to scale up evidenced-based mitigation strategies could be substantial assuming no additional steps are deployed to address rising rates.

## Using RAPID Results for Decision Making

Results from the RAPID modeling effort point to a range of public health conditions that are increasing in prevalence as indirect effects of the pandemic. For each, we have offered suggestions for evidence-based mitigation strategies that could be implemented immediately, even under continuing orders for Californians to shelter in place. For each mitigation strategy, we have provided economic projections of the direct health costs and short- and long-term savings for California. Here, we offer some considerations and suggestions for how decision makers might utilize RAPID findings in and propose additional ways that RAPID can support sound decision-making going forward.

Our forecasting analysis suggests that there could be substantial human and economic costs for failing to mitigate six health conditions known to be increasing due to the pandemic: adult depression, intimate partner violence (IPV), homelessness, excessive alcohol use, opioid use disorders, and stroke mortality. Pandemic-related increases in adult conditions related to interpersonal violence and substance abuse suggest that today's children are being exposed to elevated levels of ACEs, thus compounding harms to the population. We considered seven mitigation strategies that are evidence-based and cost-effective for the upstream mitigation of these indirect effects of the pandemic. Six out of seven of these mitigation strategies would begin to net cost-savings within 10 years. Some could achieve a net savings within just one year. There is thus a range of cost-saving mitigation strategies, offering a flexible menu of economically attractive alternatives

- **Consider Implementation Barriers:** RAPID findings estimate the cost and effectiveness of interventions, as well as the trade-offs between interventions, assuming the implementation of each intervention occurs within the general population of California. However, depending upon the condition, target population, and context, a wide range of implementation barriers will come into play. For example, mitigation strategies that require in-person contact will be challenging if specific populations are not confident in and decline to receive coronavirus vaccination, as could be the case for some of the most vulnerable populations in California. Community acceptability and geographic consideration must be considered alongside the cost-effectiveness of interventions. There exist methods for gradual scaling-up and implementation gaps analyses that can assist decision makers in anticipating and trouble-shooting these barriers.
- **Weighing Upstream and Downstream Mitigation Strategies:** Economic tools (e.g., earned income tax credit, enhanced unemployment benefits) and primary and secondary prevention are upstream interventions that have unique advantages in the current context. These upstream interventions tend to reach a broader swath of the population, address multiple health outcomes at once, and may have lower administration costs. Upstream interventions are particularly valuable for building

population resistance to stressors on health that unfold over time (e.g., exposure to family violence, depression) which are critical for preventing the long-term costs of exposure to ACEs. Our analysis shows that some ACEs (e.g., exposure to domestic violence, substance abuse) have clearly increased during the pandemic. These added exposures will result in an increased health and cost burden for decades if not mitigated as soon as possible in children. When considering results from the BRACE model, which estimates the cost and effect of each of conditions separately, one should consider leveraging upstream mitigation strategies that may generate benefits across multiple conditions. Further analyses should model the additive effects of multiple ACES because the research literature has established clear thresholds (e.g., 4+ ACEs) for predicting health consequences later in life, as well as the clear cumulative impact of multiple traumas and adversities.

- **Alignment with Existing Efforts**: The costs of interventions were calculated assuming no cost-sharing and assuming that the costs were paid by a single payer. However, there are many platforms and systems of care that are already supporting or enhancing efforts at ameliorating the indirect health impacts of the pandemic. Examples of these systems include ACEs Aware, as well as new efforts to better coordinate community agencies under Community of Caring. Far greater efforts are needed to assure that disparities and system inequities receive higher priority, particularly in communities that have experienced even greater burdens in shouldering the impacts of the pandemic. Insights from RAPID should be incorporated and synchronized with existing programs and systems of care. These efforts can leverage existing infrastructure, reduce redundancy, and potentially lead to large health impacts and cost-savings if streamlined and coordinated. For example, synergistic alignment could be obtained by working with trainers in the ACES Aware program to ensure that trainers are incorporating the most up-to-date research data in the capacity-building services they provide. This evidence can help to identify areas that improvements can be made via public health campaigns and engagement of most affected communities. We partner with state stakeholders engaged with public campaigns and mass education about the implications of our findings and to inform types of public health messaging to reach diverse populations.
- **Evaluation, Monitoring and Feedback**: In addition to ongoing planning and research that builds from RAPID, we recommend that the state establish a tracking and evaluation system, with built-in quality improvement strategies, to ascertain how policy interventions are being implemented (e.g., with fidelity to the original model, considerations of workforce availability, priority population and geographic spread). The state should use evaluation data to refine and improve interventions to assure that those needing support actually receive it. As always, it is important to demonstrate concrete returns on investment for preventative health services, which while typically

quite large, can easily become taken-for-granted. Furthermore, the state should conduct process and outcome studies, using qualitative and quantitative methods and community-engaged research approaches, to measure short- and longer-term outcomes, best practices, adaptations, and anticipated and unanticipated outcomes. An equally important action is for the state to compile cost data, including information on who is paying for the intervention and who reaps benefits.

## RAPID 2.0: Future Directions

Even after the COVID-19 pandemic subsides, the indirect effects of the pandemic and the pervasive stress of the pandemic will be felt for many years and, as this analysis suggests, for generations. We propose that the Office of the California Surgeon General (OSG) maintain an independent, authoritative, and policy-focused research group that is engaged in a number of analytic activities, ideally with external (non-state) support to assure transparency and impartiality:

- **Establish an ongoing capacity to monitor research on indirect effects of the pandemic and compile it for use by state decision makers:** Literature on the effects of the pandemic is voluminous and will continue to evolve over time. When we conducted our systematic review of literature (Review #1) in August 2020 our search strategies yielded 13,259 results, while repeating the exact same search strategy in March 2021, 60,669 were returned, about a 5 fold increase in the total number of citations being generated. As this report shows, there are many high-priority public health conditions that are thought to be worsening during the pandemic but, as yet, there is insufficient data. The RAPID team should continue to monitor COVID-19 research to alert California decisionmakers of additional indirect health impacts that warrant mitigation beyond the 5 analyzed here. Where possible, the team should identify and evaluate cost-effective strategies to minimize the burden, as well as to consider the impacts on health disparities and effects on children later in life. As time passes, we anticipate that the body of literature on the differential impacts of COVID-19 on population health will increase and therefore will allow for an analysis to address health disparities as well.
- **Establish a dynamic, interactive information resource for decision makers:** California would benefit from an online-accessible dashboard for monitoring indirect effects of the pandemic similar to those currently used for monitoring COVID-19 rates. Information on different investment levels, geographic distributions, and racial/ethnic disparities could be incorporated, as well as ongoing impacts on population health and cost savings. For example, as upstream systemic interventions that are being or should be considered are implemented (e.g., continued expansion of Earned Income Tax Credit (EITC), Paid

Family Leave, housing and rent subsidies, etc.), information is needed to track their implementation and community- and state-based result. Alternatively, regular reports, briefs, or a designated website could be used, perhaps housed within the OSG, allowing the state to keep the public aware of the cascading indirect effects of the pandemic, and to share information about potential and current investments in mitigation.

- **Proactive evaluations of limits on the service system's capacity for scaling up:** The costing methodology in the BRACE models is confined to the direct costs of each specific mitigation strategy. In some cases, lack of infrastructure – both physical and human capital – could place limits on the speed of implementation or add costs for increasing service system capacity. For example, there is ample evidence that most regions of California faced shortages of behavioral health clinicians before the pandemic. Mitigation programs that would rely on accessing cognitive therapy or other behavioral health services may be stymied without a concomitant investment in workforce expansion (e.g., recruitment, training). Our recommendations for mitigation strategies took general consideration of the implementation context within California during the pandemic. However, decision makers would benefit from more detailed modeling of implementation scenarios that consider specific constraints and the associated costs of overcoming constraints. In the case of human capital shortages, these models can include health workforce projections, gap analyses, and simulated scenarios to evaluate the best strategies to reduce demand-based and need-based shortages. In our experience, if capacity limitations are known at the outset, strategies can be identified to address barriers and can be assessed for their likelihood of overcoming limitations while maintaining the positive impacts desired (e.g., expanding scope of practice for practitioners, use of telehealth).
- **Develop a microsimulation model of the additive effects of pandemic-related stressors:** We know that when individuals experience multiple toxic stressors— e.g., four or more ACEs during childhood—the long-term health harms can be profound. We have shown that children growing up in the unprecedented conditions of the pandemic are prone to multiple ACE exposures (e.g., adult depression, opioid and alcohol use, IPV) but, so far, our analyses have only considered the independent effects of each. The RAPID team could design a microsimulation model to predict the individual and additive impacts of the COVID-19 pandemic on ACEs. Such a model would rely on parental sociodemographic and economic data and childhood ACEs data collected by OCHIN and the Family Experience during the COVID-19 pandemic Dataset designed by the American Academy of Pediatrics. Using the baseline distribution of documented ACEs, we could simulate the population of California. Then, using post-pandemic data on unemployment, IPV, mental health conditions, divorce, criminal justice encounters, and other parental experiences and characteristics, we could project the increase in ACEs

that result from the pandemic. This projection would support targeting interventions to the specific demographic groups most at risk. In addition, detailed results relating to ACEs could be used to refine the BRACE model and estimates of the cost-effectiveness of mitigating interventions.

- **Identify and simulate payer mix and funding models:** RAPID's models, as currently structured, do not take account of specific payers. To maximize impacts on population health, the State of California should consider partnering with private entities (e.g., private healthcare payers, philanthropic organizations) to support implementation of specific mitigation strategies. For some public health priorities, partnerships with federal and local governmental payers can efficiently support care through public insurance plans (e.g., Medi-Cal) and general funds (e.g., cost-sharing with local governments for homeless services). Economic modeling approaches exist for measuring and modeling different payer mix scenarios for specific mitigating interventions, allowing for projections of cost savings for different payers and providers, resulting in increased scale and efficiency.

There is now the opportunity to ameliorate both the direct and indirect impacts of COVID 19, and early and rapid intervention is more likely to mitigate long-term effects than a delayed response. Evidence-based research and modeling are important tools to guide equitable and inclusive solutions to widespread and severe pandemic impacts, particularly as the pandemic has exacerbated generations of inequality. Adopting an inter-generational vision also illuminates additional opportunities for improving the health of our communities now and for the future.

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# APPENDIX A

**PubMed search strategy**

| Search | PubMed Query: Search 1 28 July 2020 | Items found |
|---|---|---|
| **#4** | **#3 AND restrict dates to 2020-03-01 to 2021-12-31** | **6,436** |
| #3 | #1 AND #2 | 7,608 |
| #2 | Unemploy*[tiab] OR “Unemployment”[mh] OR jobless*[tiab] OR "laid off"[tiab] OR housing[tiab] OR homes[tiab] OR homeless*[tiab] OR “Homeless Persons”[mh] OR evict*[tiab] OR economic[tiab] OR economy[tiab] OR income[tiab] OR behavioral[tiab] OR lifestyle[tiab] OR loneliness[tiab] OR lonely[tiab] OR emotional[tiab] OR afraid[tiab] OR fear[tiab] OR fearful[tiab] OR "toxic stress"[tiab] OR trauma*[tiab] OR “traumatic stress”[tiab] OR “Psychological Trauma”[mh] OR stressor*[tiab] OR stressful[tiab] “Stress, Psychological”[mh] OR disruption[tiab] OR disruptive[tiab] OR psychological[tiab] OR "mental health"[tiab] OR depression[tiab] OR “Depression”[mh] OR “Depressive Disorder”[mh] OR anxiety[tiab] OR “Anxiety”[mh] OR “Anxiety Disorders”[mh] OR suicide[tiab] OR suicidal*[tiab] OR “Suicide, Attempted”[mh] OR “Suicide”[mh] OR "alcohol abuse"[tiab] OR "substance abuse"[tiab] OR "substance use"[tiab] OR "illicit drug"[tiab] OR "illegal drug"[tiab] OR opioid[tiab] OR tobacco[tiab] OR smoking[tiab] OR "well-being"[tiab] OR wellbeing[tiab] OR wellness[tiab] OR food[tiab] OR nutrition[tiab] OR “Nutrition Disorders”[mh] OR exercise[tiab] OR "physical activity"[tiab] OR postponement[tiab] OR “health insurance”[tiab] OR childcare[tiab] OR “food insecurity”[tiab] OR “child abuse”[tiab] OR “Child Abuse”[mh] OR “Physical Abuse"[tiab] OR "Emotional Abuse"[tiab] OR "Psychological Abuse"[tiab] OR "Verbal Abuse"[tiab] OR "Family conflict"[tiab] OR "Family conflict"[mh] OR maltreatment[tiab] OR parenting[tiab] OR “Parenting”[mh] OR school*[tiab] OR “Schools”[mh] OR violence[tiab] OR crime[tiab] OR hunger[tiab] OR socioeconomic[tiab] OR “socio-economic”[tiab] OR psychosocial[tiab] OR “psycho-social”[tiab] OR downstream[tiab] OR indirect[tiab] OR cardiovascular[tiab] OR “Cardiovascular Diseases”[mh] OR obesity[tiab] OR “Obesity”[mh] OR stroke[tiab] OR “Stroke”[mh] OR diabetes[tiab] OR “Diabetes”[mh] OR undocumented[tiab] OR immigration[tiab] OR immigrants[tiab] OR citizenship[tiab] OR racism[tiab] OR marginalization[tiab] OR (adverse[tiab] AND childhood[tiab]) | 6,045,754 |
| #1 | "Coronavirus"[mh] OR "SARS-COVID-2"[tiab] OR "SARS-CoV-2"[tiab] OR COVID-19[tiab] OR coronaviridae[tiab] OR coronavirus[tiab] OR COVID[tiab] | 51,310 |

| Search | Expanded Search PubMed Query: 13 August 2020 | Items found |
|---|---|---|
| **#4** | **#3 AND restrict dates to 2020-03-01 to 2020-08-13** | **2,600** |
| #3 | #1 AND #2 | |

| | | |
|---|---|---|
| #2 | Hypertension[tiab] OR “myocardial infarction”[tiab] OR “heart attack”[tiab] OR cerebrovasc*[tiab] OR tuberculosis[tiab] OR TB[tiab] OR HIV*[tiab] OR autoimmune[tiab] OR lupus[tiab] OR scleroderma[tiab] OR COPD[tiab] OR “chronic obstructive”[tiab] OR bronchitis[tiab] OR emphysema[tiab] OR allerg*[tiab] OR eczema[tiab] OR preterm[tiab] OR prematurity[tiab] OR “unintended pregnancy”[tiab] OR perinatal[tiab] OR dental[tiab] OR periodontal[tiab] | |
| #1 | "Coronavirus"[mh] OR "SARS-COVID-2"[tiab] OR "SARS-CoV-2"[tiab] OR COVID-19[tiab] OR coronaviridae[tiab] OR coronavirus[tiab] OR COVID[tiab] | |

## APPENDIX B

**Eligibility Criteria: Population, Exposure, Comparator, Outcome (PECO) Framework**

**Population:** People living in the United States during the period when pandemic started and structural interventions were implemented by federal, state and local governments to contain or mitigate the effects of the COVID-19 pandemic, March-December 2020.

**Exposures/risk factor:** We anticipated that the effects of the COVID-19 pandemic (between upstream factors and downstream health outcomes) are mediated through three main mechanisms:

- Socio-behavioral disruptions (e.g., increased fear and toxic stress due to lack of curative treatment or vaccines, widespread misinformation about the pandemic, and/or new economic uncertainties arising from measures implemented to contain the pandemic).
- Healthy lifestyle disruptions (e.g., reduced access to healthy food, access to exercise and physical activity).
- Disruptions in access to medical care (e.g., loss of income leading to loss of health insurance, postponement of cardiac stress tests, prenatal screening, postponement of other non-urgent medical appointments, Interruption in medication prescription).

**Comparators:** For most studies, unless we examined the differential effects of COVID-19 on health between populations, we considered baseline outcomes based on those of previous years, or periods of years.

**Outcomes:** We focused on conditions/outcomes anticipated to increase as early as days/weeks after the onset of the pandemic (in California and US), or within the first year(s). Outcomes listed under upstream, mid-stream, and downstream categories, are not (and cannot) be perfectly classified as there are soft distinctions – further, they do not follow a one-way causal pathway, rather they form a web of causality which can be circular. For example, while unemployment and financial insecurity can increase risk of substance use, untreated substance use may exacerbate the risk of unemployment.

**Upstream**: Societal or community level stressors known to result in negative impacts on human health such as:

- Access to health care (delayed/reduced/removed)/health insurance
- Childcare disruption
- Education disruption
- Food insecurity/hunger

- Homelessness/eviction/housing insecurity
- Loneliness/social isolation/ social support
- Unemployment/job loss
- Fear of workplace risk
- Discrimination and racism

**Mid-stream**: Community violence and crime, adverse childhood experiences (child abuse, parenting disruption, other family disruptions such as imprisonment and separation, and family violence)

**Downstream**: Our outcomes of interest will be risk factors/health conditions identified by the California Department of Public Health as being among the top 20 contributing most heavily to the state's burden of disease (CDPH 2017). For the first phase of the study, we prioritized outcomes that have already been reported to be on the rise, such as anxiety, depression, and substance and alcohol use.

# APPENDIX C

**Assessment of Strength of Evidence**

This section describes our methodology for assessing the strength of the evidence for outcomes presented in our Key Findings Table. We will denote the strength of evidence beside each effect estimate in the Key Findings Table.

We will assess the strength of the evidence by considering five domains: 1) Data quantity; 2) External validity [with three sub-domains]; 3) Risk of bias [with two sub-domains]; 4) Precision; 5) Consistency.

The intention of this tool is to provide a high-level assessment of the trustworthiness of evidence for high level decision-making in an expedited manner, and has intentionally left out a more nuanced assessment of the internal and external validity that require more intensive review of the literature, often dual-independent review by highly trained individuals in the subject matter.

See definitions below.

**1. Data quantity/Evidence of replicability*:** Number of studies or unique data points contributing to the estimate for each outcome.

- **High:** 4 or more
- **Moderate:** 2-3
- **Low:** 1

**2. External validity (direct versus indirect evidence)**:** We will assess external validity through consideration of three sub-domains, listed below (2a-2c):

**a. Population/setting applicability:** How well do the settings and populations of included studies match those of California?

