Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Estimating the impact of the COVID-19 pandemic on diagnosis and survival of five cancers in Chile from 2020 to 2030: a simulation-based analysis

Zachary J Ward, Magdalena Walbaum, Benjamin Walbaum, Maria Jose Guzman, Jorge Jimenez de la Jara, Bruno Nervi, Rifat Atun

Summary

Background The COVID-19 pandemic has strained health system capacity worldwide due to a surge of hospital admissions, while mitigation measures have simultaneously reduced patients' access to health care, affecting the diagnosis and treatment of other diseases such as cancer. We estimated the impact of delayed diagnosis on cancer outcomes in Chile using a novel modelling approach to inform policies and planning to mitigate the forthcoming cancer-related health impacts of the pandemic in Chile.

Methods We developed a microsimulation model of five cancers in Chile (breast, cervix, colorectal, prostate, and stomach) for which reliable data were available, which simulates cancer incidence and progression in a nationally representative virtual population, as well as stage-specific cancer detection and survival probabilities. We calibrated the model to empirical data on monthly detected cases, as well as stage at diagnosis and 5-year net survival. We accounted for the impact of COVID-19 on excess mortality and cancer detection by month during the pandemic, and projected diagnosed cancer cases and outcomes of stage at diagnosis and survival up to 2030. For comparison, we simulated a no COVID-19 scenario in which the impacts of COVID-19 on excess mortality and cancer detection were removed.

Findings Our modelling showed a sharp decrease in the number of diagnosed cancer cases during the COVID-19 pandemic, with a large projected short-term increase in future diagnosed cases. Due to the projected backlog in diagnosis, we estimated that in 2021 there will be an extra 3198 cases (95% uncertainty interval [UI] 1356–5017) diagnosed among the five modelled cancers, an increase of nearly 14% compared with the no COVID-19 scenario, falling to a projected 10% increase in 2022 with 2674 extra cases (1318–4032) diagnosed. As a result of delayed diagnosis, we found a worse stage distribution for detected cancers in 2020–22, which is estimated to lead to 3542 excess cancer deaths (95% UI 2236–4816) in 2022–30, compared with the no COVID-19 scenario, among the five modelled cancers, most of which (3299 deaths, 2151–4431) are projected to occur before 2025.

Interpretation In addition to a large projected surge in diagnosed cancer cases, we found that delays in diagnosis will result in worse cancer stage at presentation, leading to worse survival outcomes. These findings can help to inform surge capacity planning and highlight the importance of ensuring appropriate health system capacity levels to detect and care for the increased cancer cases in the coming years, while maintaining the timeliness and quality of cancer care. Potential delays in treatment and adverse impacts on quality of care, which were not considered in this model, are likely to contribute to even more excess deaths from cancer than projected.

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See Comment pages 1350 and 1352

For the Spanish translation of the abstract see Online for appendix 1

For the Portuguese translation of the abstract see Online for appendix 2

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Introduction

The COVID-19 pandemic has had major adverse health and economic consequences worldwide. Latin America in particular has been severely affected by the pandemic, with more than 1 000 000 reported deaths due to COVID-19 by the end of May, 2021.[1] In Chile, more than 1·6 million people have been diagnosed with COVID-19 to date, with more than 36 000 deaths.[2] However, nearly 80% of the population has completed the local vaccine programme.[2] Other serio-us collateral effects include economic impacts, with an estimated reduction of 7·4% in gross domestic product in Latin America and the Caribbean in 2020 according to the International Monetary Fund.[3] Additionally, diagnosis, early referrals, and treatment for non-COVID-19-related illnesses have experienced a notable decrease due to foregone and delayed care and difficulty in accessing services when needed, especially for people with non-communicable diseases such as cancer.[4,5] The decrease in health system access due to foregone, delayed, and unavailable care presents a large threat to public health as the global cancer burden is rising, especially in low-income and middle-income countries; this is particularly true in Latin America and the Caribbean where cancer is the second leading cause of death[6] and where the COVID-19 pandemic has strained health systems responding to the

Research in context

Evidence before this study

Previous studies have estimated the impact of the COVID-19 pandemic on cancer diagnosis and mortality in various settings, finding large decreases in cancers diagnosed during the pandemic. We searched PubMed for studies published between Feb 1, 2020, and July 1, 2021, using the search terms "COVID-19", "cancer", and "Chile" or "Latin America". We found studies that examined administrative data and reported large declines in the number of cancer cases diagnosed and cancer services provided during the COVID-19 pandemic in Latin America. However, we found no studies that projected the number of future cancer cases diagnosed as cancer detection rates revert to normal, or that estimated survival outcomes for patients affected by delayed diagnosis. Administrative data on cancers in Chile have also shown a notable decrease in cancer diagnosis, but it remains unclear what the longer-term impact of the COVID-19 pandemic will be on cancer outcomes.

Added value of this study

We developed a novel microsimulation model of cancer incidence and progression for five cancers (breast, cervix, colorectal, prostate, and stomach) that accounts for COVID-19 competing mortality and the impact of delayed diagnosis on the stage distribution of detected cancers. We provide the first estimates of the adverse impact of the COVID-19 pandemic on cancer diagnosis and survival in Chile. These findings provide timely information for policy makers who have to make decisions under uncertainty and ensure that appropriate levels of capacity are available to manage the projected surge of diagnosed cancers due to delays in cancer detection during the pandemic.