- **High:** at least one California data point, and the vast majority (as a rule of thumb, 75%-80% or more) of all data coming from the US
- **Moderate:** no California data, but the vast majority of data coming from the US
- **Low:** vast majority of data coming from countries other than the US [ Note: these data are selectively included if CA/US data not available]

**b. Contextual relevance:** How well does the identified evidence reflect the COVID-19 era?

- **High:** COVID-19 era data
- **Moderate:** Pre-COVID-19 era data but sufficient contextual similarities

- **Low:** Pre-COVID-19 era data, but unclear contextual similarities [Note: we may consider selectively include these data as a placeholder when no other contextually relevant data are available]

**c. Outcome measure relevance:** How well does the included indicator predict the intended outcome? For example, the extent to which high blood pressure (the reported indicator) may be a proxy for myocardial infarction (the intended outcome); or to which police calls may be a proxy for substantiated domestic violence.

- **High:** Reported indicator and intended outcome are the same
- **Moderate:** Reported indicator is a strong proxy for the intended outcome
- **Low:** Reported indicator is a weak proxy for the intended outcome

**Overall external validity score (based on 2a-2c):**

- High: If there is at least one of 2a-2c scored "High, and none of 2a-2c are scored "Low."
- Moderate: If all are scored "Moderate"; OR if one is scored "High," one "Moderate" and one "Low"; OR if two are scored "High" and one is scored "Low."
- Low: None of the above

**3. Risk of bias (internal validity)**:** We assess risk of bias through consideration of two sub-domains (3a-3b).

**a. Outcome measurement.** What is the extent to which subjectivity of the outcome can affect the validity of the results? For example, measures like "number of ED visits" from hospital records are more objective than self-reported non-standard mental health measures.

- **High:** Objective/hard outcome (e.g. number of ED visits, or stroke), easy to quantify
- **Moderate:** Subjective outcome measured via a standardized or widely recognized tool (e.g. depression, anxiety)
- **Low:** Subjective outcome without a clear indication of how the outcome was measured

**b. Assessment of baseline risk.** What study methodology was used in obtaining the baseline and outcome data, and how similar are the two groups being compared? For example, did the study take raw data from 2019 and compare it to 2020 data, or did they do some statistical adjustments? Are the participants in baseline data similar to the later (e.g. COVID-19 era) participants?

- **High:** At least one study with baseline data from the same cohort or population; others may include data from different cohorts but with reasonable comparison groups
- **Moderate:** No cohort data of the same population, but vast majority of studies with baseline data from a different cohort (e.g. serial cross-sections); with

reasonable comparators and using consistent survey methods and/or advanced statistical adjustments

- **Low:** Vast majority of studies with baseline data from different population / study

**Overall internal validity score (based on 3a-3b):**

- **High:** If at least either 3a-3b scored "High", and none of 2a-2c are scored "Low."
- **Moderate:** If both scored "Moderate"; OR if one is scored "Low," the other is "High."
- **Low:** None of the above

**4. Uncertainty/precision*:** Effect sizes with tighter confidence intervals (or range) are preferred over those with wide CIs, or those with no CIs.

**a. High:** Tight CIs (range < 0.4)

**b. Moderate:** Wide CIs (range > 0.40) but not crossing the null

**c. Low:** Wide CIs AND crossing the null; OR no CI reported

**5. Consistency/statistical heterogeneity*:** What is the extent to which data points are consistent in the direction and overall magnitude of the effect?

**a. High:** Vast majority (> 75%) of data points in the same direction

**b. Moderate:** More than half (50%-74%) of data points in the same direction

**c. Low**: Data points are highly heterogeneous in regard to direction and magnitude of effect

**Note:** If there is only a single data point, we rate it as "High."

**Overall Strength of Evidence score based on 1-5, above:**

- **High:** If no "Low" and at least one "High"
- **Moderate:** All "Moderate" OR no more than one is "Low"
- **Low:** Two are "Low"
- **Very low:** Three or more are "Low"

**Note:** If #3 (RoB) is "Low" for Moderate or Low, downgrade one level

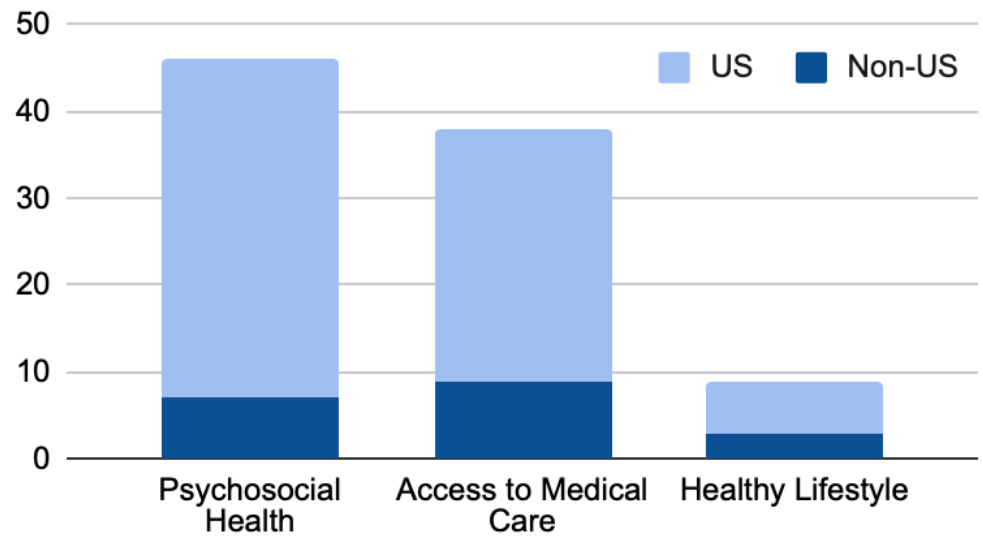
*Domain assessed at the aggregate level only

** Data extracted at individual data point to help assess overall scoring.

## APPENDIX D

Figure 5 shows the distribution of studies into across three key causal pathway that help account for changes in indirect health outcomes during the pandemic: medical care access disruptions, which includes loss of health insurance because of unemployment or economic hardship and postponing or choosing not to seek medical treatment because of fear of COVID-19 infection at a hospital or clinic, clinic schedule disruptions, or cost; psychological distress and stress, which includes the social, emotional, financial, and psychological stresses and strains of both the pandemic itself and related factors such as job loss and social isolation; and healthy lifestyle disruptions, which includes difficulty in maintaining healthy exercise and dietary habits because of facility closures, staying at home to avoid potential infection, economic disruptions, and grocery shortages.

**Figure 6. Extracted studies categorized by mechanism of COVID-19 disruption**



# APPENDIX E

**Expanded summaries of the articles included for extraction**

## Mental health (thirteen US studies, three non-US studies)

- Almandoz 2020: Investigators surveyed patients with obesity (n=123) at a Texas obesity medicine clinic regarding their health behaviors during stay-at-home orders and found high reported rates of anxiety (72.8%) and depression (83.6%).

- Alonzi 2020: Investigators surveyed a sample of young adults aged 18 to 35 years old (n=616) in the United States and Canada in order to determine prevalence of anxiety and depression symptomatology among those that may be more at risk. The found that self-identified female and nonbinary individuals and those with preexisting mental and physical health conditions reported statistically significant higher levels of depression and anxiety following COVID-19 pandemic declaration compared to their male peers or those without underlying conditions.

- Asmundson 2020: Investigators surveyed a population-representative sample of adults from the US and Canada to determine impact of COVID-19 stress on those who reported having mental health conditions compared to a random sample of respondents. Those with anxiety-related disorders reported greater fears about danger and contamination, socioeconomic consequences, xenophobia, and traumatic stress symptoms. Respondents with anxiety-related or mood disorders were more likely to voluntarily self-isolate and were more likely to report greater self-isolation stressors and distress than those without a mental health disorder. There were no major differences in perceived effectiveness of coping strategies across groups.

- Czeisler 2020: Investigators from the Centers for Disease Control and Prevention (CDC) detailed the results of a US adult population survey (n=5,470) conducted in June 2020 that found 31% of respondents experienced symptoms of anxiety or depression. Respondents who reported treatment for diagnosed anxiety, depression, or PTSD at the time of the survey reported higher prevalence of adverse mental and behavioral health conditions compared with those who did not.

- Di Tella 2020: Investigators in Italy found that healthcare professionals (n=145, 72 medical doctors and 73 nurses) who worked in COVID-19 wards reported higher levels of both depressive symptoms (p=0.005) and posttraumatic stress symptoms (p=0.015) in standardized depression, PTSD, and anxiety surveys compared to healthcare professionals working in non-COVID-19 facilities.

- Farewell 2020: Investigators in this mixed methods study looked at the mental health and well-being effects of the COVID-19 pandemic among women during the perinatal period (n=31). 12% of participants reported high depressive symptomatology and 60% reported moderate or severe anxiety. Forty percent reported being lonely. The primary themes related to stress were uncertainty surrounding perinatal care, exposure risk for both mother and baby, inconsistent messaging from information sources and lack of support networks.

- Fitzpatrick 2020: Investigators surveyed a representative US adult population (n=10,368) using the Center for Epidemiological Studies Depression (CESD) Scale. Respondents indicated increased depressive symptomatology, with average scores one point higher than standard cutoff value (16+) and nearly a third of respondents had scores greater than 25. Multiple regression revealed significantly higher scores for those that self-identified as female, non-White, Hispanic, unmarried, or not working.

- Flentje 2020: Investigators looking at the experiences of sexual and gender minorities found that participants had a mean increase in depression symptoms (+1.21; $p<0.001$) and anxiety symptoms (+3.11; $p<0.001$) when compared to scores obtained from the same cohort in 2019. Interestingly, those who screened positive for depression in 2019, had a mean decrease in their score (-1.08; $p<0.001$) but there were mean increases in those previously screened negative for anxiety and depression (+3.93; $p<0.001$ and +2.17; $p<0.001$, respectively).

- Hamm 2020: Investigators in this mixed methods study looking at the feelings and depression scores of 73 older adults living with major depressive disorder 2 months into the pandemic found no significant difference in Patient Healthcare Questionnaire (PHQ-9) scores between pre-pandemic and the current evaluations (8.8 vs 8.7, $p=0.8$); however, subjectively they reported that their quality of life was lower and worried that their mental health would suffer with continued physical distancing.

- Huckins 2020: Investigators used a smartphone app to track lifestyle habits and media consumption and a patient health questionnaire to assess symptoms of anxiety or depression, researchers found that college students from one US university were more sedentary and reported increased anxiety and depression symptoms ($p<0.001$) during the Winter 2020 term when compared to previous academic terms. They also found that anxiety ($p<0.001$) and depression ($p=0.03$) were significantly associated with viewing COVID-19 related news.

- Kaparounaki 2020: Investigators in Greece found that during lockdown, major depression was present in 12.43% of university students with 13.46% experiencing

severe distress. Risk factors were female sex, history of self-injury, suicidal attempts and following theoretical studies (RR=2–5.71). Females with a history of suicidal attempt were at a 5.71-times (44.07% vs 7.71%; RR=5.71) higher risk to develop depression during the lockdown in comparison to males without such a history.

- Leeb 2020: Investigators from the CDC examined national syndromic surveillance data to compare pediatric mental health-related emergency department (ED) visits from 2019 to 2020. They found that despite the total number of pediatric ED visits, (including total number of pediatric mental-health related ED visits) being down, the proportion of mental health-related visits for children less than 18 years old increased by 44% when March 15 to October 17, 2020 when compared to the same time period the year prior.

- Liu 2020: Investigators used a cross-sectional online survey of young adults (n=898) approximately one month after the US declared a state of emergency and found reported high levels of depression (43.3%, PHQ-8 scores ≥ 10), high anxiety scores (45.4%, GAD-7 scores ≥10), and high levels of PTSD symptoms (31.8%, PCL-C scores ≥45).

- Patrick 2020: Investigators developed a probability sample of US households and surveyed those with at least one child under age 18 in June 2020. Compared to March 2020, respondents (n=1,011) reported worsening of parental mental health (27%) and children's behavioral health (14%). Worsening mental health for parents occurred alongside worsening behavioral health for children in nearly 1 in 10 families, among whom 48% reported loss of regular childcare, 16% reported change in insurance status, and 11% reported worsening food security.

- Pierce 2020: Investigators in the United Kingdom performed a secondary analysis of the UK Household Longitudinal Study that surveys those aged 16 or older for general mental health using the 12-item General Health Questionnaire (GHQ-12) in April 2020 and found mean scores increased over time from 11.5 (95% CI 11.3-11.6) in 2018-2019 to 12.6 (95% CI 12.5-11.8). There was a rise in clinically significant levels of mental distress from 18.9% (95% CI 17.8-20) in 2018-19 to 27.3% (95% CI 26.3-28.2) in April 2020. GHQ-12 scores rose the most for young adults less than 35 years old, women, and people living with young children.

- Twenge 2020: Investigators from the US Census Bureau surveyed adults from several nationwide probability samples from January 2019 and May 2020 (n=336,525) using standardized mental health screening tools and found that those in the latter period were more than three times as likely to screen positive for depressive disorders or anxiety disorders. One-third of those screening positive for either condition also screened positive for the other.

## Stroke (thirteen US studies, one non-US study)

- Agarwal 2020: Investigators studying discharge outcomes of stroke patients presenting to a NYC stroke center found that compared to pre-pandemic, discharge outcomes were significantly worse: good disposition, defined as discharged home or to an acute inpatient rehabilitation facility, decreased (80.6% vs 90.7%, p=0.01), and mortality increased (7.5% vs 2.5%, p=0.004). The time from symptom onset to presentation was not significantly different. Among eligible patients who received time-sensitive clot dissolving medication (alteplase) and/or surgical removal of stroke-causing blood clots (mechanical thrombectomy, MT), stroke time metrics were not different between pre-pandemic and pandemic cohorts except for the slightly longer door to head CT time (16 vs 12 min; p= 0.05) and a trend towards longer door to groin puncture for MT (71 vs 79.5 min, p= 0.06). These time metrics are critically important in acute stroke treatment and greatly affect disability outcomes.

- de Havenon 2020: Investigators performed a retrospective analysis of 65 academic and community hospitals assessing the monthly count of stroke and acute coronary syndrome (ACS) presentations from Feb-Mar 2020 compared to the same months in previous years found that the number of patients admitted with stroke and ACS decreased, 17.6% and 25.7% respectively. They also found a related decrease in interventions for stroke and ACS: -3.3% for administration of tPA (the time-sensitive medication used to break up blood clots), -18.8% for mechanical thrombectomies (surgical removal of blood clot), and -14.7% for percutaneous coronary interventions (surgical opening of clogged arteries causing ACS).

- Desai 2020: Investigators at a stroke center in Pittsburgh found a decrease in total emergency department encounters (-22%, p=0.005), acute ischemic strokes (-40%, p=0.001), and transient ischemic attacks (-60%, p=0.163) in March 2020 when compared to the previous 3 years.

- Esenwa 2020: Investigators looking at stroke admission rates at three New York City hospitals found decreased admission rates by an average of 4.4 per week (p=0.005), with weekly admissions down 44% compared to baseline from January 1, 2020 through April 17, 2020.

- Friedlich 2021: Investigators analyzed acute stroke presentations in Southwest Healthcare System (SHS) in Riverside County, California; California (CA); and the United States (US) from February to June 2020 compared to 2019. The total number of code strokes decreased by approximately 15% in the US and CA (p=0.01 and p=0.02, respectively), but increased in SHS during the COVID-19 study period (p=0.007). The US

and SHS demonstrated no change in stroke mortality, but CA demonstrated an increased stroke mortality of approximately 22% during the COVID-19 pandemic. There was also greater loss of independence with increased stroke morbidity noted in the US during the COVID-19 pandemic.

- Ghanchi 2020: Investigators analyzed demographic data from stroke patients presenting in the State of California, Pacific Coast hospitals, Western Region hospitals, and all hospitals in the United States from February to May 2020 compared to the same time period in 2019. Similar to other studies they found the overall presentation of stroke had decreased, with mean drops of approximately 15 percent. They also found a statistically significant increase in the proportion of racial minorities presenting in 2020 when compared to matched calendar months in 2019. There was no statistically significant change in the proportion of Caucasian patients presenting with stroke in 2020. Of note, this article was later retracted due to authors being unable to get permission from the American Heart Association for use of its data for publication.
- Hsiao 2020: Investigators compared volume of stroke consultation in Kentucky, Ohio, and Indiana to the volume 10 weeks prior and found that consultations declined by 39% (95% CI 32% to 46%) in the 5 weeks after announcement of statewide school and restaurant closures in the aforementioned states.
- Jasne 2020: Investigators analyzed data from three Connecticut hospitals to quantify trends in stroke code calls and treatment in two time periods: January 1 to April 28, 2019 and the corresponding dates in 2020. Investigators observed a 30% decline in stroke code calls in the latter period, beginning with week 7 (February 11-17). There were no differences in stroke severity or early outcomes.
- Kerleroux 2020: Investigators in France examined the rates of mechanical thrombectomy (surgical removal of stroke-causing blood clots), performed at multiple centers during the COVID pandemic era compared to years prior and found a significant decrease (21%, $p<0.001$) in case volumes, as well as delays in care.
- Nagamine 2020: Investigators at the University of California, Irvine compared acute ischemic stroke presentations between March-April 2020 and the same time period in 2019. They found a decreased number of stroke cases—48 in 2020 compared to 64 in 2019—and delayed presentation in comparison to the same time period in 2019. The average last known well to arrival time (±SD) for stroke codes was 1,041 (±1682.1) minutes in 2020 and 554 (±604.9) minutes in 2019. Of the patients presenting directly to the emergency department, only 27.8% presented in the first 4.5 hours in the 2020

cohort, in contrast to 40.5% in 2019. Mortality rates also increased from 6.3% in the 2019 cohort compared to 10.4% in 2020.

- Nguyen-Huynh 2020: Investigators analyzed stroke data from 21 stroke centers across Northern California and found decreased stroke alert volumes when comparing pre-shelter-in-place (SIP) data. Weekly stroke alert volume post-SIP decreased by approximately 26% (post-SIP mean, 98 [95% CI 92–104]; pre-SIP mean, 132 [95% CI, 130–136]; p<0.001). Compared with pre-SIP, post-SIP patients had higher National Institutes of Health Stroke Scale scores (p=0.003), lower comorbidity scores (p<0.001), and arrived more often by ambulance (p<0.001). Post-SIP, more patients had large vessel occlusions (p=0.03), and there were fewer stroke mimics (p=0.001). There were no differences in patient demographics and inpatient mortality noted in this study.
- Siegler 2021: Investigators analyzed data from a New Jersey tertiary care hospital to quantify trends in new ischemic stroke diagnoses in two time periods spanning across the national emergency declaration for the COVID-19 pandemic and found 38% decline.
- Siegler 2020: Investigators analyzed acute stroke management data from 14 comprehensive stroke centers in the United States from Jan 1, 2019 to July 31, 2020. They found that patients treated during COVID-19 were at lower odds of receiving clot breaking medication within 60 minutes of arrival (OR 0.61 [95% CI, 0.38–0.98]; p=0.04), with a median delay in door-to-needle time of 4 minutes (p=0.03) and that the delay appeared driven by the longer delay from time of imaging to administration of the clot breaking medication (median, 29 versus 22 minutes; p=0.02). There was no significant delay in door-to-operative procedure time for patients who underwent surgical removal of the clot (median, 83 versus 90 minutes; p=0.30).
- Uchino 2020: Investigators analyzed data from 19 hospital emergency departments (ED) in Ohio, comparing acute stroke presentations between January 1 and March 8, 2020 with those between March 9 and April 2, 2020. There was a 26% to 30% reduction in acute stroke presentations during the latter period, as measured by total stroke alerts, ED stroke diagnoses, and stroke telemedicine activations.

### Acute stress, fear, and loneliness (nine US studies)

- Civantos 2020: Investigators surveyed otolaryngology residents and attending physicians (n=349) to evaluate burnout, anxiety, distress, and depression. Anxiety, distress, burnout, and depression were reported in 167 (47.9%), 210 (60.2%), 76 (21.8%), and 37 (10.6%) physicians, respectively. Attendings had decreased burnout relative to residents (OR 0.28, [95% CI 0.11-0.68]; p=0.005). Females had increased burnout (OR 1.93, [95% CI 1.12.-3.32], p=0.018), anxiety (OR 2.53, [95% CI 1.59-4.02], p<0.005), and distress (OR

2.68, [95% CI 1.64-4.37], p<0.005). Physicians in states with greater than 20,000 positive cases had increased distress (OR 2.01, [95% CI 1.22-3.31]; p=0.006).

- Emerson 2020: Investigators examined the impact of sheltering in place and social distancing on US adults aged 60 and older during the COVID-19 pandemic. A large portion reported being stressed (36%), and/or being lonely (42.5%). Nearly one-third stated that their sense of loneliness increased during the time of social distancing. Respondents reported engaging in more solitary activity (and fewer in-person activities), using email and text messages more than usual, and spending more time on computers/tablets than usual. Approximately two-thirds reported using more social media than usual. These differed significantly by younger (age 60-70) and older (71+) respondents (73.2 vs 54.4, p=0.000). Additionally, decrease in physical activity (33.8 vs 43.3, p=0.000), increased drinking (14.9 vs 7.7, p=0.001), and decreased sleep (18.2 vs 11.9, p=0.010) differed by age.

- Fitzpatrick 2020: Investigators surveyed a representative US adult population (n=10,368) near the end of March 2020 and found that average fear of COVID-19 scores on a 10-point scale was high (average of 7) with more than 25% of the sample endorsing moderate to severe anxiety symptoms. Significant relationships were noted between higher fear of COVID-19 and those self-reported as female, Asian, Hispanic, foreign-born, or in families with children.

- Killgore 2020a: Investigators surveyed US, English-speaking adults and found lower rates of psychological resilience (CD-RISC scale: M = 66.84, SD=17.48; t (1579)=16.29, p<0.00001) when compared to published normative data. Lower scores for resilience were associated with more severe depression and anxiety scores, as well as, increased worries about effects of COVID-19. There was a linear and positive association with resilience and time spent outside (β =0.07, p=0.012), daily exercise (β =0.09, p=0.0004), lower severity of insomnia (β = −0.18, p<0.00001), and greater frequency of prayer (β =0.23, p<0.00001).

- Killgore 2020b: Investigators surveyed US adults (n=1,013) during the third week of shelter-in-place guidelines using the UCLA Loneliness Scale-3 and Public Health Questionnaire (PHQ-9) and found 43% of respondents above published cutoffs for loneliness with strong associations between loneliness severity and depression and suicidal ideation.

- Luchetti 2020: Investigators surveyed US adults (mean age 54; 22% living alone) to assess loneliness at three time points: January and February 2020, late March 2020, and

late April 2020. Overall, loneliness increased slightly by the second survey wave in adults over age 65 but did not further increase.

- Park 2020: Investigators surveyed a US adult, English-speaking population to determine the immediate impact of COVID-19 on American's stress, coping, and guideline adherence. They found that the most commonly experienced stressors were reading/hearing about the severity and contagiousness of COVID-19 (96.6%), uncertainty about length of quarantine and social distancing requirements (88.3%), and changes to social/daily personal care routines (80.1%). Financial concerns were rated most stressful by respondents. Those who were younger, female gender, or a caregiver had increased risk for stressor exposure and reported a greater degree of stress from these exposures.

- Schechter 2020: Investigators used a cross-sectional web survey of healthcare providers during peak inpatient admissions for COVID-19 in New York City at one large medical center (n=657) and found positive screens for acute stress (57%), depressive symptoms (48%), and anxiety symptoms (33%). Nurses and advanced practice providers screened positive at higher rates when compared to attending physicians. A majority (61%) reported increased sense of meaning or purpose.

- Tull 2020: Investigators studied a nationwide US community adult sample (n=500) to analyze the relationship between COVID-19 stay-at-home orders, perceived impact of the pandemic, and psychological outcomes (depression, health anxiety, financial worry, social support, and loneliness). They found a statistically significant association with greater self-reported health anxiety, financial worry, and loneliness with the stay-at-home orders.

## Heart disease (seven US studies, two non-US studies)

- Advani 2020: Investigators used an online survey to determine changes in sleep patterns during the pandemic that may correlate to the decrease in myocardial infarctions noted in emergency departments seen across the nation. In the 131 respondents who completed the survey, they found shifts in the sleeping patterns led to an average nightly increase of 44 minutes or 11% ($p<0.0001$) during the pandemic when compared to pre-pandemic sleep duration.

- AlMufleh 2020: Investigators studied a group of heart failure patients in Massachusetts and found increased pulmonary artery pressure (PAP) volatility (from a median of 4 per patient (2–24) to 10 (4–26), $p=0.170$) during the post-COVID period when compared to prior. Elevated pulmonary artery pressures are associated with adverse prognoses and

increased risk for hospitalization in patients with heart failure. The investigators, however, noted fewer worsening heart failure events (1 vs 11, p=0.024) for the cohort in the post-COVID period.

- Bhatt 2020: Investigators at a tertiary care center in Boston found a significant decline of 43.4% (95% CI -27.4% to 56.0%) in the total number of cardiovascular hospitalizations in March 2020 compared with March 2019 (260 hospitalizations vs 475 hospitalizations; p<0.001). Investigators also found a significant decline in daily cardiovascular admissions across the health system in this time period (-5.9% per day [95% CI -7.6% to -4.3%]; p<0.001).

- Braiteh 2020: Investigators found a 40.7% (p <0 .05) decrease of total acute coronary syndrome cases during the COVID-19 pandemic with 36.4% of NSTEMI patients (a specific type of myocardial infarction or heart attack) presenting >24 hours of having symptoms during the COVID-19 pandemic in comparison with 2019 when 27.1% presented late (p=0 .033).

- de Havenon 2020: Investigators in this retrospective analysis of 65 academic and community hospitals found that patients presenting with acute coronary syndrome (a range of conditions resulting in reduced blood flow to heart which includes myocardial infarction or “heart attacks”) decreased by 25.7% in March 2020 compared to similar pre-COVID months. They found a related decrease in percutaneous coronary interventions (surgical opening of clogged arteries causing ACS), which decreased by 14.7%.

- Jabri 2020: Investigators in the Cleveland Clinic health system in Northeast Ohio examined the incidence of stress cardiomyopathy in patients presenting with acute coronary syndrome who underwent coronary arteriography found a significant increase in the incidence of stress cardiomyopathy during the COVID-19 period (n=1,914; incidence proportion, 7.8%), compared with pre-pandemic timelines, which ranged from 5 to 12 patients with stress cardiomyopathy (incidence proportion range, 1.5%-1.8%). The rate ratio comparing the COVID-19 pandemic period to the combined pre-pandemic period was 4.58 (95% CI 4.11-5.11; p<0.001). Patients with stress cardiomyopathy during the COVID-19 pandemic had a longer median hospital length of stay compared with those hospitalized in the pre-pandemic period (COVID-19 period: 8 [6-9] days; March-April 2018: 4 [3-4] days; January-February 2019: 5 [3-6] days; March-April 2019: 4 [4-8] days; January-February: 5 [4-5] days; p =0.006). There were no significant differences between the COVID-19 period and the overall pre-COVID-19 period in mortality or 30-day rehospitalization.

- Kessler 2020: Investigators in Germany examined the hospital admissions for acute coronary syndrome (a range of conditions resulting in reduced blood flow to heart which includes myocardial infarction or “heart attacks”) during the early days of the COVID-19 pandemic compared to pre-pandemic levels and found a significant reduction in number of daily admissions (41.1 vs 55.9; $p< 0.001$).

- Lai 2020: Investigators examined the characteristics associated with out-of-hospital cardiac arrests and death during the COVID-19 pandemic in New York City and found a three-fold increase in the incidence compared to 2019 with fatality rates exceeding 90%. Patients with out-of-hospital cardiac arrests in 2020 were less likely to be White (32.9% vs 20.4%) and more likely to be Black (28.6% vs 34.3%) or Hispanic (20.6% vs 25.5%).

- Legutko 2020: Investigators in Poland examined the number of coronary angiography and percutaneous coronary interventions (surgical opening of clogged arteries causing ACS) performed in patients presenting with acute myocardial infarction found significant decreases in both interventions (-34.8% and -28.3%, respectively) during the COVID-19 pandemic.

## Intimate partner violence (five US studies, two non-US studies)

- Boserup 2020: Investigators found many preliminary reports of increased domestic violence (DV) arrests in Portland (+22%), increased family violence calls in San Antonio (+18%), increased DV calls in Jefferson County Alabama (+27%), and increased DV reports in NYC (+10%).

- Bullinger 2020: Investigators found that stay at home (SAH) orders in the city of Chicago lead to a decrease in total calls for police service, but an increase in domestic violence (DV)-related calls for police service. Effects were larger in areas with a high proportion of renters. The increase in DV calls was not reflected in the percentage of reported domestic-related crimes and arrests by police officers. Official reports and arrests for DV crimes fell by 8.7% and 26.3%, respectively. Overall, investigators estimated that nearly 1,000-cases of DV crimes went underreported between March and April 2020.

- Buttell 2020: Investigators from Tulane University surveyed New Orleans residents (n=275) regarding the COVID-19 pandemic and experiences of interpersonal violence (IPV). 88% of survey participants felt nervous and stressed in the past month, 95% expressed worry about the ongoing impacts of COVID-19, and 59% reported an escalation of intimate partner violence among those who experienced this prior to the pandemic.

- Johnson 2020: Investigators in the United States, United Kingdom, and Kenya looked at the impact of the COVID-19 pandemic on clinical care and forensic medical documentation for sexual and gender-based violence survivors. They found that in the first six weeks of the UK's lockdown, sexual assault referral centers saw a 50% decrease in the number of referrals for forensic examinations. Similar decreases were also seen in Kenya, although no numbers were reported.

- Leslie 2020: Investigators analyzed data from 14 large US cities to quantify trends in domestic violence service calls before and after social distancing began, relative to trends during the same period in 2019. They found a 7.5% increase in domestic violence service calls in the 12 weeks after social distancing began. Effects were largest in the first five weeks after social distancing began, when DV calls increased by nearly 10%. The increase in reported DV incidents began before official stay-at-home orders were mandated. This increase appeared to be driven by households without a previous history of DV, but not driven by any particular demographic group.

- Piquero 2020: Investigators in Dallas, Texas found that incidence of domestic violence increased in the first two weeks after stay-at-home orders were implemented but decreased thereafter. They also acknowledge an upward trend in domestic violence incidents prior to the stay-at-home orders leading to caution when interpreting their results.

- Usher 2020: Investigators in this Australian review article, reported on the rising rates of family violence seen in Australia and other nations around the world in the COVID-19 era. Australia saw a 40% decrease in overall crime but a 5% increase in domestic abuse call-outs and a 75% increase in internet searches relating to support for domestic abuse. France saw a 32-36% increase in domestic abuse complaints. The United States saw a 21-35% increase in domestic abuse incidents. The United Kingdom saw a 25% increase in calls to the National Domestic Abuse Hotline and at least 8 family-violence related deaths were reported.

## Social determinants of health (seven US studies)

- Ashby MPJ 2020: Investigators in several states found mixed results related to the COVID-19 impact on crime ranging from 54% decline in Nashville, TN to a 40% increase in Louisville, KY with all estimates falling within the 99% CI of predicted crime rates.

- Elser 2020: Investigators in this Bay Area social media survey found that from March 14 to April 1, 2020 respondents of a social media survey in the Bay Area and other states

reported increased difficulty in obtaining food (Bay Area 13.3% vs US 8.2%); wage decreases (Bay Area 4.7% vs US 6.4%); and job loss (Bay Area 1.2% vs US 1.6%).

- Halford 2020: Investigators used Google trends data and found that search inquiries related to upstream factors associated with suicide risk factors. These search terms included:
    - “Loan” (37%; 95% CI 17% to 58%)
    - “I lost my job” (226%; 95% CI 120% to 333%)
    - “Laid off” (1164%; 95% CI 395% to 1932%)
    - “Unemployment” (1238%; 95% CI 560% to 1915%)
    - “Furlough” (5717%; 95% CI 2769% to 8665%)

- Mohler 2020: Investigators analyzed trends in the volume of calls for police service from January 2 to April 21, 2020 in Los Angeles and Indianapolis. They reported P values for changes in means across two study periods. The second study period began March 20 in Los Angeles and March 24 in Indianapolis. The most robust patterns to emerge, in both Los Angeles and Indianapolis, were a substantial decrease in traffic stops and a substantial increase in domestic violence calls-for-service in both settings. However, the increase in domestic violence calls did not appear to seriously impact reported aggravated assaults. There was no statistically significant change in volume-of-calls for vandalism, burglary, and assault/battery in either city.

- Niles 2020: Investigators in Vermont conducted a statewide survey (n=3219) during the beginning of their stay-at-home order and found a 32.6% increase in household food insecurity with 35.5% of food insecure households being newly food insecure. Of those food insecure households two-thirds reported eating less since COVID-19. Respondents from households with new food insecurity were significantly less likely to accept food or money from friends/family, sign up for government programs, or get food from a food pantry.

- Patrick 2020: Investigators developed a probability sample of US households in June, 2020 and surveyed those with at least one child under age 18. Compared to their recollection of these outcomes in March 2020, respondents (n=1011; 50% of sample) reported worsening of parental mental health (27%), children's behavioral health (14%), parental physical health (18%) and children's physical health (4%). Slightly smaller proportions of Black and Hispanic respondents reported worsening of parental or child mental health status, though a slightly larger proportion of Hispanic respondents reported worsened physical health status for both parents and children. Overall,

respondents also reported significantly worsened access to health care and child care and worsened food security.

## Substance use (six US studies, one non-US study)

- Czeisler 2020: Investigators at the Centers for Disease Control and Prevention (CDC) detailed the results of a survey to 5,470 US adults and reported that 13.1% of respondents had started or increased substance use to cope with stress related to COVID-19. Increased substance use was more likely among those 18-24 years old, those who identified as Black or Hispanic, those who were employed, and among essential workers when compared to their peers. A longitudinal analysis of subset from this cohort found that among those not reporting substance use in May, the group of "unpaid caregivers of adults" had approximately three times more risk of reporting substance use in June (adjusted OR 3.33, [95% CI 1.75 to 6.31]).

- Dumas 2020: Investigators in Canada examined self-reported substance use in 1,054 Canadian adolescents three weeks prior to and after the pandemic and social distancing orders and found no significant change in the percentage of teens who reported using alcohol (28.6% vs 30.1%, p=0.21) but did find increases in number of substance-using days for both alcohol (0.76 vs 0.96, p=0.02) and cannabis (0.94 vs 1.10, p=0.01) among those who used substances. Notably half of the teens reported solitary substance use which correlated with reports of depressive symptoms and fear of COVID-19. Nearly a third of teens reported using substances with friends via technology and up to a quarter were still using substances with friends in-person despite social distancing guidelines.

- Friedman 2020: Investigators using data from the National EMS Information System (NEMSIS), found that from January through August 1, 2020, overdose-related cardiac arrests totaled 49.5 per 100,000 EMS activations (48.5% above baseline). These trends corresponded temporally with a sharp drop in cell phone-based mobility, which was used as a measure of social distancing, beginning March 16, reaching a minimum of −51.8% of baseline by April 13 and slowly increasing to −24.3% by July 27. The temporal similarities suggested that social isolation as a result of stay at home orders, contributed to an acceleration in fatal overdose trends.

- Glober 2020: Investigators in an urban emergency medical services (EMS) system in Indiana found that despite a mild 4% increase (p<0.001) in all EMS calls for service, overdose specific calls increased by 43% (p<0.001), and calls where naloxone was administered (reversal agent for opioid overdoses) increased 61% (p<0.001) after state stay-at-home orders were issued. Additionally, deaths from drug overdoses increased by

47% (p<0.001). They did not find significant changes in age distribution, race/ethnicity, or zip code in individuals who overdosed after the stay-at-home order was issued.

- Lechner 2020: Investigators found a significant increase in reported alcohol consumption during the week prior to and after campus closure at a public university in Northeast Ohio. Analysis of data from 1,958 students, demonstrated that alcohol consumption (amount and frequency) increased as time progressed. A significant main effect for time indicated that alcohol consumption increased as time progressed (b=0.369, [95% CI 0.316-0.423], p<0.001). Significant main effects for symptoms of depression (b=0.027, [95% CI 0.017-0.037], p<0.001), and anxiety (b=0.026, [95% CI 0.014-0.038], p<0.001), indicated that higher psychological distress was associated with higher alcohol consumption overall. Social support demonstrated a significant negative effect, indicating that those with more social support, consumed less alcohol overall (b=−0.009, [95% CI −0.015 to −0.002], p=0.013).