Implications of all the available evidence

Due to delays and foregone care that lead to backlogs, we estimate a short-term increase in diagnosed cases of nearly 14% among the five modelled cancers in 2021, with excess cancer cases declining thereafter each year. Despite this surge in short-term cancer cases, we estimate that there will be fewer cumulative cancers diagnosed during 2020–30 overall than would have occurred without the COVID-19 pandemic, owing to competing mortality, including deaths from COVID-19 that affect older population groups who are at an increased risk of developing cancer. However, due to stage migration (ie, worse stage at diagnosis) as a result of delayed diagnosis, we predict an excess of more than 3500 deaths among the five modelled cancers during 2022–30, compared with a no COVID-19 scenario, occurring predominantly before 2025. Potential delays in treatment and adverse impacts on quality of care due to the pandemic, which are not considered in the model, are likely to lead to even more excess deaths.

large increases in the number of hospital admissions and patients needing intensive care.[7]

The COVID-19 pandemic, which has led to major access problems in health systems, has also produced substantial reductions in cancer diagnoses and referrals,[3,4,8] which are likely to lead to patients with cancer being diagnosed at later stages of disease and having a worse prognosis, including shorter survival and decreased quality of life.[9] In most countries, cancer treatments for diagnosed patients have been postponed, especially immunosuppressive therapies and invasive procedures, such as surgery, which require hospitalisation and admission to intensive care units in some cases.[10] WHO has reported that cancer services have been partially or completely disrupted in a third of countries in Europe.[11] For example, the Netherlands experienced a 25% decrease in cancer diagnoses during the first COVID-19 wave in February to April, 2020.[12] In the UK, it was estimated that 45% of those who experienced cancer symptoms did not seek medical care between March and May, 2020, alongside an 80% decrease in patients with cancer referred via the 2-week-wait pathway, leading to a projected 15% increase in colorectal cancer deaths and 9% increase in breast cancer deaths over the next 5 years.[4,13] Brazil has also reported a 35% reduction in newly diagnosed cancer cases, a 45–55% decline in cancer care appointments, a more than 50% decrease in patients undergoing systemic treatment, and a 60% decrease in cancer surgeries.[14] In Chile, which has reliable data for several cancers both before and during the COVID-19 pandemic, administrative data suggest that there has been a reduction of more than 60% in the number of new cancer diagnoses, as well as a 50% reduction in surgical procedures for individuals with cancer between April and June, 2020,[15] shortly after the introduction of a national lockdown in March, 2020. In this study, based on data provided by the Chile Ministry of Health, we estimate the impact of delayed diagnosis on cancer outcomes in Chile using a novel modelling approach to provide information for decision makers that can inform policies and planning to mitigate the forthcoming cancer-related health impacts in Chile.

Methods

Overview

We developed the Chile COVID-19 Cancer Projections and Outcomes (C3PO) model, a microsimulation (individual-level) model of cancer incidence and progression in Chile for five cancers (breast, cervix, colorectal, prostate, and stomach) that are estimated to account for 46% of diagnosed cancer cases and 45% of cancer-related mortality in Chile each year.[16] These cancers were selected because reliable data on trends over several years were available for these cancer sites from the Ministry of Health. These five cancers are also relevant for Chile, with breast cancer the most common cancer for women and prostate cancer the most common

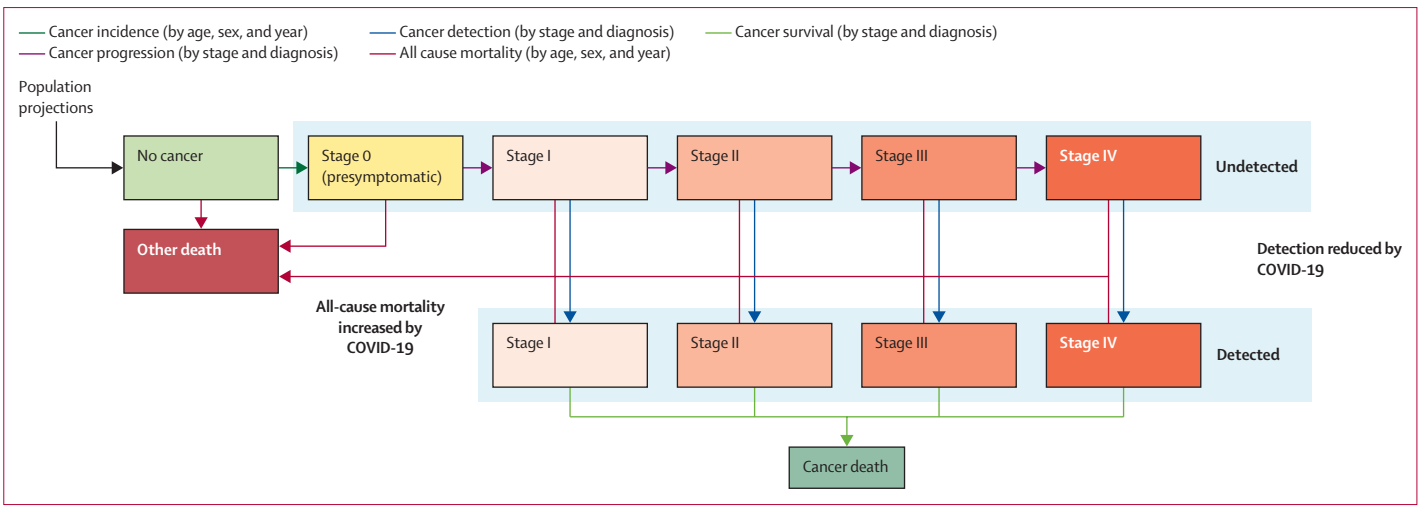

Figure 1: **Conceptual model**

for men, while gastric cancer has a high mortality rate for both sexes. The model follows a monthly cycle and simulates cancer incidence, stage progression, stage-specific detection probabilities (ie, diagnosis), and stage-specific survival. The model accounts for competing all-cause mortality (ie, risk of death from causes other than cancer) and the impacts of the COVID-19 pandemic on cancer detection and risk of death (figure 1). Model inputs were synthesised from various sources, described below (see appendix 3 p 2 for a summary of model inputs). Using the model, we projected diagnosed cancer cases and outcomes up to 2030. For comparison, we simulated a no COVID-19 scenario in which the impacts of COVID-19 on excess mortality and cancer detection were removed.

Population data

We obtained estimates of the Chilean population size and age structure by sex and year from the UN World Population Prospects.[17] We initialised the model with a nationally representative virtual population in the year 2000 and simulate an open population by introducing new infants (ie, births) in each cycle (appendix 3 p 2). All-cause annual mortality rates for Chile by year, age, and sex were also obtained from the UN World Population Prospects,[17] and were converted to monthly probabilities (appendix 3 p 2).

Cancer incidence, progression, detection, and survival

Trends in cancer incidence rates by sex, year (1998–2012), and age group were obtained from the Chile-Valdivia registry, as reported in Cancer Incidence in Five Continents, published by the International Agency for Research on Cancer.[18] We estimated secular trends in sex-specific and age group-specific cancer incidence rates, and used natural cubic splines to interpolate the predicted incidence rates by continuous age in the model. The number of monthly incident cancer cases was sampled for each age and sex from a (log) binomial distribution based on the estimated incidence rates (appendix 3 pp 2–5).

Incident cancer cases initially enter a presymptomatic health state (stage 0) and are assumed to remain undetected in the model while in this state. Patients with undetected cancer face a monthly risk of progressing to the next stage (stages I–IV), inferred via model calibration (appendix 3 p 5). Given a patient's stage, the model simulates the probability of the cancer being detected (ie, the patient receiving a diagnosis), also inferred via calibration (appendix 3 p 5). We set weakly informative uniform priors for cancer progression and detection probabilities (appendix 3 p 5).

See Online for appendix 3

Once a patient with cancer is diagnosed, they face cancer-specific mortality (in addition to other-cause mortality), based on survival curves. We based survival curve priors for stage-specific relative 5-year survival on studies from Chile for breast and stomach cancer,[19,20] and used estimates from the Surveillance, Epidemiology, and End Results (SEER) Program in the USA to set priors for the other cancers for which no Chile-specific estimates were available.[21] Based on the modelled 5-year net survival probabilities, we adjusted 10-year stage-specific survival curves from SEER (2000–16)[21] and sampled a (relative) survival period for each diagnosed cancer case, assuming that if the patient survived 10 years they would not die from the cancer (appendix 3 pp 5–6). All patients, with and without cancer, faced competing mortality risks from all-cause mortality.

COVID-19 impacts

To account for mortality from COVID-19, we obtained estimates of monthly excess mortality in Chile by age group (six different age groups: 0–29, 30–49, 50–59, 60–69, 70–79, and ≥80 years) from the Ministry of Health of Chile.[22] These empirical estimates of excess mortality were calculated against mean monthly deaths in each age group from 2016–19 and were available for February, 2020, to