- Pollard 2020: Investigators studied US adult alcohol during the COVID-19 pandemic and found a 14% increase in the overall frequency of alcohol consumption from the same time period in 2019 (+0.74 days; 95% Cl 0.33-1.15 days). Women reported a 17% increase in frequency of alcohol consumption (+0.78 days; 95% CI 0.41-1.15) and a significant 41% increase in frequency of heavy drinking (+0.18 days; 95% CI 0.04-0.32 days), which equated to an increase of 1 days for 1 in 5 women. Adults aged 30 to 59 years, reported a 19% increase in frequency of alcohol consumption (+0.93 days; 95% CI 0.36-1.51 days). Non-Hispanic White individuals reported a 10% increase in alcohol consumption (+0.66 days; 95% CI 0.14-1.17 days). On average, alcohol was consumed 1 day more per month by 3 of 4 adults.

- Smalley 2020: Investigators retrospectively examined emergency department visits in a large sample of midwestern hospitals between March and April in 2019 and 2020 and found that while the total number of alcohol related visits to the emergency department decreased (971 in 2019 vs 829 in 2020, -14.62%), the percentage of alcohol-related emergency visits increased by 53% (1.72% of visits in 2019 vs 2.64% in 2020).

### Suicide and self-harm (six US studies, one non-US study)

- Bryan 2020: Investigators surveyed a general US adult population sample (n=10,625) and failed to support their hypothesis that physical distancing measures correlated with worse mental health outcomes but did find that multiple life stressors were associated with increased rates of probable depression (OR 1.81, [95% CI 1.59-2.05], p<0.001) in this. Past-month suicidal ideation was significantly higher among participants reporting ongoing arguments with a partner, serious legal problems, or concerns about life-

threatening illness or injury of close family member or friend (OR 1.46, [95% CI 1.16 to 1.83], p=0.001; OR -1.85, [95% CI 1.31 to 2.62], p<0.001; and OR 2.26, [95% CI 1.48 to 3.46], p<0.001, respectively).

- Czeisler 2020: Investigators surveyed a representative US adult population (n=5,412) during June 2020 to assess mental health, substance use, and suicidal ideation during the pandemic. 40.9% of respondents reported at least one adverse mental or behavioral health condition, including symptoms of anxiety disorder or depressive disorder (30.9%), symptoms of a trauma and stressor-related disorder (TSRD) related to the pandemic (26.3%), and having started or increased substance use to cope with stress or emotions related to COVID-19 (13.3%). They found that 10.7% of participants reported having seriously considered suicide in the preceding 30 days. This finding was significantly higher among respondents aged 18-24 years (25.5%), minority racial/ethnic groups (Hispanic respondents [18.6%], non-Hispanic Black respondents [15.1%]), self-reported unpaid caregivers for adults (30.7%), and essential workers (21.7%).

- Fitzpatrick 2020: Investigators surveyed a representative US adult population (n=10,368) near the end of March 2020 using the Suicide Behaviors Questionnaire-Revised (SBQ-R) and found that nearly 15% scored in the high risk category. Regression results identified significantly increased scores among those who self-identified as Black, Native American, Hispanic, or unmarried (p<0.000). Those in families with children and younger adult respondents also reported significantly higher scores (p<0.000).

- Gratz 2020: Investigators surveyed a sample of US adults across 45 states (n=500) between the end of March and early April 2020 to assess the impact of COVID-19 shelter-in-place orders and job loss on factors such as thwarted belongingness, perceived burdensomeness, loneliness, and suicide risk. They found at that time that 82.4% of participants were under a stay-at-home order and 11% reported a recent job loss related to the pandemic. Using the Depression Symptom Index-Suicide Subscale they found that 11.6% of respondents met criteria for high suicide risk. Through statistical analysis they found an indirect relationship between stay-at-home orders and job loss with increased suicide risk.

- Halford 2020: Investigators used Google Trends data to examine search terms between March 3, 2019 and April 18, 2020 and found that search inquiries related specifically to the act of suicide were lower than predicted. They did, however, find increases in the following search terms:
    - “Depression” (+3%; 95% CI 1% to 6%),
    - “Panic attack” (+12%; 95% CI 2% to 21%),

- "Loneliness" (+24%; 95% CI 12% to 37%),
- "National suicide hotline" (+9%; 95% CI 1% to 18%),
- "Crisis text line" (+36%; 95% CI 18% to 54%)
- "Disaster distress helpline" (+3021%; 95% CI 873% to 5169%).

- McIntyre 2020: Investigators used prediction modeling to project number of excess suicides in Canada based on unemployment rates using previous data from 2000-2018 that showed a proportional increase in suicide and unemployment. In one of their scenarios, with an increase in unemployment of 10.7% in 2020 followed by a 1.2% increase in 2021, they projected 2,114 excess suicides.

- Smalley 2020: Investigators analyzed data from 20 hospital emergency departments in the Midwest, with attention to psychiatric ED visits, between March 25, 2020 and April 24, 2020. During the one-month study period, the hospital system had 31,387 ED encounters with 2477 (7.9% of visits) behavioral health (BH) visits, compared to 56,453 visits with 3438 (6.1% of visits) BH visits during the same period in 2019. Overall, between 2019 and 2020, there was 44.4% decrease in overall ED visits and 28.0% decrease in BH visits. When comparing 2019 to 2020, SI encounters decreased by 60.6%. As a percentage of all ED encounters, SI encounters decreased from 2.03% to 1.44% from 2019 to 2020. Encounters for suicidal ideation (SI) fell from 33.28% in 2019 to 18.21% in 2020 ($p<0.001$) when examining the percentage of overall BH encounters within the system.

**Dietary and exercise habits (four US studies, two non-US studies)**

- Almandoz 2020: Investigators surveyed patients (n=123) at a Texas obesity clinic regarding their habits and 69.6% reported their weight loss goals were hard to achieve since shelter-in-place with 47.9% reporting decreased physical activity duration and 55.8% reporting decreased physical activity duration. Stress eating was reported by 61.2% of respondents.

- Ashby NJS 2020: Investigators analyzed anonymized geographical positioning system data representing 65% of counties in the US from Dec 2019 - April 2020 and found that patronage to unhealthy eating establishments declined by approximately 4% overall but counties with the highest obesity rates observed less of a decline ($p=0.001$) and observed a faster rate of rebound to increased patronage back to pre-pandemic levels in these counties as well..

- Di Stefano 2020: Investigators in Italy surveyed subjects (n=268) to estimate the levels of physical activity among patients with neuromuscular disease (NMD) before and

during the last week of quarantine. They found a significant decrease of the total weekly physical activity level during COVID-19 quarantine in both patients with NMD and healthy controls.

- Ding 2020: Investigators in this study examined Google Trends data in the UK, Australia, and the US to assess community interest in physical activity before and during the COVID-19 pandemic. They found that community interest in exercise surged immediately following the lockdown and peaked within the first 2 week. Researchers found that it did decline again but remained at a higher level than before the lockdown ($p<0.01$).

- Gallo 2020: Investigators in Australia examined the effect of isolation measures during the early phase of the COVID-19 pandemic in Australia (March-April 2020) on diet (24-hr recall) and physical activity (Active Australia Survey) patterns in third-year university students. Findings were compared with students enrolled in the same university course in the previous two years. In females, but not males, energy intake was 20% greater during the pandemic, and snacking frequency and energy density of consumed snacks also increased compared with 2018 and 2019. Physical activity was impacted for both sexes during the pandemic with 30% fewer students achieving "sufficient" levels of activity, defined by at least 150 min over at least five sessions, compared with the previous two years.

- Huckins 2020: Investigators used smartphone data to track lifestyle habits of college students and found increased rates of sedentary behavior during the Winter 2020 term when compared to previous academic terms ($p<0.001$).

## Emergency care (three US studies, two non-US studies)

- Bram 2020: Investigators studying pediatric emergency department presentations at a Level 1 trauma center in Philadelphia found a decrease in the incidence of pediatric fractures during the pandemic when compared to a pre-pandemic cohort in 2018 and 2019 (22.5±9.1/d vs 9.6±5.1/d, $p<0.001$). The presenting age for all fractures decreased during the pandemic (7.5±4.3 vs 9.4±4.4, $p<0.001$) because of decreased fracture burden among adolescents. There was an increase in the proportion of injuries occurring at home (57.8% vs 32.5%, $p<0.001$) or on bicycles (18.3% vs 8.2%, $p<0.001$), but a decrease in those related to sports (7.2% vs 26.0%, $p<0.001$) or playgrounds (5.2% vs 9.0%, $p<0.001$).

- Cheek 2020: Investigators in Australia compared pediatric emergency department (ED) visits in the two months following the closure of the country's borders to non-residents

in 2020 to the same period in 2019. They found a 47.2% decrease in total ED presentations (26871 vs 14170), with a significant difference in daily means (440.5 vs 232.3, difference -208.2, [95% CI -221.7 to -194.7], p<0.001). Conversely, there was a 35% (485 vs 656) increase in mental health patients (daily means 8.0 vs 10.8, difference 2.8, [95% CI 1.7-3.9], p<0.001).

- Franchini 2020: Investigators in Italy compared emergency department (ED) attendance from February 1 to March 31, 2020, to the same time period in 2019. They found ED attendance dropped by 37% in 2020. Two-thirds of this reduction occurred early after the identification of the first COVID-19 case in Lombardy, before lockdown measures were enforced. Hospital admissions of non-COVID patients fell by 26%. During the peak of COVID-19 attendance, the ED faced an extraordinary increase in the following: patients needing oxygen (+239%, p<0.0001) or noninvasive ventilation (+725%, p<0.0001), transfers to the intensive care unit (+57%, p=0.0315), and in-hospital mortality (+309%, p<0.0001), compared with the same period in 2019. A total of 7824 patients were admitted in 2020, compared with 12,422 in 2019 (-37%, p<0.0001).

- Hartnett 2020: Investigators from the CDC examined national syndromic surveillance data to compare overall emergency department visits in March to April 2020 compared to the same time period in 2019. Emergency department visits declined by 42% in the latter period. Diagnostic categories that were recorded less commonly during the latter period included influenza, no immunization or under immunization, otitis media, and neoplasm-related encounters.

- Lange 2020: Investigators from the CDC examined national syndromic surveillance data to compare hospital emergency department (ED) admissions for three life-threatening conditions in two time periods: the first 10 weeks of 2020 and the 10 weeks following the March 13 declaration of COVID-19 as a national emergency. In the latter period, ED admissions for heart attack, stroke and uncontrolled high blood sugar declined by 23%, 20% and 10%, respectively.

## Diabetes mellitus (four non-US studies)

- Kamrath 2020: Investigators in Germany found increased incidence of diabetic ketoacidosis (DKA; a complication of uncontrolled type 1 diabetes mellitus that can result in significant morbidity and mortality) and severe DKA presentation among children and adolescents diagnosed with type 1 diabetes during the COVID era when compared to prior years [DKA: 44.7% in 2020 vs 24.5% in 2019 (aRR 1.84, 95%CI 1.54-2.21; p<0.0001) and Severe DKA: 19.4% in 2020 vs 13.9% in 2019 (aRR 1.37, 95%CI 1.04-1.81; p=0.03)]

- Fernandez 2020: Investigators in Spain found that glycemic control (blood glucose levels in ideal range) was improved among the 307 adult patients with type 1 diabetes included in their analysis (estimated HbA1c declined from 7.4 ± 1.0 to 7.1 ± 1.0%, p<0.001).

- Christoforidis 2020: Investigators in Greece did not find a major difference in mean blood glucose values among children with type 1 diabetes mellitus on an insulin pump during the COVID lockdown (168.76 ± 21.87 mg/dl before lockdown versus 170.26 ± 22.79 during lockdown, p=0.466), but did appreciate changes in the timing of meals, which can impact the dosing and effect of insulin as prescribed. They found the percentage of breakfast consumed before 10:00 AM had fallen from 80.67% to 41.46% (p<0.001) during the lockdown.

- Bonora 2020: Investigators in Italy monitoring the glucose levels of 33 adult patients with type 1 diabetes examined the differences in glycemic control (blood glucose levels in ideal range) among patients who continued to work during the lockdown (n=13) to those that stopped working (n=20) and found that those who stopped working demonstrated improved glycemic control as measured by average glucose decline from 177 ± 45 mg/dL (week before lockdown) to 160 ± 40 mg/dL (lockdown; p=0.005) and the standard deviation improved significantly with increased time in range from 54.4 to 65.2% (p=0.010), and decreased time in hyperglycemia from 42.3 to 31.6% (p=0.016). In 13 patients who continued working, none of the measures of glycemic control changed during lockdown.

### Child maltreatment (one US study, one non-US study)

- Sidpra 2020: Investigators in the United Kingdom (UK) found an increase in incidence of pediatric abusive head trauma to 10 cases in the month that the UK entered a period of national self-isolation, compared with the incidence (mean of 0.67 cases per month) in the same time period over the previous three years. All families lived in areas with higher than average Index of Multiple Deprivation (national mean 15,200; cohort mean 19,867), and 70% of parents had significant underlying vulnerabilities: two had previous criminal histories, three had mental health disorders, and four had financial concerns.

- Swedo 2020: Investigators from the CDC examined national syndromic surveillance data to quantify trends in pediatric emergency department (ED) visits related to child abuse and neglect from January 6, 2019 to September 6, 2020. They found that the total number of ED visits related to child abuse and neglect averaged 53% less than the number that occurred during the corresponding 2019 period during week 11 (March 15–March 22, 2020), coinciding with the declaration of a national emergency on March

13, however, the proportion of these visits per 100,000 ED visits began increasing above the 2019 baseline for all age groups. While the weekly number of these visits resulting in hospitalization remained stable in 2020, the yearly percentage of ED visits related to child abuse and neglect resulting in hospitalization increased significantly among all age groups, from 2.1% in 2019 to 3.2% in 2020 ($p<0.001$). Hospitalizations for child abuse and neglect did not decrease in 2020, suggesting that injury severity did not decrease during the pandemic, despite decreased ED visits.

## Chronic respiratory disease (two US studies)

- Oreskovic 2020: Investigators in Boston found that despite an increase in hospital admissions for COVID-19 between February and April 2020, there was a decline in pediatric asthma-related emergency department visits compared to the same time period in 2019 (-8%, 38.8%, and 84.8% in February, March, and April, respectively). This sharp decrease may reflect families avoiding health care institutions for fear of contracting COVID-19, structural contributing factors based on health care provider recommendations, or early evidence of improved asthma control or beneficial environmental shifts such as improved air quality.

- Kaye 2020: Investigators used an electronic medical monitoring system to evaluate daily inhaler use among a sample of adult patients with chronic obstructive pulmonary disease or asthma (n=7,578) and found 14.5% increase (53.7% to 61.5%) in mean daily controller medication adherence between the first week of January 2020 and the last week of March 2020.

## Communicable diseases (two US studies)

- Bramer 2020: Investigators reviewing the vaccine registry in Michigan found a decline in coverage in all milestone age cohorts, except for birth-dose hepatitis B coverage, which is typically administered in the hospital setting prior to discharge after birth. The up-to-date status of children aged 5 months decreased from two-thirds (66.6%, 67.4%, 67.3%, 67.9%, respectively) in the years prior to just under half (49.6%) in May 2020. They found that measles-containing vaccination coverage decreased from 76.1% in May 2019 to 70.9% in May 2020. The number of non-influenza vaccine doses administered and reported for children aged ≤18 years decreased 21.5%, and the number of doses administered to children aged ≤24 months decreased 15.5% during January–April 2020, compared with the same averaged periods in 2018 and 2019. Notably there was a difference seen between payor status, with lower up-to-date status for Medicaid-enrolled children than for those children not enrolled in Medicaid, with the largest difference seen in the age 7 months cohort (34.6% vs 55.0%).

- Kalichman 2020: Investigators surveyed young adults living with HIV (n=162) and found that nearly 1 in 5 participants reported missing a scheduled HIV care appointment either due to personal or clinic cancellation. They found reports of decreased access to both food and medications but statistically significant increase in adherence to antiretroviral therapy.

## Organ donation (two US studies)

- Ahmed 2020: Through a web-based survey distributed to 19 organ procurement organizations throughout the United States, investigators found an 11% decrease in organ authorization (n=1379 vs n=1552, p=0.0001), 17% reduction in organ recovery for transplantation (p=0.0001), with a further 18% decrease in the number of organs transplanted (p=0.0001). Trauma as a cause of donor death declined by 4.5%, however substance use as a cause of death increased by 35% during the COVID-19 period.

- Boyarsky 2020: Investigators studied data from the Scientific Registry of Transplant Recipient (SRTR) and found a significant drop in the number of new organ donor listings, deceased donor kidney transplants, and live donor kidney transplants (18%, 24%, and 87% below the expected value respectively, all $p<0.001$). The number of waitlist deaths was more than twice as high as expected in the five states that had the highest COVID-19 burden ($p<0.001$).

## Cancer (one US study)

- Frey 2020: Investigators surveyed women with ovarian cancers (n=555) to evaluate treatment interruptions and quality of life during the COVID-19 pandemic. A total of 175 participants (33%) experienced a delay in some component of their cancer care. 10 (26.3%) of the 38 participants scheduled for surgery experienced a delay, as did 18 (8.3%) of the 217 participants scheduled for nonsurgical cancer treatment. A total of 133 participants (24.0%) had a delayed physician appointment, 84 (15.1%) laboratory tests, and 53 (9.6%) cancer-related imaging. Among the cohort, 88.6% (489) reported significant cancer worry, 51.4% (285) borderline or abnormal anxiety, and 26.5% (147) borderline or abnormal depression.

## Musculoskeletal disorders (one US study)

- Brown 2020: Investigators at six centers in the United States distributed surveys to patients whose elective orthopedic procedures had been canceled due to the COVID-19 pandemic (n=358), to assess pain, anxiety, physical function, and economic ability of patients to undergo a delayed operation. The majority of patients (86%) had their surgery postponed or canceled by the surgeon or hospital, whereas 14% of patients

initiated the cancellation. Older patients were more likely to have initiated the cancellation of their operation than younger patients (18% vs 10%, p=0.013). The cancellation reason was significantly different in the Northeast and South, with 18% and 25% of cancellations initiated by the patient compared with 3% for Midwest (p<0.0001).

## Risk of violence (one US study)

- Schleimer 2020: Investigators studied the association between changes in firearms purchases and interpersonal firearm violence in the US during the COVID-19 pandemic. They found an estimated 2.1 million excess firearms purchases nationally between March and May 2020 (63% increase over expected volume). Multivariable regression models showed that changes in firearm purchasing within states was significantly associated with changes in firearm violence during this period. They found a relative rate of death and injury from firearm violence of 1.015 (95% 1.005-1.025) for every 100 excess purchases per 100,000. Using model predictions, investigators found an estimated increase of 776 injuries (95% CI 216-1,335) across the US from March through May 2020 over what would have been expected had no increase in purchasing occurred (+7.8%, [95% CI 1.7%-13.9%]).

## APPENDIX F

**Examining the literature for health disparity data**

- A New York City study examined a decline in stroke admissions and favorable treatment outcomes (Agarwal 2020). Investigators do not analyze differences in stroke admissions among ethnic groups. Visually inspecting the reported estimates, however, it appears that a somewhat larger proportion of African-Americans was admitted for stroke in the first period than in the second period (14.2% and 10.9% respectively). Investigators do not disaggregate stroke outcomes by ethnic group.
- A US nationwide survey of parent and child well-being in households with at least one child (Patrick 2020) reported considerable data. Investigators do not analyze differences in responses among ethnic groups. Visually inspecting the estimates, however, there is apparently little difference in the proportions of White non-Hispanic, Black non-Hispanic and Hispanic respondents reporting worsened mental/behavioral or physical status for parents or children. Children's physical health in Hispanic households was more often reported to have worsened, compared to White or Black households (5.2%, 2.7% and 2.1%, respectively). Apart from this, physical and mental/behavioral status for parents and children in Black and Hispanic respondents generally seemed similar those in White households (perhaps not significantly different). Notwithstanding this, more respondents identifying as "other" than the above-named ethnic groups (n=103) reported what seem to be significantly worsened parental mental and physical health status and worsened child physical health status. Households with <$25k income (n=91) and those with $25k-$50k income (n=164) seemed generally to have slightly better parental health status and slightly worse child health status, compared to those in the other income strata.

# APPENDIX G

## COVID era findings for modeled conditions, from consolidated summary sheet

### Alcohol

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| COVID-19 | Alcohol use prevalence (adolescents) | RR 1.06 (0.93 - 1.21) | Canada | Mod | High | Dumas 2020 | NO - population not generalizable |
| | Binge drinking prevalence (adolescents) | RR 0.62 (0.50 - 0.79) | Canada | Mod | High | | NO - population not generalizable |
| | Mean # of standard drinks (university students) | RR 1.44 (1.31 - 1.58) | Northeast Ohio | High | High | Lechner 2020 | NO - population not generalizable |
| | Mean # of drinking days (university students) | RR 1.43 (1.34 - 1.52) | Northeast Ohio | High | High | | NO - population not generalizable |
| | # of drinking days | Risk 1.14 (1.00 - 1.29) | USA | High | High | Pollard 2020 | YES |
| | # of drinks, past month | Risk 1.00 (0.73 - 1.39) | USA | High | High | Pollard 2020 | YES |
| | # of binge drinking days, past month | Risk 1.19 (0.78 - 1.82) | USA | High | High | Pollard 2020 | YES |
| | Adverse consequences associated with alcohol use (SIP score, past 3 months) | Risk 1.30 (0.88 - 1.91) | USA | High | High | Pollard 2020 | YES |
| | % ED visits with alcohol as the chief complaint and diagnosis | RR 1.53 (1.40 - 1.69) | Midwest | High | High | Smalley 2020 | YES |
| | **Summary - Median (IQR)** | **1.19 (1.07 - 1.415)** | | High | High | | **Overall SoE: HIGH** |

### Depression

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| COVID-19 | Depression | RR 3.73 | USA | High | Mod | Czeisler 2020 | NO - no CI |
| | | RR 3.56 (3.36 - 3.77) | USA | High | Mod | Twenge 2020 | YES* |
| | | RR 3.65 (3.44 - 3.88) | USA | High | Mod | | YES* |
| | | RR 3.70 (3.49 - 3.92) | USA | High | Mod | | YES* |
| | | RR 3.77 (3.56 - 4.00) | USA | High | Mod | | YES* |
| | | RR 1.23 (0.98 - 1.51) | USA | High | Low | Bryan 2020 | NO - poor IV |
| | Google searches for depression | Risk 1.03 (1.01 - 1.06) | USA | Mod | High | Halford 2020 | NO - poor proxy for depression |
| | Prevalence with clinically significant mental distress | RR 1.44 (1.35 - 1.55) | UK | Mod | High | Pierce 2020 | YES |
| | Non-specific mental distress | RR 1.10 (1.08 - 1.12) | UK | Mod | High | | YES |
| | Proportion of childrens' ED visits that are mental health-related | RR 1.44 (1.34 - 1.55) | USA | High | High | Leeb 2020 | NO - population not generalizable |
| | | RR 1.31 (1.25 - 1.37) | | | | | |
| | | RR 1.24 (1.13 - 1.37) | | | | | |
| | % ED visits that are behavioral health encounters | RR 1.30 (1.23 - 1.36) | Midwest | Mod | High | Smalley 2020 | YES |
| | **Summary - Median (IQR)** | **1.37 (1.20 - 2.56)** | | High | Mod | | **Overall SoE: HIGH** |

## Homelessness

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| Great Recession | # of households receiving housing vouchers (federal rental assistance for low-income households) | Risk 6.67 | USA | Low | High | ICPH 2013 | YES |
| | **Summary - Value (range)** | **6.67 (5.336 - 8.004)** | | **Low** | **High** | | **Overall SoE: VERY LOW** |

## Intimate Partner Violence

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| COVID-19 | Domestic violence arrests | RR 0.73 (0.65 - 0.81) | Chicago, IL | Mod | High | Bullinger 2020 | NO - poor proxy |
| | | 1.22 | Portland, OR | Mod | High | Boserup 2020 | NO - poor proxy |
| | Domestic violence police reports | RR 1.10 (1.05 - 1.14) | Dallas, TX | Mod | High | Piquero 2020 | NO - poor proxy |
| | | RR 1.10 (1.05 - 1.16) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.12 (1.06 - 1.18) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.10 (1.04 - 1.17) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.02 (1.01 - 1.03) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.02 (1.01 - 1.03) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.02 (1.01 - 1.03) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | RR 1.02 (1.01 - 1.03) | Dallas, TX | Mod | High | | NO - poor proxy |
| | | 0.92 (0.88 - 0.95) | Chicago, IL | Mod | High | Bullinger 2020 | NO - poor proxy |
| | | 1.10 | New York, NY | Mod | High | Boserup 2020 | NO - poor proxy |
| | Police calls for service for domestic violence | 1.15 (1.08 - 1.22) | Los Angeles, CA | Mod | High | Mohler 2020 | YES |
| | | 1.16 (1.09 - 1.24) | Indianapolis, IN | Mod | High | | YES |
| | | 1.07 (1.05 - 1.10) | Chicago, IL | Mod | High | Bullinger 2020 | YES |
| | | 1.18 | San Antonio, TX | Mod | High | Boserup 2020 | NO - no CI |
| | | 1.27 | Jefferson County, AL | Mod | High | | NO - no CI |
| | Aggraveted domestic assault | Risk 1.37 | New Orleans, LA | Mod | Low | Buttell 2020 | NO - no CI |
| | | Risk 1.16 | New Orleans, LA | Mod | Low | | NO - no CI |
| | Domestic abuse | Risk 1.21 - 1.35 | USA | Mod | Low | Usher 2020 | NO - poor IV |
| | **Summary - Median (IQR)** | **1.11 (1.045 - 1.155)** | | **Mod** | **High** | | **Overall SoE: HIGH** |

## Opioids

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| COVID-19 | In-hospital stroke mortality | RR 3.03 (1.37 - 6.69) | New York City, NY | High | High | Agarwal 2020 | YES |
| | | RR 3 | New Jersey | High | High | Siegler 2020 | NO - no CI |
| | | RR 1.41 (0.74 - 2.70) | Massachusetts | High | High | Bhatt 2020 | YES |
| | | RR 0.75 (0.51 - 1.09) | Greece | Mod | High | Kerleroux 2020 | NO - not US |
| | | RR 1.40 (1.30 - 1.51) | California | High | High | Friedlich 2021 | YES |
| | | RR 0.92 (0.56 - 1.52) | Northern California | High | High | Nguyen-Huynh 2020 | YES |
| | | RR 1.67 (0.47 - 5.88) | Irvine | High | High | Nagamine 2020 | YES |
| | | RR 1.64 (1.16 - 2.31) | 9 US states | High | High | Siegler 2021 | YES |
| | **Summary - Median (IQR)** | **1.525 (1.40 - 1.67)** | | High | High | | **Overall SoE: HIGH** |

## Stroke

| Risk Factor | Outcome | Risk Ratio & 95%CI | Location | Strength of Evidence | | Author and year | Include for BRACE input |
|---|---|---|---|---|---|---|---|
| | | | | External Validity | Internal Validity | | |
| COVID-19 | Overdose deaths | 2.04 | Indianapolis | High | High | Glober 2020 | YES |
| | Overdose incidence (as determined by EMS provider) | 1.3 | Indianapolis | High | High | Glober 2020 | YES |
| | Naloxone administration | 1.91 | Indianapolis | High | High | Glober 2020 | YES |
| | Organ donor cause of death substance abuse | Risk 1.35 (1.16 - 1.57) | USA | High | High | Ahmed 2020 | YES |
| | **Summary - Median (IQR)** | **1.63 (1.325 - 1.975)** | | High | High | | **Overall SoE: MODERATE** |

# APPENDIX H

**Table 11. Interventions included in BRACE modeling**

| Condition | Intervention | Outcome | Risk Ratio & 95% CI | Location | Author & Year |
|---|---|---|---|---|---|
| Depression | SSRI medications | Significant improvement (50% decrease in score) | RR 0.75 (0.62 - 0.90) | USA/Europe (meta-analysis) | Arroll 2009 |
| Depression | Cognitive-Behavioral Treatment (CBT) | Remission of depression | RR 0.65 (0.51 - 0.83) | Worldwide (meta-analysis) | Cuijpers 2014 |
| Depression | Mindfulness | Multiple health conditions among those with 3+ ACEs | PR 0.66 (0.51 - 0.85) | Pennsylvania | Whitaker 2014 |
| Depression | Mindfulness | Poor health behavior among those with 3+ ACEs | PR 0.60. (0.38 - 0.95) | Pennsylvania | Whitaker 2014 |
| Depression | Mindfulness | Poor health-related quality of life among those with 3+ ACEs | PR 0.43 (0.25 - 0.75) | Pennsylvania | Whitaker 2014 |
| Intimate Partner Violence | Nurse-Family Partnership Home Visiting | IPV within 4 years | RR 0.79 (0.99 – 0.64) | USA | Miller 2015 |
| Homelessness | Rent subsidies | # of households receiving housing vouchers | 6.67 (NA) | USA | ICPH 2013 |
| Opioid use disorder | Medication-Assisted Treatment (MAT) | Overdose mortality during treatment | RR 0.12 (0.07 – 0.22) | Worldwide (meta-analysis) | Ma 2019 |
| Opioid use disorder | Medication-Assisted Treatment (MAT) | All-cause mortality during treatment | RR 0.39 (0.26 – 0.58) | Worldwide (meta-analysis) | Ma 2019 |
| Excess alcohol use | Brief intervention (as in SBIRT) | Alcohol consumption | -50g of alcohol/week (-65 - -34); 15% greater decrease than controls | Worldwide (meta-analysis) | Bertholet 2005 |
| Stroke | Public awareness campaigns | ER stroke admissions | RR 1.07 (1.001 – 1.14) | England | Flynn 2014 |
| Stroke | Public awareness campaigns | ER stroke admissions within 5 hours of symptoms | RR 1.11 (1.03 – 1.21) | Canada | Hodgson 2007 |

# APPENDIX I

## BRACE model detailed analysis: case study on depressive symptoms

We applied the BRACE modeling approach to six different priority public health conditions for which there is evidence of increased prevalence during the pandemic: adult depression, excessive alcohol use, opioid use disorder, housing insecurity, intimate partner violence (IPV), and stroke mortality. Below, we provide a detailed discussion of the results for adult depression, as a case study, to illustrate the range of findings possible using this approach.

**BRACE results for effects of COVID-19 on depressive symptoms in adults and secondarily in children exposed to a depressed caregiver**: Our BRACE model analysis of **adult depression** (including depressive symptoms not necessarily meeting formal diagnostic criteria for depression) is presented in Supplemental Table 12. Input values derive from the most relevant studies in our literature review. Sources for all input values, including notes on their interpretation, are available in RAPID spreadsheets provided separately to the OSG. Due to imperfect internal validity (study precision and accuracy for study subjects) and external validity (applicability to COVID-19 in California), we conducted extensive sensitivity analyses to quantify the impact of uncertainty in input values on results.

Prevalence prior to COVID-19 is estimated at 18.5%. Direct medical costs (all costs inflated to 2020) are estimated at $12,806 per case in the short term, and non-medical direct costs at $1,130. With a recurrence risk of 45% and estimated four episodes of depression, if there is recurrence, the anticipated long-term costs are approximately twice as high as short-term. For children, costs are estimated at one-tenth of parent's costs, assuming one tenth likelihood, based on a ten-fold difference in long-term morbidity (see below). Discounted at 3%, total direct cost per episode is $34,157.

Morbidity is quantified in health state utility (0 to 1, where 1 indicates perfect health) and is incorporated into QALYs. Studies suggest a 0.5 drop in utility during the episode, which persists for 0.5 years, the mean duration of a depressive episode. The drop is similar in subsequent episodes if they occur (45%), and we spread these drops in utility over two years. For children, the observed utility drop is one-tenth as much, reflecting a sporadic risk of depressive episodes, and ongoing for ten years. We could not find reliable and usable data on concurrent (short-term) utility drop for children.

Mortality, largely due to suicide, is estimated at 4 per 1,000 in the short-term and similar risk for multiple subsequent episodes. Mortality risks for the children are 4 per 10,000 short-term and 3 per 10,000 long-term.

COVID-19 increases the risk of depression by an estimated 37% (median of identified studies). This increased risk results in a depression prevalence of 25.3%, of which 6.9% is due to

COVID-19. The resulting added direct cost per capita is $2,338, and there are 0.078 lost QALY per capita.

We examined two interventions that could mitigate the effects of increases in adult depression: 1) cognitive-behavior therapy with selective serotonin reuptake inhibitor medications (CBT + SSRI) and 2) a mindfulness meditation intervention for children of affected adults (hereafter mindfulness). These interventions, like all examined in the BRACE model, are not COVID-specific, for three reasons. First, the interventions were designed and tested before COVID; we found no reports of COVID-adapted versions. Second, we believe it is challenging to definitively attribute a specific case of depression or other conditions we examine to COVID. A detailed clinical assessment *might* suggest a likelihood of COVID etiology, e.g., if depressive symptoms start soon after a job layoff due to COVID, but the determination would not be definitive in the presence of other risk factors and related medical history. Third, we can identify no compelling reason to limit interventions to those individuals who appear more likely to have COVID as a substantial contributing cause; rather, we believe that interventions will be tailored to diagnosis, whatever the etiology.

CBT + SSRI has an estimated cost of $878 per client, with 25% efficacy. Assuming 20% coverage in a population of one million, the cost is $45 million. This leads to a 1.3% reduction in prevalence (from 25.3% to 24.1%), with 14 thousand QALYs gained. The savings (averted direct costs) are estimated at $433 million, yielding net savings of $61 million within a year and $236 million by 10 years. By traditional economic criteria, the intervention appears quite promising, i.e., both mitigating indirect health harms of COVID-19 and producing substantial economic savings, even in the first year.

Mindfulness for a child exposed to a depressed caregiver can also be implemented. Cost is an estimated $200, with 17% efficacy in reducing ACE-related harm (extrapolated from benefits of mindfulness for ACEs in observational studies). With 20% coverage, the cost is $10 million, and 1,200 QALYs are gained. Savings are $13 million, with net savings projected after 10 years.

**Table 12: BRACE results *for effects of COVID-19 on depression in adults and secondarily in children.***

| Adult Depression 16-Dec-2020 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.185 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $12,806 | $17,150 | | $1,432 |
| Non-medical direct (social svcs, law enforcement) | $1,130 | $1,513 | | $126 |
| *Total direct* | ***$13,936*** | ***$18,663*** | | ***$1,558*** |
| Productivity loss | $11,936 | $8,880 | | |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0.53 | 0.2385 | 0 | 0.026 |
| Duration (yrs) | 0.5 | 2 | 1 | 10 |
| QALY burden morbidity | **0.27** | **0.35** | | **0.12** |
| **Mortality:** added deaths per case | 0.004 | 0.018 | 0.00042 | 0.0003 |
| QALY burden mortality | **0.10** | **0.28** | **0.01** | **0.00** |
| QALY total | **0.36** | **0.64** | **0.01** | **0.13** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 1.37 | | | |
| Prevalence under COVID | **0.25345** | | | |
| Add prevalence under COVID | **0.0685** | | | |
| Added direct cost per capita | **$954** | **$1,277** | | **$107** |
| Added QALYs lost per capita | **0.025** | **0.044** | **0.001** | **0.009** |

| BRACE = Broad & Rapid Analysis of COVID indirect Effects | | |
|---|---|---|
| **Intervention Outcomes** | | |
| **Effect of intervention** | **Intervention 1** | **Intervention 2** |
| | CBT + SSRI | Mindfulness (for child) |
| Reduction in prevalence (efficacy) | 0.25 | 0.17 |
| Cost | $878 | $200 |
| Prevalence after intervention | 0.190 | n/a |
| Partial Implementation level | 0.20 | 0.20 |
| Prevalence after partial implementation | 0.2408 | n/a |
| Reduction in prevalence | 0.0127 | n/a |
| **Costs & Savings** (per person affected) | | |
| Cost of **partial** implementation | $176 | $40 |
| Savings (direct) from partial implementation | $1,708 | $53 |
| QALY gain from partial intervention | 0.0569 | 0.0048 |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) | Dominant (cheaper+better) |
| | -$26,939 | -$2,727 |
| **Scaled up** | 1,000,000 | 1,000,000 |
| Cost | $44,505,820 | $10,138,000 |
| Savings (direct) | $432,858,736 | $13,427,792 |
| Net (red / parenthetical = savings) | ($388,352,916) | ($3,289,792) |
| Cumulative projected net at 1 year | ($61,456,556) | $10,138,000 |
| Cumulative projected net at 3 years | ($161,739,349) | $7,452,442 |
| Cumulative projected net at 10 years | ($246,458,642) | $3,424,104 |
| QALY gain | 14,416 | 1,207 |

## Sensitivity analyses

We conducted one-way and multivariate sensitivity analyses for all results to address uncertainty in key inputs. Projections were conducted assuming an eligible population of one million individuals and 20% intervention coverage of the affected population. In multivariate analyses, we varied all input variables based on defined probability distributions and ranges. In one-way sensitivity analyses, each input was varied individually while all others were kept constant. The values included in the sensitivity analyses were obtained through a robust review of the literature; in cases where a reliable value could not be identified, expert opinion was used to inform input values.