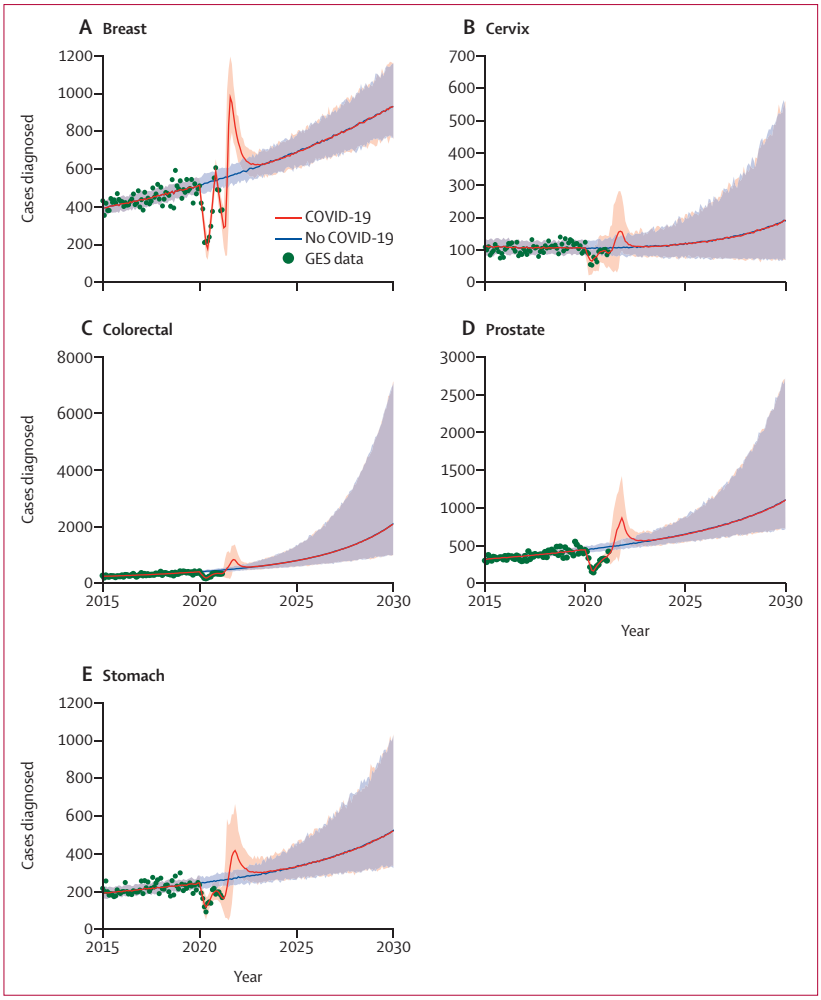

Figure 2: **Estimated cases diagnosed per month in the COVID-19 vs no COVID-19 scenarios, 2015–30**
The COVID-19 scenario describes the status quo, whereas the no COVID-19 scenario is a counterfactual scenario in which the impacts of COVID-19 on excess mortality and cancer detection were removed. Shaded regions indicate 95% uncertainty intervals. GES=Garantías Explícitas en Salud.

April, 2021, after which we projected trends in excess mortality rates, assuming they would revert to zero over the future course of the pandemic, accounting for uncertainty around this endpoint (appendix 3 p 6). Excess COVID-19 mortality by age group was applied to both the population without cancer (ie, at risk for developing a cancer) and patients with cancer (both detected and undetected). Due to lack of data on the impact of COVID-19 on mortality for patients with cancer, we assumed that COVID-19-related mortality was independent of cancer status (ie, cancer versus non-cancer) and stage.

In addition to excess mortality, we simulated the impact of the COVID-19 pandemic on cancer detection. The pandemic is likely to have affected cancer outcomes in several ways, including decreases in diagnosis (eg, due to mobility restrictions and constrained health system capacity), increased waiting time for treatment after diagnosis (eg, due to a backlog of diagnosed cases), and potential declines in quality of care (eg, due to decreased health system capacity). However, owing to data limitations on treatment and quality, we only modelled the impact of the pandemic on cancer detection, applying a cancer-specific scalar to the modelled stage-specific detection probabilities. We allowed the detection scalar to vary by cancer to account for potential differences in modes of detection (ie, screening *vs* emergency presentation), but assumed that the detection scalars were non-differential by stage (ie, we assumed that although the underlying cancer detection probabilities might vary by stage, the impact of COVID-19 on these detection probabilities did not vary by stage). To account for differences between the first (May to July, 2020) and second (March to July, 2021) waves of the pandemic in Chile, we fit four control timepoints (ie, knots in the model), and estimated cancer detection scalars for each point, assuming that detection probabilities changed linearly between each timepoint (appendix 3 p 7).

	Breast			Cervix			Colorectal		
	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess
2020	4588 (4241 to 4924)	6343 (6069 to 6657)	–1756 (–2167 to –1384)	1014 (788 to 1194)	1267 (1125 to 1487)	–253 (–508 to –51)	3522 (3185 to 3911)	5234 (4816 to 5768)	–1712 (–2263 to –1115)
2021	7567 (6952 to 8408)	6725 (6411 to 7137)	841 (187 to 1398)	1468 (1129 to 1954)	1283 (1061 to 1552)	185 (–76 to 475)	6877 (5805 to 8434)	5901 (5200 to 6862)	976 (–166 to 1793)
2022	7869 (7160 to 8612)	7128 (6658 to 7707)	741 (329 to 1198)	1370 (1055 to 1842)	1306 (1069 to 1708)	63 (–67 to 254)	7250 (5889 to 9028)	6706 (5777 to 8367)	543 (–39 to 1496)
2023	7584 (7049 to 8279)	7569 (7037 to 8329)	15 (–222 to 265)	1335 (1038 to 1883)	1346 (1026 to 1901)	–11 (–113 to 91)	7683 (6298 to 10 886)	7668 (6327 to 10 693)	14 (–203 to 247)
2024	7989 (7262 to 8954)	8024 (7351 to 8938)	–34 (–256 to 242)	1390 (1011 to 2125)	1387 (984 to 2124)	3 (–83 to 105)	8887 (6854 to 13 766)	8899 (6852 to 13 709)	–12 (–256 to 274)
2025	8488 (7629 to 9690)	8516 (7603 to 9629)	–27 (–271 to 287)	1467 (959 to 2502)	1474 (952 to 2518)	–6 (–105 to 104)	10 397 (7546 to 18 383)	10 421 (7623 to 18 446)	–24 (–279 to 257)
2026	9036 (8033 to 10 521)	9035 (8013 to 10 541)	0 (–224 to 216)	1561 (953 to 3017)	1566 (959 to 3039)	–5 (–94 to 77)	12 310 (8407 to 25 212)	12 330 (8292 to 25 142)	–20 (–322 to 260)

(Table 1 continues on next page)