Based on one-way sensitivity analyses for depression, costs related to implementing either intervention were most impacted by variation in costs of the interventions themselves, followed by the prevalence of depression under COVID-19. Net savings associated with CBT + SSRI were most influenced by the efficacy of this intervention, prevalence of depression under COVID-19, and medical cost per episode of depression. Net savings associated for mindfulness training were most impacted by the cost and efficacy of the intervention, as well as the long-term medical costs accrued by children as a result of the toxic stress resulting from the ACE. Shown below in Figures 7a, 7b, 7c and 7d are the one-way sensitivity analyses for net savings with CBT + SSRI, net savings with mindfulness, QALY gain per million with CBT + SSRI, and QALY gain per million with mindfulness.

**Figure 7a. One-way sensitivity analyses for net savings with CBT + SSRI intervention for adult depression. Net savings range from $300 to $700 million in a one-way SA for CBT + SSRI.**

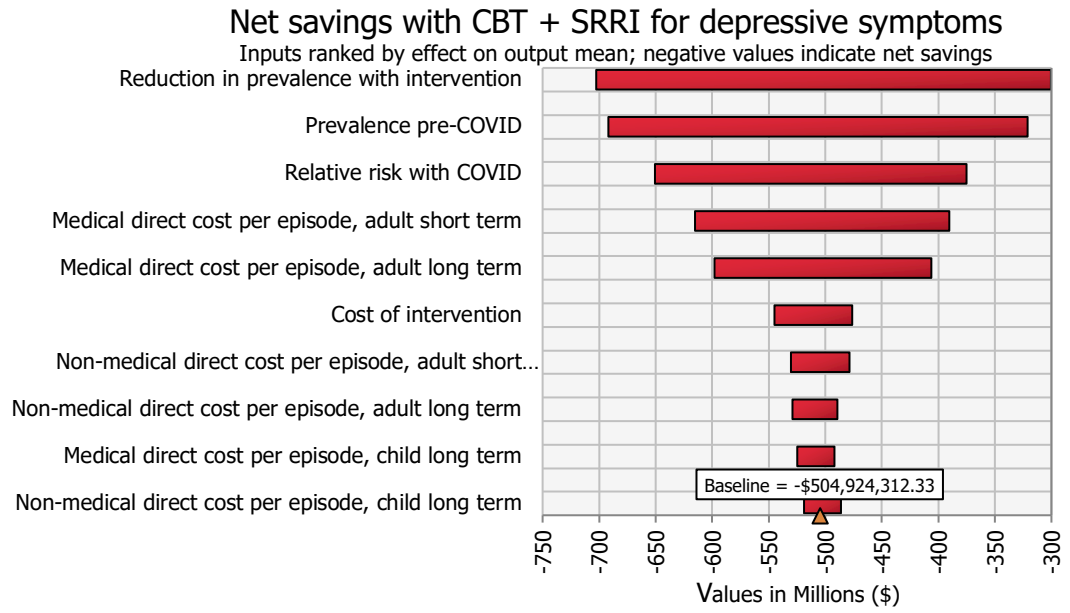



**Figure 7b. One-way sensitivity analyses for net savings with mindfulness intervention for children of adults with depression. Net savings range from no savings to $9 million in a one-way SA for mindfulness.**

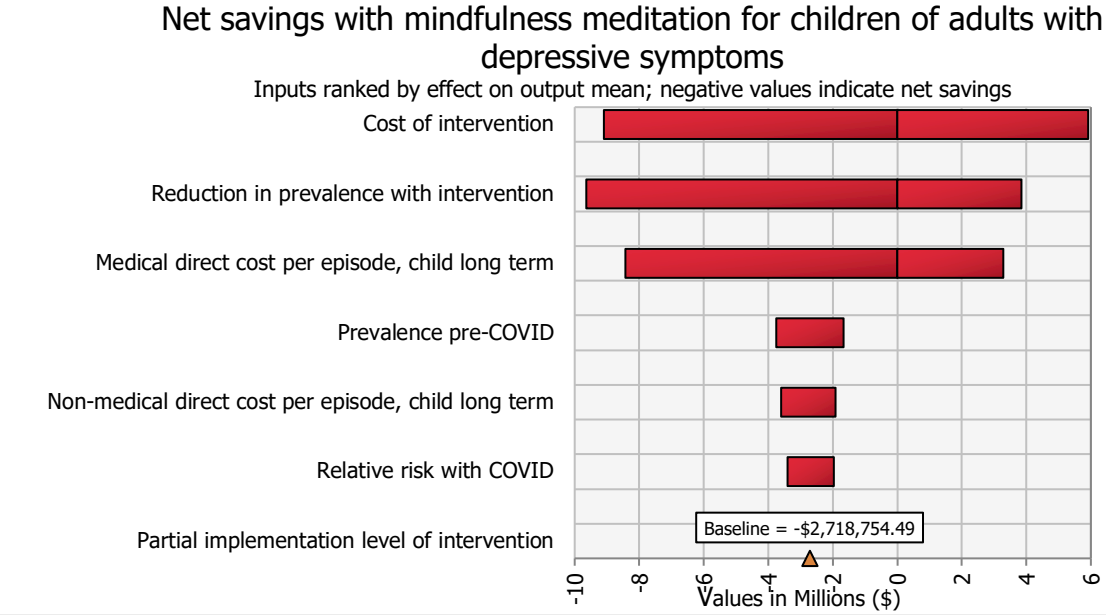


**Figure 7c. One-way sensitivity analyses for QALYs gained per 1 million people with CBT + SSRI intervention for adult depression. QALY gains range from 12,000 to 26,000 in one-way SAs for CBT + SSRI.**

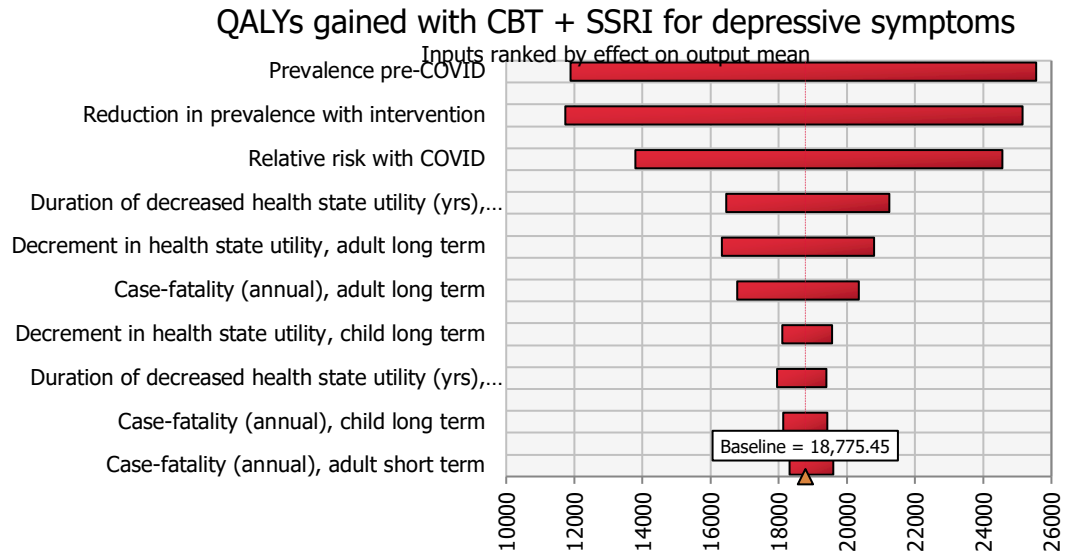
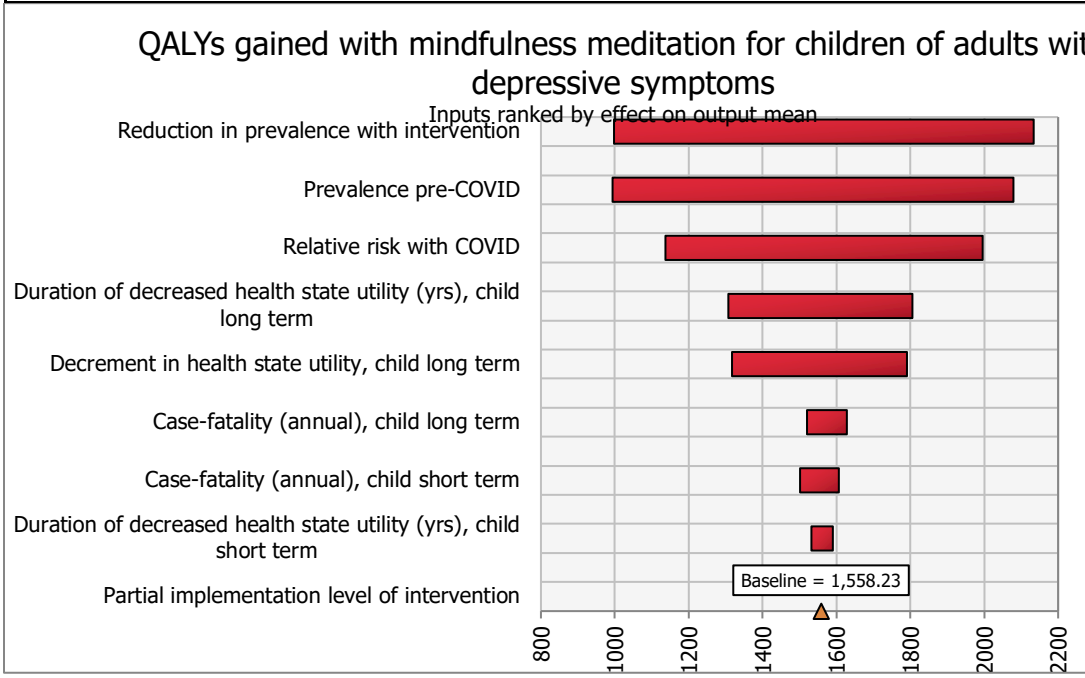



**Figure 7d. One-way sensitivity analyses for QALYs gained per 1 million people with mindfulness intervention for children of adults with depression. QALY gains range from 1,000 to 2,100 when the input that has the most effect on this output is varied in a one-way SA for mindfulness.**



**BRACE model detailed analysis: Overview of findings**

Our analysis of **adult depression/depressive symptoms** is presented in full detail above. We estimate a 37% increase in this condition due to COVID-19, resulting in a prevalence near 25%. The cost per case, including short-term and long-term consequences in the affected adult and their child, is nearly $34,000. The cost per case translates to a COVID-19-associated added direct cost per capita of nearly $2,300. CBT + SSRI medications have an estimated cost of $878 per case, with 25% efficacy. Assuming 20% coverage in a population of one million, the cost is $45 million. This intervention leads to a 1.3% reduction in prevalence (from 25.3% to 24.1%), with 14,000 QALYs gained. The savings (averted direct costs) are estimated at $433 million, yielding net savings of $61 million within a year and $246 million by 10 years. By traditional economic criteria, this finding makes the intervention quite promising, i.e., both mitigating indirect health harms of the pandemic and producing substantial economic savings for California. A mindfulness intervention (efficacy extrapolated from observed benefits of mindfulness for ACEs in observational studies) for an exposed child costs an estimated $200, with 17% efficacy in reducing ACE-related harm. With 20% coverage, the cost is $10 million, and 1,200 QALYs are gained. Savings are $13 million, with net savings projected after 10 years.

## Intimate partner violence

**IPV (supplemental table 13)**: We estimate an 11% increase in this condition due to COVID-19, resulting in a prevalence of 6%. The cost per case, including short-term and long-term consequences in the affected adult and their child, is $122,000; this cost per case translates into a COVID-associated added direct cost per capita of $740. Nurse-family partnership (NFP) home visiting program has an estimated cost of $13,000 per family, with 21% efficacy. Assuming 20% coverage in a population of one million, the cost is $165 million. This intervention, if implemented, is projected to reduce the prevalence of IPV by approximately 0.3% (to 5.8%), with 24,000 QALYs gained. The savings (averted direct costs) are estimated at $313 million, yielding net costs of $70 million within a year and net savings of $59 million by 10 years. The results highlight that implementing this intervention may not only mitigate indirect health harms of COVID-19 but also produce substantial economic savings.

## Supplemental Table 13. BRACE results for effects of COVID-19 on IPV

| DV / IPV 2-Mar-2020 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.055 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $45,247 | $41,621 | | $5,701 |
| Non-medical direct (social svcs, law enforcement) | $16,453 | $12,241 | | $991 |
| *Total direct* | ***$61,700*** | ***$53,862*** | | ***$6,692*** |
| Productivity loss | $788 | $528 | | $13,180 |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0.4 | 0.4 | 0.02 | 0.05 |
| Duration (yrs) | 1 | 27 | 1 | 30 |
| QALY burden morbidity | **0.40** | **8.04** | **0.02** | **0.72** |
| **Mortality:** added deaths per case | 0.00017 | 0.01364 | | 0.0045 |
| QALY burden mortality | **0.0041** | **0.2131** | | **0.05** |
| QALY total | **0.40** | **8.25** | **0.02** | **0.77** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 1.11 | | | |
| Prevalence under COVID | **0.06105** | | | |
| Add prevalence under COVID | **0.0061** | | | |
| Added direct cost per capita | **$373** | **$326** | **$0** | **$40** |
| Added QALYs lost per capita | **0.002** | **0.050** | **0.000** | **0.005** |

| BRACE = Broad & Rapid Analysis of COVID indirect Effects | |
|---|---|
| **Intervention Outcomes** | |
| **Effect of intervention** | **Intervention 1** |
| | NFP Home visiting |
| Reduction in prevalence | 0.21 |
| Cost | $13,489 |
| Prevalence after intervention | 0.048 |
| Partial Implementation level | 0.20 |
| Prevalence after partial implementation | 0.0585 |
| Reduction in prevalence | 0.0026 |
| **Costs & Savings** (per person affected) | |
| Cost of **partial** implementation | $2,698 |
| Savings (direct) from partial implementation | $5,135 |
| QALY gain from partial intervention | 0.3965 |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) |
| | -$6,145 |
| **Scaled up** | 1,000,000 |
| Cost | $164,700,690 |
| Savings (direct) | $313,470,457 |
| Net (red / parenthetical = savings) | ($148,769,767) |
| Cumulative projected net at 1 year | $69,777,708 |
| Cumulative projected net at 3 years | ($5,305,232) |
| Cumulative projected net at 10 years | ($58,937,215) |
| QALY gain | 24,208 |

## Homelessness

**Homelessness (supplemental table 14):** Nearly seven-fold increase is projected in this condition due to COVID-19, resulting in a prevalence of 2.5%. The cost per case, including short-term and long-term consequences in the affected adult and their child, is $102,000, resulting in a COVID-associated added direct cost per capita of $2,200. Rent subsidies have an estimated cost of $9,000 per client, with 43% efficacy in reducing consequences (accounting for intervention delivery after experiencing homelessness). Assuming 20% coverage in an eligible population of one million, the cost is $47 million. This leads to a reduction in prevalence of homelessness to 2.3%, with 3,000 QALYs gained. The savings (averted direct costs) are estimated at $221 million, yielding net costs of $5 million within a year and net savings of $95 million by 10 years. Thus, the intervention appears to be dominant, or achieves a cost-savings.

**Supplemental Table 14. BRACE results for effects of COVID-19 on housing insecurity**

| Homelessness 21-Dec-2020 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.0038 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $14,132 | $46,403 | | $2,390 |
| Non-medical direct (social svcs, law enforcement) | $18,626 | $20,808 | | |
| *Total direct* | ***$32,758*** | ***$67,211*** | | ***$2,390*** |
| Productivity loss | | | | |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0.36 | 0.22 | 0.038 | 0.015 |
| Duration (yrs) | 1 | 1 | 1 | 20 |
| QALY burden morbidity | **0.360** | **0.164** | **0.038** | **0.14** |
| **Mortality:** added deaths per case | 0.01 | | 0.0125 | 0.0125 |
| QALY burden mortality | **0.24** | **0.00** | **0.36** | **0.14** |
| QALY total | **0.601** | **0.164** | **0.403** | **0.287** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 6.67 | | | |
| Prevalence under COVID | **0.0253** | | | |
| Add prevalence under COVID | **0.0215** | | | |
| Added direct cost per capita | **$706** | **$1,448** | **$0** | **$51** |
| Added QALYs lost per capita | **0.0130** | **0.0035** | **0.0087** | **0.006** |

BRACE = Broad & Rapid Analysis of COVID indirect Effects

| **Intervention Outcomes** | | |
|---|---|---|
| **Effect of intervention** | **Intervention 1** | **Intervention 2** |
| | Pay mean cost of housing | |
| Reduction in prevalence | 0.43 | |
| Cost | $9,282 | |
| Prevalence after intervention | 0.0146 | |
| Partial Implementation level | 0.20 | |
| Prevalence after partial implementation | 0.0232 | |
| Reduction in prevalence | 0.0022 | |
| **Costs & Savings** (per person affected) | | |
| Cost of **partial** implementation | $1,856 | |
| Savings (direct) from partial implementation | $8,701 | |
| QALY gain from partial intervention | 0.1237 | |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) | |
| | -$55,351 | |
| **Scaled up** | 1,000,000 | |
| Cost | $47,052,314 | |
| Savings (direct) | $220,542,115 | |
| Net (red / parenthetical = savings) | ($173,489,801) | |
| Cumulative projected net at 1 year | $4,704,082 | |
| Cumulative projected net at 3 years | ($46,462,379) | |
| Cumulative projected net at 10 years | ($94,979,917) | |
| QALY gain | 3,134 | |

## Opioid use disorder

**Opioid use disorder (supplemental table 15):** A 63% increase is expected in this condition due to COVID-19, resulting in a prevalence of 1.8%. The cost per case, including short-term and long-term consequences in the affected adult and their child, is $82,000, resulting in a COVID-associated added direct cost per capita of $571. Medication-assisted treatment (MAT) with methadone or buprenorphine has an estimated cost of nearly $16,000 per client, with 39% efficacy in reducing negative health and financial (e.g., medical and non-medical direct cost) consequences. Assuming 20% coverage in an eligible population of one million, the cost is $56 million. This intervention, if implemented, is estimated to lead to 0.14% reduction in prevalence of opioid use disorder (to about 1.7%), with 6,300 QALYs gained. The savings (averted direct costs) are estimated to be $115 million, with $36 million net costs in the first year and net savings of $16 million by 10 years.

**Supplemental Table 15. BRACE results for effects of COVID-19 on opioid use disorder.**

| Opioid Use Disorder 21-Dec-2020 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.011 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $16,608 | $34,208 | | $2,390 |
| Non-medical direct (social svcs, law enforcement) | $7,378 | $21,357 | | $508 |
| *Total direct* | ***$23,986*** | ***$55,565*** | | ***$2,898*** |
| Productivity loss | $16,233 | | | |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0.306 | 0.193 | 0.085 | 0.028 |
| Duration (yrs) | 1 | 25 | 1 | 25 |
| QALY burden morbidity | **0.31** | **3.59** | **0.09** | **0.33** |
| **Mortality:** added deaths per case | 0.006692 | | 0.000326 | 0.000101 |
| QALY burden mortality | **0.16** | **0.00** | **0.01** | **0.00** |
| QALY total | **0.47** | **3.59** | **0.09** | **0.34** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 1.63 | | | |
| Prevalence under COVID | **0.0179** | | | |
| Add prevalence under COVID | **0.0069** | | | |
| Added direct cost per capita | **$166** | **$385** | **$0** | **$20** |
| Added QALYs lost per capita | **0.003** | **0.025** | **0.001** | **0.002** |

| BRACE = Broad & Rapid Analysis of COVID indirect Effects | | |
|---|---|---|
| **Intervention Outcomes** | | |
| **Effect of intervention** | **Intervention 1** | **Intervention 2** |
| | MAT Buupr / Methadone | |
| Reduction in prevalence | 0.39 | |
| Cost | $15,669 | |
| Prevalence after intervention | 0.011 | |
| Partial Implementation level | 0.20 | |
| Prevalence after partial implementation | 0.0165 | |
| Reduction in prevalence | 0.0014 | |
| **Costs & Savings** (per person affected) | | |
| Cost of **partial** implementation | $3,134 | |
| Savings (direct) from partial implementation | $6,431 | |
| QALY gain from partial intervention | 0.3500 | |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) | |
| | -$9,420 | #DIV/0! |
| **Scaled up** | 1,000,000 | |
| Cost | $56,189,034 | |
| Savings (direct) | $115,307,398 | |
| Net (red / parenthetical = savings) | ($59,118,364) | |
| Cumulative projected net at 1 year | $36,061,806 | |
| Cumulative projected net at 3 years | $10,051,017 | |
| Cumulative projected net at 10 years | ($15,547,014) | |
| QALY gain | 6,276 | |

## Excessive alcohol use

**Excessive alcohol use (supplemental table 16):** A 19% increase in this condition is estimated due to COVID-19, resulting in a prevalence of 7.3%. The estimated cost per case, including short-term and long-term consequences in the affected adult and a child exposed to a caregiver who drinks excessively, is $298,000, resulting in a COVID-associated added direct cost per capita of $1,140. A screening and brief alcohol intervention (SBIRT) has an estimated cost of $450 per client, with 15% efficacy in reducing consequences. Assuming 20% coverage in an eligible population of one million, the cost is $7 million. This intervention, if implemented, is estimated to reduce the prevalence by 0.2% (to about 7.0%), with 5,600 QALYs gained. The savings (averted direct costs) are estimated at $214 million, making the intervention "dominant," with net savings of $9 million within a year and $112 million by 10 years.

**Supplemental Table 16. BRACE results for effects of COVID-19 on excessive alcohol use.**

| Alcohol 21-Dec-2020 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.061 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $4,425 | $48,336 | | $2,390 |
| Non-medical direct (social svcs, law enforcement) | $7,456 | $33,787 | | $1,925 |
| *Total direct* | ***$11,881*** | ***$82,123*** | | ***$4,315*** |
| Productivity loss | | | | |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0.43 | 0.11 | 0.085 | 0.028 |
| Duration (yrs) | 1 | 10 | 1 | 20 |
| QALY burden morbidity | **0.43** | **0.82** | **0.09** | **0.27** |
| **Mortality:** added deaths per case | 0.00338 | 0.057 | 0.00022 | 0.0003 |
| QALY burden mortality | **0.08** | **0.89** | **0.01** | **0.00** |
| QALY total | **0.51** | **1.71** | **0.09** | **0.27** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 1.19 | | | |
| Prevalence under COVID | **0.07259** | | | |
| Add prevalence under COVID | **0.0116** | | | |
| Added direct cost per capita | **$138** | **$952** | **$0** | **$50** |
| Added QALYs lost per capita | **0.006** | **0.020** | **0.001** | **0.003** |

| BRACE = Broad & Rapid Analysis of COVID indirect Effects | | |
|---|---|---|
| **Intervention Outcomes** | | |
| **Effect of intervention** | **Intervention 1** | **Intervention 2** |
| | Brief Intervention | |
| Reduction in prevalence | 0.15 | |
| Cost | $452 | |
| Prevalence after intervention | 0.062 | |
| Partial Implementation level | 0.20 | |
| Prevalence after partial implementation | 0.0704 | |
| Reduction in prevalence | 0.0022 | |
| **Costs & Savings** (per person affected) | | |
| Cost of **partial** implementation | $90 | |
| Savings (direct) from partial implementation | $2,950 | |
| QALY gain from partial intervention | 0.0775 | |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) | |
| | -$36,697 | #DIV/0! |
| **Scaled up** | 1,000,000 | |
| Cost | $6,562,136 | |
| Savings (direct) | $214,110,178 | |
| Net (red / parenthetical = savings) | ($207,548,042) | |
| Cumulative projected net at 1 year | ($8,961,816) | |
| Cumulative projected net at 3 years | ($54,371,177) | |
| Cumulative projected net at 10 years | ($112,135,917) | |
| QALY gain | 5,625 | |

## Stroke mortality

**Stroke mortality (table 17):** Due to COVID-19, in-hospital mortality for patients admitted with stroke symptoms have increased 53%, to 0.02 (i.e., the likelihood of dying in hospital if presenting with a stroke). In Table X, the prevalence shown (0.00015) is adjusted for the likelihood of hospital admission for stroke. The cost per case is $17,000 and the COVID-19 associated added direct cost per capita is just below $1. These costs do not include long term costs for the child since stroke typically occurs later in life (e.g. age 60-70), when offspring are adult, and thus does not lead to an ACE. A public awareness campaign encouraging people to seek care if they experience symptoms is estimated to cost nearly $100 per person at risk for stroke and has an estimated 11% efficacy in reducing consequences. Rolled out to a population of one million, this intervention is projected to cost $14,000 and lead to 388 QALYs gained. The savings (averted direct costs) are estimated at $270,000, with net savings of $148,000 within a year and $242 by 10 years. The intervention remains dominant even with an efficacy one-tenth as much.

**Supplemental Table 17. BRACE results for effects of COVID-19 on stroke mortality.**

| Stroke Mortality 05-Mar-2021 | | | | |
|---|---|---|---|---|
| **Added Burden** | | | | |
| **Prevalence pre-covid** | 0.00009588 | | | |
| | Adult | | Child | |
| | Short-term | Long-term | Short-term | Long-term |
| **Cost per episode** | | | | |
| Medical direct | $16,773 | | | |
| Non-medical direct (social svcs, law enforcement) | | | | |
| *Total direct* | ***$16,773*** | ***$0*** | ***$0*** | ***$0*** |
| Productivity loss | | | | |
| **QALY burden per episode** | | | | |
| **Morbidity:** drop in health state utility | 0 | | | |
| Duration (yrs) | 0 | | | |
| QALY burden morbidity | **0.00** | **0.00** | **0.00** | **0.00** |
| **Mortality:** added deaths per case | 1 | | | |
| QALY burden mortality | **24.11** | **0.00** | **0.00** | **0.00** |
| QALY total | **24.11** | **0.00** | **0.00** | **0.00** |
| Discount factor | | 0.744 | | 0.478 |
| **Effect of COVID-19** | | | | |
| Relative risk | 1.525 | | | |
| Prevalence under COVID | **0.00015** | | | |
| Add prevalence under COVID | **0.0000503** | | | |
| Added direct cost per capita | **$0.844** | **$0** | **$0** | **$0** |
| Added QALYs lost per capita | **0.001214** | **0.000** | **0.000** | **0.000** |

| BRACE = Broad & Rapid Analysis of COVID indirect Effects | | |
|---|---|---|
| **Intervention Outcomes** | | |
| **Effect of intervention** | **Intervention 1** | **Intervention 2** |
| | Awareness Campaign | |
| Reduction in prevalence | 0.11 | |
| Cost | ***$98*** | |
| Prevalence after intervention | 0.000 | |
| Partial Implementation level | 1.00 | |
| Prevalence after partial implementation | 0.0001 | |
| Reduction in prevalence | 0.0000 | |
| **Costs & Savings** (per person affected) | | |
| Cost of **partial** implementation | $98 | |
| Savings (direct) from partial implementation | $1,845 | |
| QALY gain from partial intervention | 2.6521 | |
| Cost-effectiveness ratio (ICER) | Dominant (cheaper+better) | |
| **Scaled up** | 1,000,000 | |
| Cost | $14,335 | |
| Savings (direct) | $269,775 | |
| Net (red / parenthetical = savings) | ($255,440) | |
| Cumulative projected net at 1 year | ($147,530) | |
| Cumulative projected net at 3 years | ($228,462) | |
| Cumulative projected net at 10 years | ($241,951) | |
| QALY gain | 388 | |

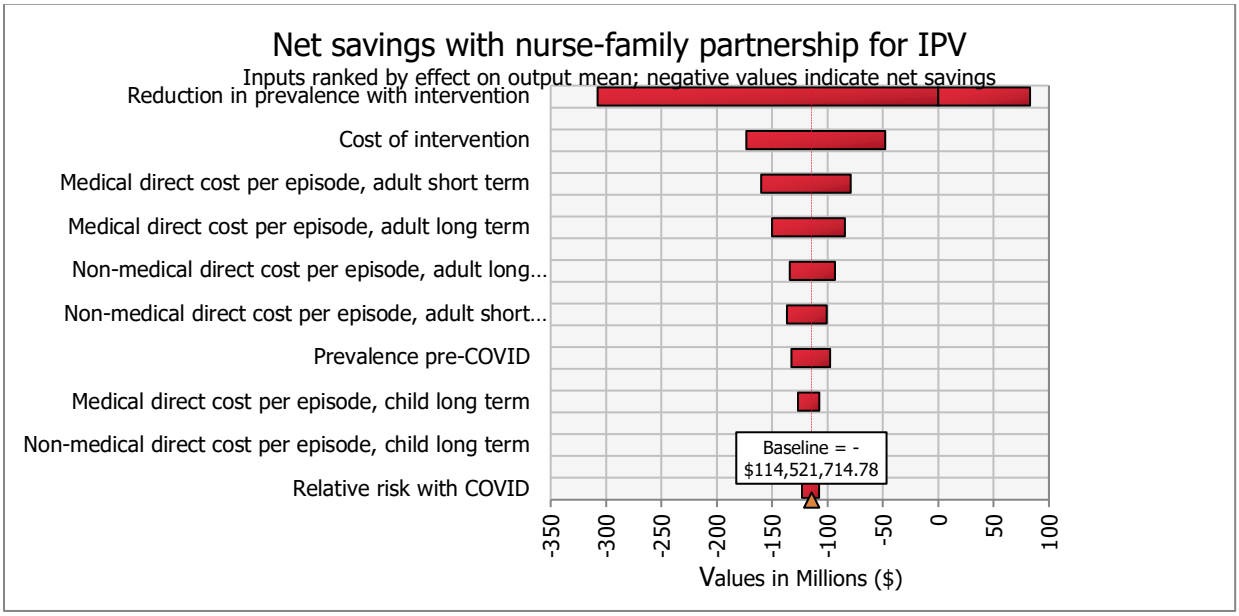
**Note:** We did not attempt to model racial/ethnic disparities due to concerns about the poor quality of current data. For example, for IPV, studies report lower growth in police reports by Black women compared with White and Hispanic women. Data on IPV reporting from the pre-COVID-19 period data suggest that IPV may be 60% higher among Hispanic women and 90% higher among Black women compared to White women. If this difference in pre-COVID-19 rates leads to larger differences in the rise in IPV rates due to COVID-19, the economic analyses will find that per capita health and economic burdens will be higher (e.g., 60% greater among Hispanics than Whites), as will intervention costs and benefits. The cost-effectiveness ratio would stay the same. In fact, post-COVID-19 increases in IPV may be even greater among Black and Hispanic women due to the heightened exposure of ethnic minority families to the economic fallout of the pandemic – an extreme stressor on families, which could increase IPV risk.

## BRACE Sensitivity Analyses

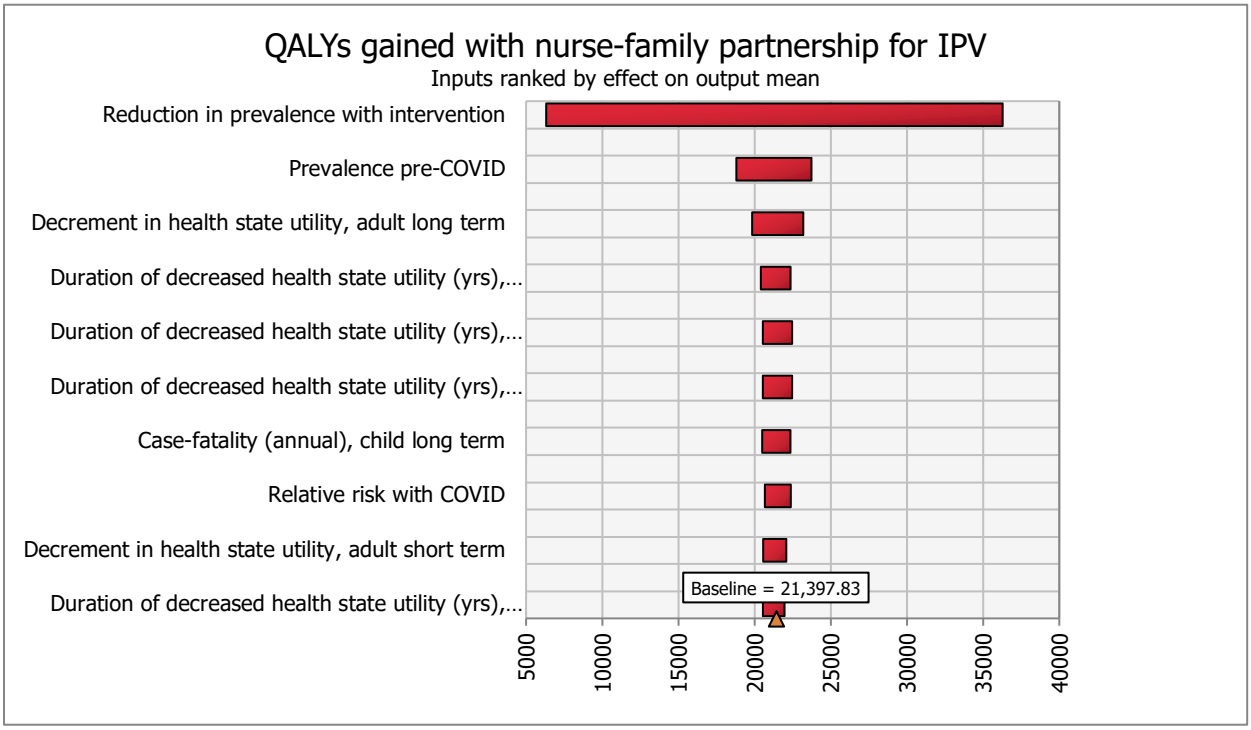
These pages present "tornado" diagrams to summarize the one-way sensitivity analyses (SAs). These figures indicate how two key outcomes – net overall cost and QALYs gained – vary according to uncertainty in the values of the most influential health and cost inputs. As with the multivariate analyses, these analyses suggest that the results are qualitatively robust – usually net savings (i.e., "dominant") and substantial QALY gains. A full (very large) set of one-way and multivariate SAs is available as a technical supplement on request.

## Intimate Partner Violence

The nurse-family partnership intervention appears to yield net savings up to $300 million or net costs up to $75 million in one-way SAs.

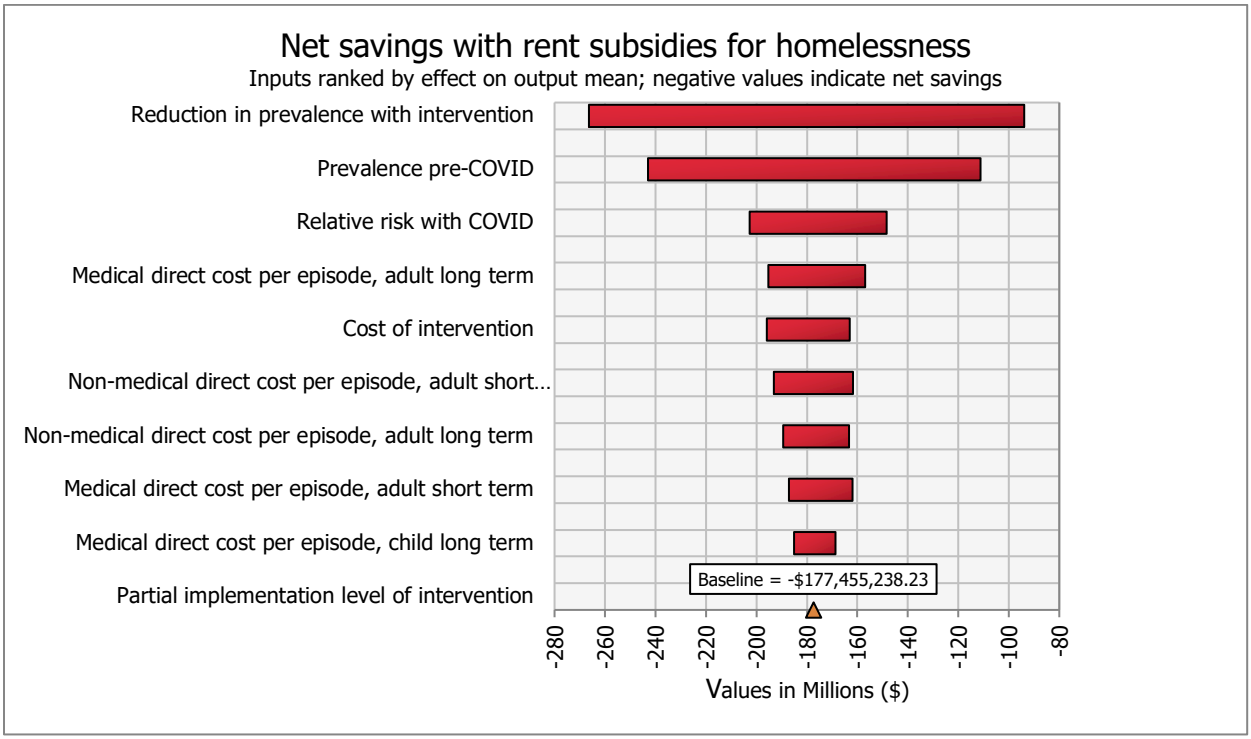



QALY gain ranges from 6,000 to 36,000 in one-way SAs.