	Breast			Cervix			Colorectal		
	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess
(Continued from previous page)									
2027	9584 (8279 to 11 429)	9599 (8484 to 11 361)	–15 (–294 to 239)	1694 (921 to 3678)	1710 (935 to 3701)	–17 (–155 to 88)	14 787 (9269 to 34 900)	14 833 (9224 to 34 994)	–46 (–354 to 265)
2028	10 201 (8717 to 12 221)	10 214 (8806 to 12 356)	–13 (–300 to 234)	1886 (896 to 4529)	1885 (911 to 4613)	1 (–122 to 118)	18 016 (10 300 to 49 113)	18 066 (10 242 to 49 629)	–50 (–614 to 248)
2029	10 833 (9108 to 13 387)	10 841 (9196 to 13 292)	–8 (–304 to 241)	2126 (886 to 5901)	2140 (901 to 6019)	–13 (–153 to 97)	22 292 (11 403 to 70 156)	22 373 (11 521 to 70 384)	–80 (–475 to 240)
2030	11 552 (9667 to 14 682)	11 562 (9643 to 14 643)	–10 (–305 to 264)	2474 (858 to 7520)	2475 (867 to 7536)	–2 (–129 to 124)	27 996 (12 743 to 99 795)	28 036 (12 765 to 99 969)	–40 (–433 to 365)
Total: 2020–30	95 291 (85 271 to 109 875)	95 557 (85 598 to 110 320)	–266 (–1049 to 601)	17 784 (10 887 to 34 411)	17 839 (10 914 to 34 420)	–54 (–367 to 214)	140 016 (88 844 to 342 042)	140 467 (89 096 to 342 995)	–451 (–1419 to 325)
Total: 2022–30	83 137 (73 535 to 97 187)	82 488 (72 830 to 96 696)	648 (–283 to 1715)	15 302 (8717 to 31 768)	15 289 (8698 to 31 683)	13 (–301 to 380)	129 618 (78 907 to 330 423)	129 332 (78 864 to 330 737)	286 (–873 to 1625)

Data are mean cases (95% uncertainty interval).

Table 1: **Estimated number of diagnosed breast cancer, cervical cancer, and colorectal cancer cases, 2020–30**

	Prostate			Stomach			Total		
	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess
2020	3290 (3010 to 3606)	5519 (5228 to 5919)	–2228 (–2578 to –1930)	2099 (1859 to 2323)	3010 (2847 to 3242)	–910 (–1261 to –590)	14 513 (13 920 to 15 025)	21 373 (20 727 to 22 097)	–6860 (–7768 to –6045)
2021	6978 (5802 to 8203)	5932 (5541 to 6528)	1045 (–187 to 1931)	3327 (2505 to 4112)	3176 (2912 to 3548)	150 (–803 to 828)	26 216 (24 306 to 28 887)	23 017 (22 075 to 24 295)	3198 (1356 to 5017)
2022	7220 (6146 to 8653)	6395 (5892 to 7404)	826 (109 to 1751)	3876 (3240 to 4901)	3375 (3040 to 3905)	501 (48 to 1231)	27 584 (25 426 to 30 453)	24 910 (23 553 to 27 071)	2674 (1318 to 4032)
2023	6950 (6163 to 8440)	6898 (6239 to 8386)	52 (–213 to 407)	3662 (3105 to 4575)	3573 (3103 to 4387)	88 (–140 to 406)	27 213 (25 230 to 30 587)	27 055 (25 018 to 30 361)	158 (–373 to 746)
2024	7446 (6489 to 9853)	7478 (6561 to 9635)	–33 (–252 to 194)	3850 (3235 to 5096)	3829 (3267 to 4940)	21 (–132 to 199)	29 562 (26 787 to 34 792)	29 617 (26 592 to 34 717)	–54 (–605 to 419)
2025	8115 (6915 to 11 486)	8152 (6935 to 11 606)	–37 (–282 to 220)	4123 (3354 to 5785)	4134 (3365 to 5793)	–10 (–146 to 162)	32 591 (28 413 to 40 644)	32 696 (28 620 to 40 837)	–105 (–566 to 318)
2026	8896 (7348 to 14 040)	8936 (7275 to 13 945)	–40 (–330 to 200)	4445 (3500 to 6685)	4452 (3553 to 6700)	–7 (–180 to 152)	36 247 (30 747 to 48 572)	36 320 (30 768 to 48 727)	–72 (–570 to 378)
2027	9812 (7659 to 17 539)	9844 (7744 to 17 481)	–32 (–318 to 311)	4852 (3622 to 7898)	4866 (3656 to 7969)	–14 (–190 to 178)	40 728 (32 906 to 60 266)	40 852 (32 958 to 60 709)	–123 (–634 to 509)
2028	10 938 (8124 to 22 334)	10 970 (8160 to 22 313)	–32 (–287 to 199)	5315 (3738 to 9124)	5334 (3760 to 9262)	–19 (–228 to 175)	46 355 (35 350 to 77 072)	46 469 (35 489 to 77 474)	–114 (–724 to 375)
2029	12 310 (8522 to 28 751)	12 364 (8492 to 28 812)	–54 (–355 to 250)	5895 (3930 to 11 019)	5910 (3930 to 11 035)	–15 (–188 to 181)	53 457 (37 962 to 100 726)	53 627 (37 762 to 100 803)	–170 (–716 to 401)
2030	14 050 (9013 to 37 512)	14 105 (9076 to 37 703)	–55 (–527 to 215)	6583 (4064 to 13 615)	6596 (4074 to 13 442)	–12 (–237 to 212)	62 655 (40 774 to 133 741)	62 774 (41 206 to 134 221)	–119 (–737 to 504)
Total: 2020–30	96 005 (77 180 to 168 766)	96 594 (77 265 to 168 979)	–589 (–1270 to 74)	48 027 (37 713 to 74 006)	48 254 (37 972 to 74 061)	–228 (–889 to 323)	397 123 (323 993 to 594 227)	398 711 (325 095 to 596 798)	–1588 (–3313 to –79)
Total: 2022–30	85 737 (66 611 to 157 916)	85 143 (66 314 to 156 928)	594 (–504 to 1883)	42 601 (32 243 to 67 696)	42 068 (32 104 to 67 154)	532 (–237 to 1678)	356 394 (283 618 to 551 615)	354 321 (282 236 to 551 442)	2073 (–86 to 4310)

Data are mean cases (95% uncertainty interval).

Table 2: **Estimated number of diagnosed prostate cancer, stomach cancer, and total cancer cases, 2020–30**

Model calibration

Calibration involves comparing the model predictions with observed estimates to identify parameter sets that achieve a good fit to empirical data. In addition to accounting for parameter uncertainty, simulating the underlying age and sex distribution of the Chilean population and calibrating the model to nationally representative cancer estimates helps to address any potential sources of bias in the model inputs. We calibrated the C3PO model using a Bayesian approach in

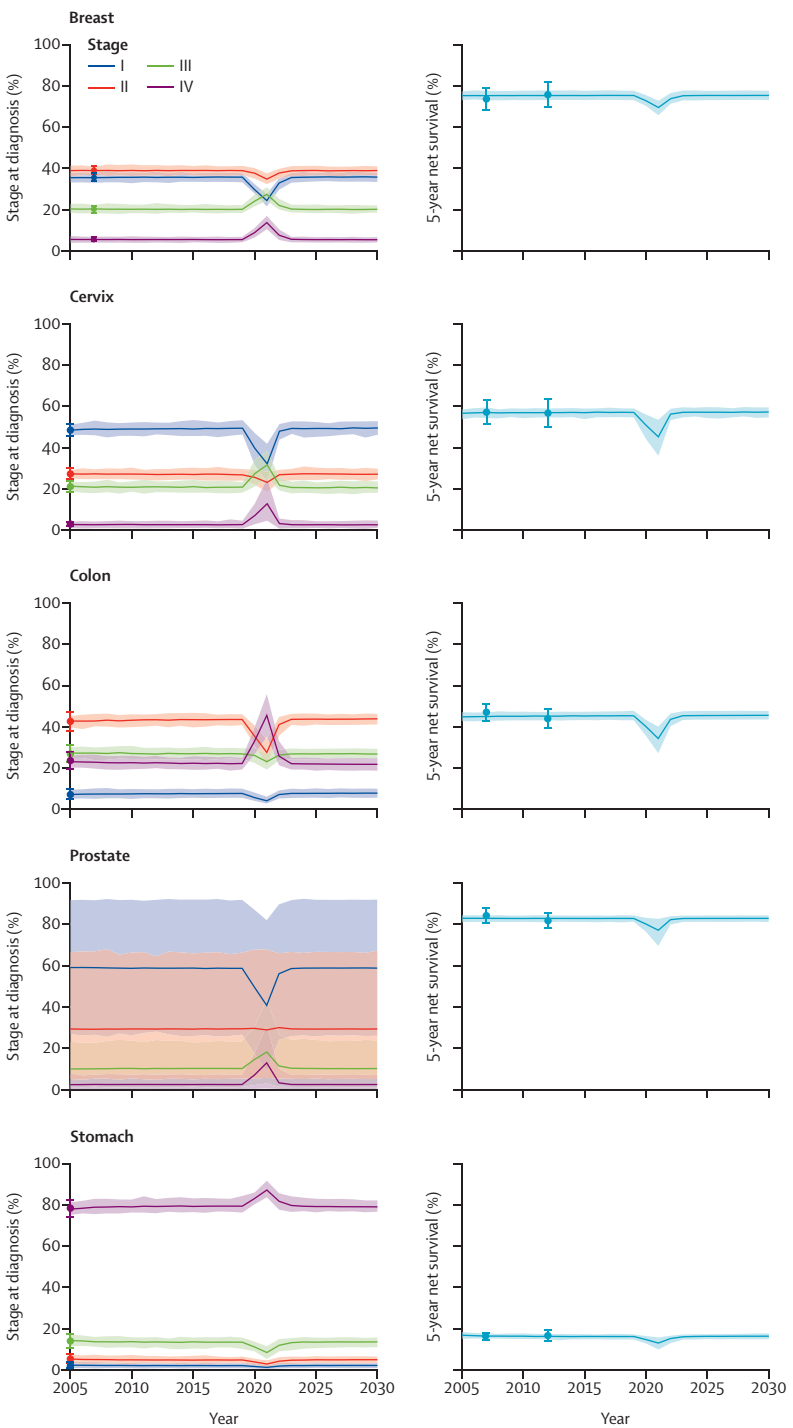

Figure 3: **Estimated stage distribution at diagnosis and 5-year net survival by cancer, 2005–30**
The COVID-19 scenario describes the status quo, whereas the no COVID-19 scenario is a counterfactual scenario in which the impacts of COVID-19 on excess mortality and cancer detection were removed. Shaded regions indicate 95% uncertainty intervals. Datapoints for empirical mean estimates from the medical literature are shown, with reported 95% CIs.

which the empirical data are considered fixed and the model parameters are random variables. We set prior probability distributions on all model parameters, and calibrated the model to empirical data on cancer cases, stage distribution, and survival (appendix 3 p 8).

We obtained estimates of the total number of diagnosed incidence cases by month from the Garantías Explícitas en Salud (GES; Explicit Health Guarantees) for each cancer for January, 2015, to March, 2021. In Chile, the GES regime guarantees universal access, opportunity of care, and financial protection for people with specific prioritised health problems, regardless of whether the individual receives care in public or private health facilities. GES records of diagnosed cancer cases and notifications of treatment delays were provided by the Ministry of Health of Chile and the National Health Fund.