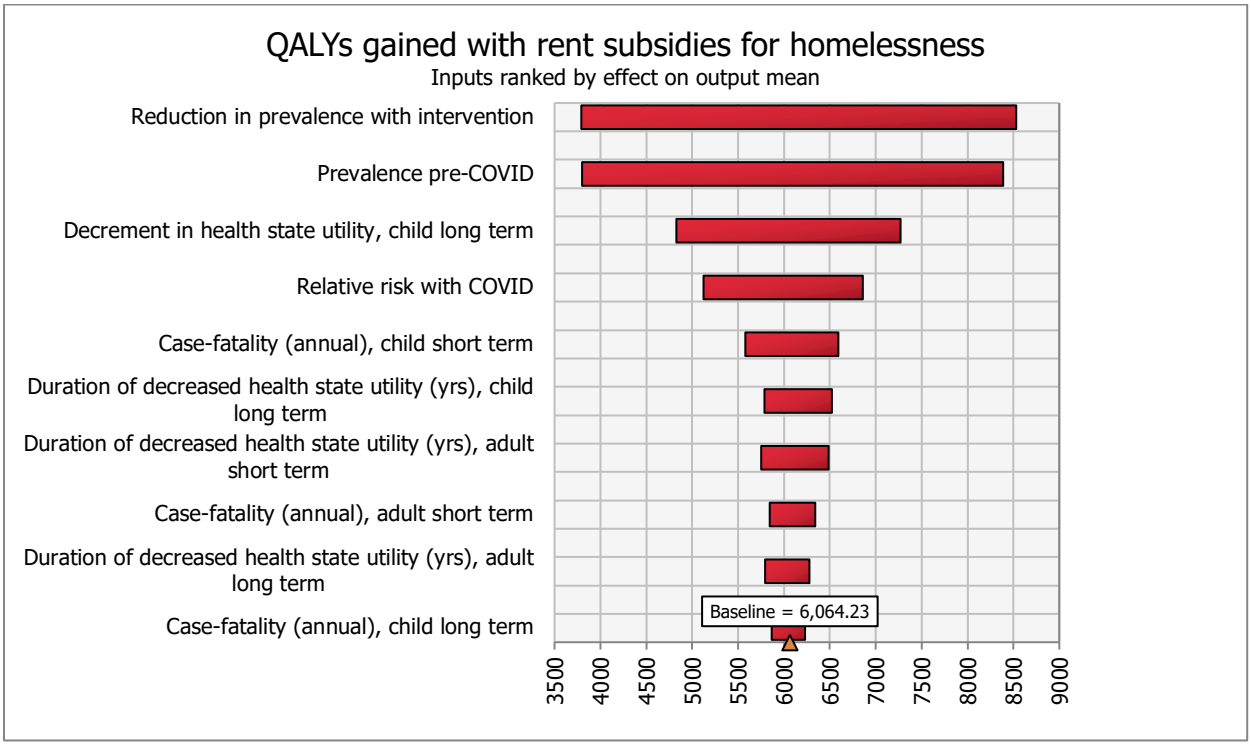


## Homelessness

The intervention has savings between $95 - $270 million for all one-way SAs.

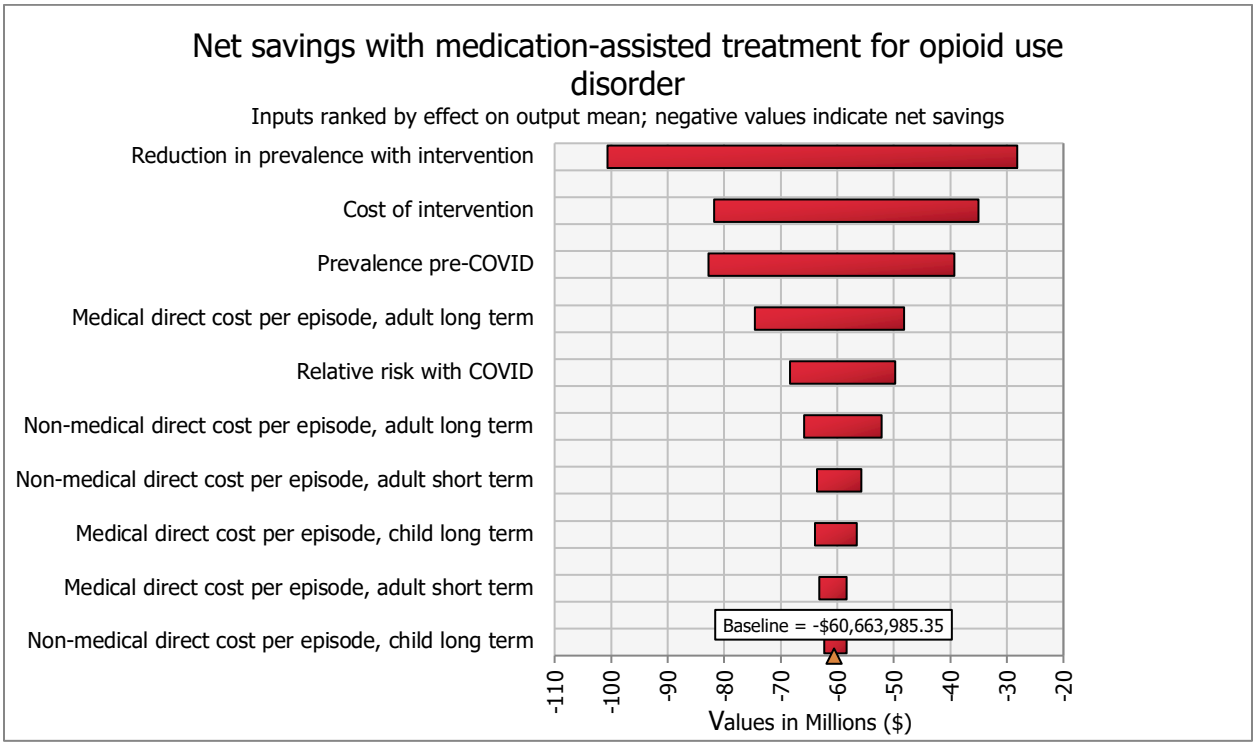



QALY gain ranges from 3,700 to 8,500 in one-way SAs.

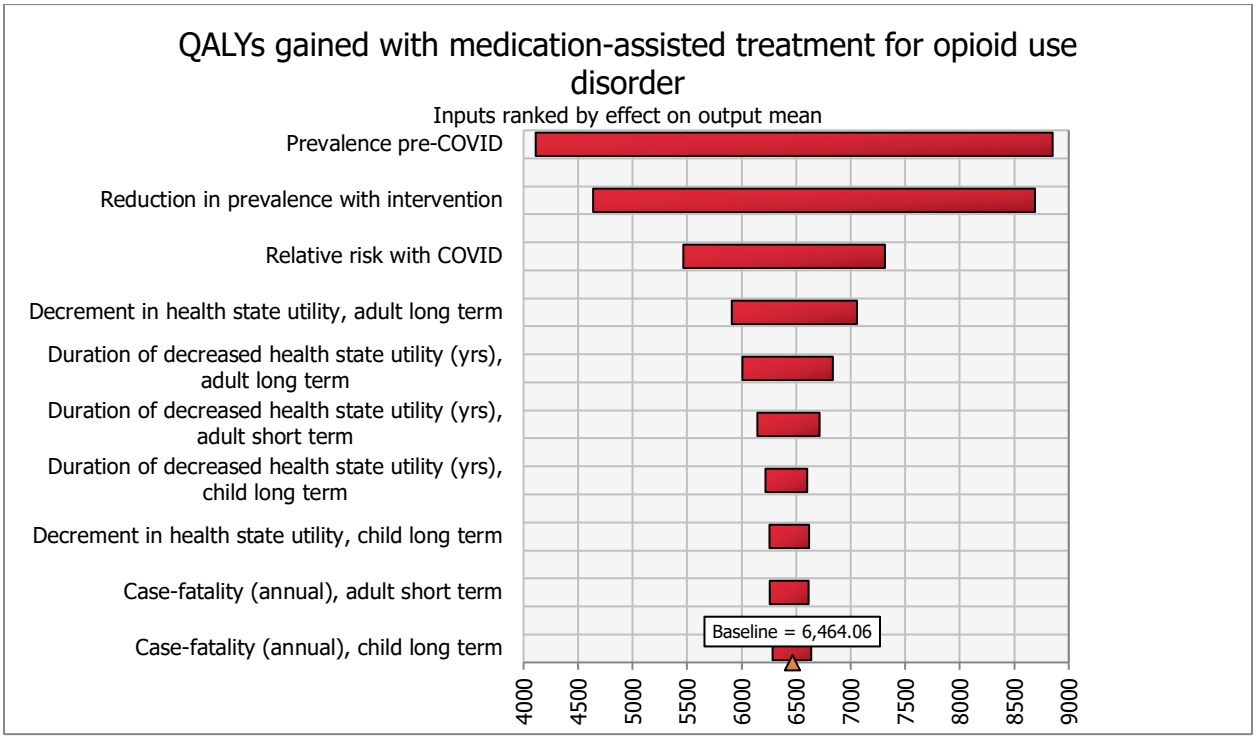


## Opioid Use Disorder

The intervention appears to yield net savings of $30 to 100 million in one-way SAs.

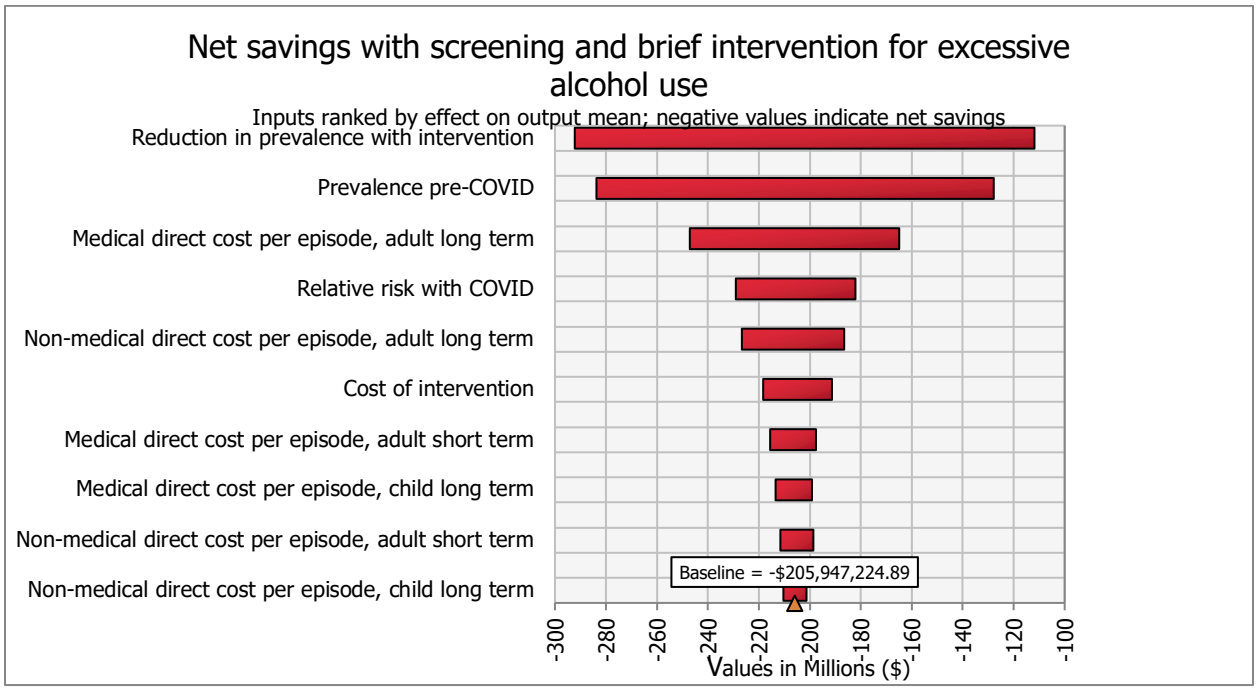



QALY gain ranges from 4,000 to 9,000 in 1-way SAs.

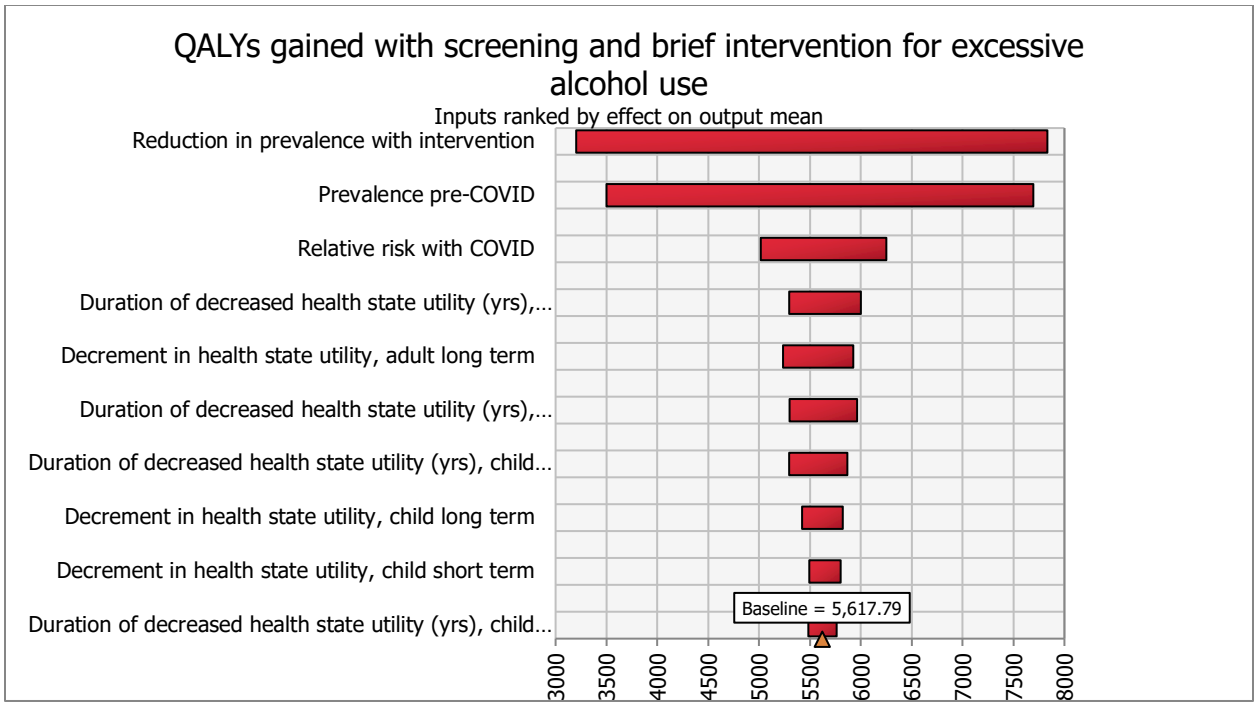


## Excessive Alcohol Use

The intervention appears to yield net savings $110-290 million in one-way SAs.

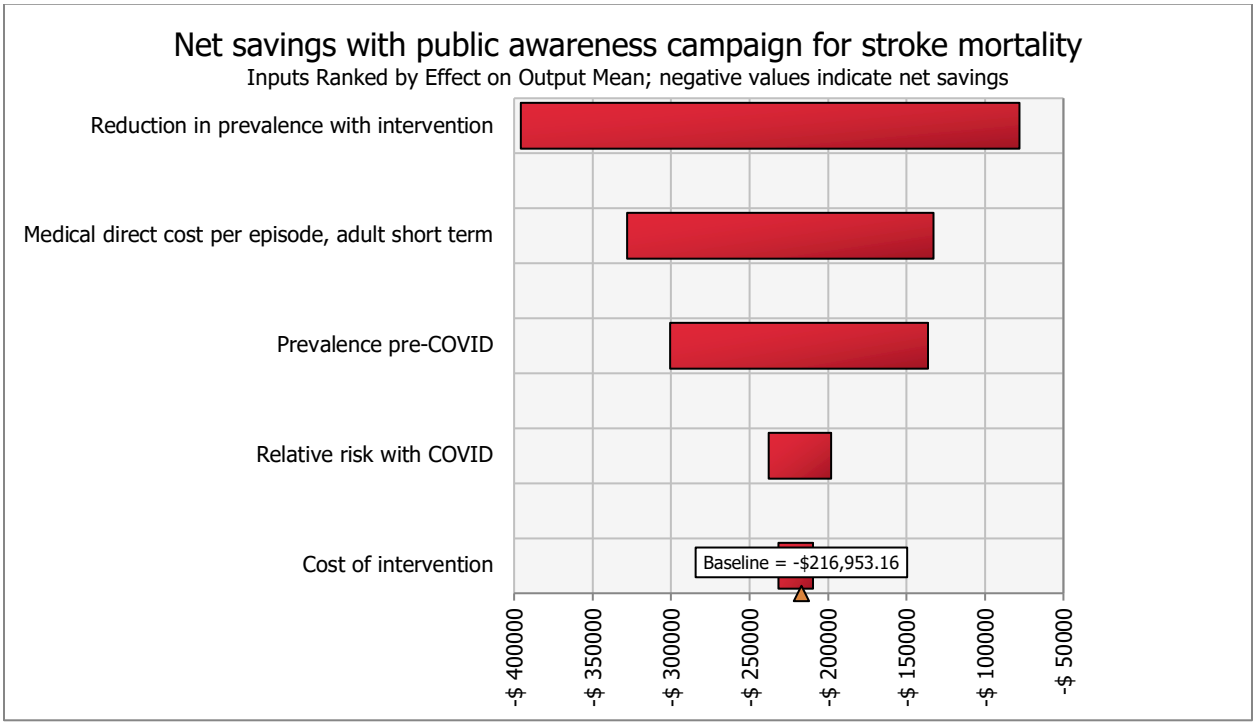



QALY gain ranges from 3,200 to 7,800 in 1-way SAs.



## Stroke Mortality

The intervention appears to yield net savings $80 to $400 thousand in one-way SAs.




QALY gain ranges from 140 to 650 in 1-way SAs.