We also obtained estimates of the stage distribution at diagnosis in Chile from the published medical literature.[19,20,23,24] We calibrated stage-specific relative survival for each cancer to estimates of overall 5-year net survival (ie, across all stages) from the CONCORD programme for the global surveillance of cancer survival for 2005–09 and 2010–14, on the basis of data from four registries in Chile.[25] We used a stochastic optimisation algorithm (simulated annealing) to fit the model, scoring each proposed parameter set as the sum of the distance squared between the model predictions and empirical target means. We ran 1000 search chains and selected the best-fitting 100 parameter sets to explore parameter uncertainty when running the final model simulations (appendix 3 pp 8–9).

To assess the performance of our model, we compared the reported number of monthly GES cancer cases with our model predictions. We calculated the mean error, mean absolute error, mean relative error, and coverage probabilities (ie, how often the observed value fell within our modelled 95% uncertainty intervals [UIs]). We also compared our model predictions with estimates of the stage distribution at diagnosis and 5-year net survival for each cancer, calculating the same performance indicators described above, as well as how often our mean predicted values fell within the estimated 95% CIs of the empirical data.

Model outcomes

Using the model, we estimated the number of cases of each cancer diagnosed per month, the stage distribution at diagnosis by year, 5-year net survival by year, and cancer deaths per month. We simulated two scenarios with the model: the status-quo (COVID-19) scenario and a counterfactual (no COVID-19) scenario in which the impacts of COVID-19 on excess mortality and cancer detection were removed. To create the no COVID-19 scenario, excess mortality was set to 0 and cancer detection scalars were set to 1·0 for the entire period. We estimated excess numbers of cancer cases diagnosed and cancer deaths compared with the no COVID-19 scenario. We projected the model outcomes up to 2030 and report

the mean across the 100 parameter sets and the 95% UIs (calculated as the 2·5 and 97·5 percentiles of the simulation results) for all model outcomes. All model predictions were generated from the posterior predictive distributions (ie, simulated based on the joint posterior distribution of all model parameters, accounting for first-order [stochastic] patient-level uncertainty). Our 95% UIs therefore indicate the sensitivity of our results to different parameter values and account for their joint distribution. Total excess cancer cases and deaths were estimated for two time periods: the entire period from 2020 to 2030, and a forward-looking period from 2022 to 2030, assuming no future waves of COVID-19 in Chile. The model was developed in Java (version 1.8.0).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The calibrated model fitted well to empirical data. Compared with reported detected monthly cancer cases, the model had an overall mean error of 0·004 cases (SD 29·9), a mean absolute error of 22·3 cases (SD 20·0; a relative error of 8·7%), and a coverage probability of 79·5%. Compared with estimates of stage distribution at diagnosis from the medical literature, our modelled estimates had a coverage probability of 100%, fell within the empirical 95% CIs 100% of the time, and had a mean absolute error of 0·2 percentage points (SD 0·1; a relative error of 1·1%). Our estimates of 5-year net survival had a coverage probability of 90% compared with estimates from CONCORD-3,[25] and fell within the empirical 95% CIs 100% of the time with a mean absolute error of 0·9 percentage points (SD 0·7; a relative error of 1·7%). Model performance was similar by cancer type (appendix 3 p 10). The calibrated model parameters are presented in appendix 3 (pp 11–18).

The model results reveal a sharp decrease in the number of diagnosed cancer cases during the waves of the COVID-19 pandemic in 2020 and 2021, with a large projected short-term increase in future diagnosed cases as detection probabilities return to normal levels (figure 2).

Among the five modelled cancers, we estimate that 6860 fewer cases (95% UI 6045–7768) were diagnosed in 2020 due to COVID-19, a 32·1% reduction compared with the no-COVID-19 scenario (tables 1, 2). Due to the projected backlog in diagnosis, we estimate that in 2021 there will be an extra 3198 cases (1356–5017) diagnosed among the five modelled cancers, an increase of nearly 14% compared with the no COVID-19 scenario. The excess diagnosed cases are projected to decrease in 2022 to an extra 2674 cases (1318–4032), an estimated increase of more than 10% compared with the no COVID-19 scenario. However, although we find a projected short-term increase in the number of diagnosed cases compared with the no COVID-19 scenario, the cumulative number of cancer cases detected from 2020 to 2030 is estimated to be 1588 cases (79 to 3313) fewer than expected, due to high competing mortality in 2020 and 2021. Looking forward to the period between 2022 and 2030, we estimate a total of 2073 excess cases (–86 to 4310) due to backlogs of undetected cases in 2020 and 2021.

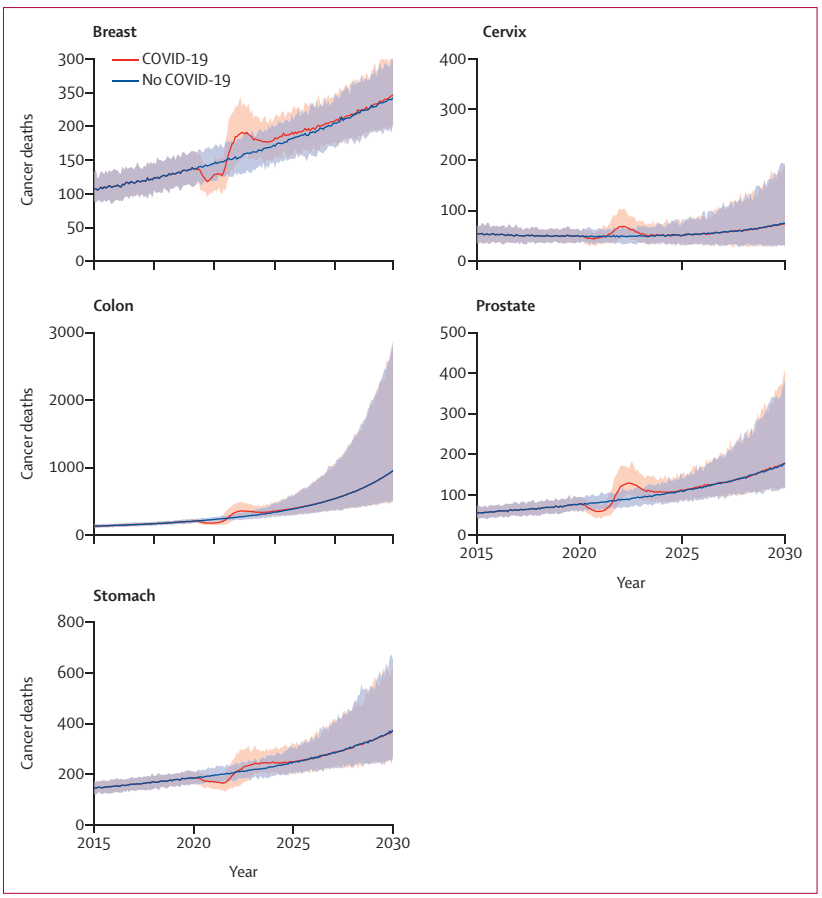

Figure 4: **Estimated cancer deaths per month, 2015–30**
Shaded regions indicate 95% uncertainty intervals.

As a result of decreased cancer detection, we find a worse stage distribution (ie, a larger proportion of patients diagnosed at advanced stages) for detected cancers in 2020–22 compared with the no COVID-19 scenario, leading to lower 5-year net survival (figure 3). Although we estimate that cancer mortality decreased compared with the no COVID-19 scenario during the pandemic due to increased competing mortality from COVID-19, we find that cancer deaths are projected to increase in the near future due to worse stage at diagnosis (figure 4). This stage migration is estimated to lead to 3542 excess cancer deaths (95% UI 2236–4816) among the five modelled cancers in 2022–30, compared with the no COVID-19 scenario, led by colorectal cancer (1389 excess deaths [95% UI 364–2567]) and breast cancer (869 excess deaths [418–1301]; tables 3, 4). Most of these deaths

	Breast			Cervix			Colorectal		
	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess
2020	1544 (1413 to 1677)	1693 (1534 to 1845)	–149 (–205 to –94)	558 (495 to 620)	588 (523 to 671)	–30 (–82 to 12)	2275 (2127 to 2429)	2593 (2404 to 2857)	–319 (–466 to –181)
2021	1702 (1485 to 1984)	1786 (1634 to 1931)	–84 (–267 to 123)	663 (510 to 852)	590 (514 to 682)	73 (–81 to 233)	2638 (2042 to 3539)	2908 (2624 to 3319)	–269 (–811 to 506)
2022	2250 (1881 to 2698)	1891 (1701 to 2067)	359 (102 to 705)	760 (603 to 1012)	594 (501 to 719)	166 (26 to 375)	4173 (3297 to 5468)	3280 (2829 to 3991)	893 (349 to 1827)
2023	2150 (1942 to 2384)	1998 (1809 to 2188)	152 (–4 to 300)	623 (488 to 845)	600 (508 to 751)	23 (–41 to 114)	4080 (3360 to 5250)	3718 (3145 to 4842)	362 (–63 to 778)
2024	2236 (2024 to 2471)	2122 (1934 to 2339)	114 (–19 to 259)	618 (486 to 892)	615 (480 to 844)	3 (–62 to 72)	4439 (3617 to 6301)	4290 (3480 to 6282)	148 (–112 to 402)
2025	2325 (2095 to 2617)	2249 (2025 to 2556)	77 (–55 to 222)	633 (458 to 966)	635 (451 to 954)	–2 (–62 to 68)	5032 (3809 to 8036)	4969 (3820 to 8076)	63 (–164 to 270)
2026	2432 (2168 to 2734)	2369 (2114 to 2691)	63 (–65 to 177)	665 (456 to 1080)	667 (442 to 1148)	–2 (–73 to 71)	5845 (4229 to 10 629)	5828 (4258 to 10 670)	17 (–220 to 259)
2027	2557 (2311 to 2999)	2522 (2253 to 2956)	36 (–97 to 145)	709 (430 to 1374)	710 (443 to 1357)	–1 (–45 to 62)	6916 (4683 to 14 244)	6929 (4581 to 14 259)	–13 (–219 to 236)
2028	2696 (2378 to 3230)	2683 (2368 to 3180)	13 (–145 to 149)	761 (415 to 1601)	768 (432 to 1632)	–8 (–86 to 87)	8314 (5180 to 19 939)	8336 (5091 to 20 000)	–22 (–243 to 186)
2029	2864 (2468 to 3463)	2828 (2465 to 3411)	37 (–90 to 196)	842 (413 to 2016)	853 (413 to 2096)	–10 (–95 to 62)	10 174 (5639 to 28 046)	10 198 (5763 to 28 074)	–23 (–237 to 193)
2030	3038 (2604 to 3770)	3017 (2607 to 3666)	21 (–126 to 182)	951 (410 to 2533)	949 (405 to 2521)	2 (–72 to 83)	12 617 (6363 to 39 626)	12 654 (6292 to 39 910)	–37 (–317 to 262)
Total: 2020–30	25 795 (23 141 to 29 303)	25 159 (22 812 to 28 477)	636 (179 to 1102)	7783 (5406 to 13 187)	7569 (5216 to 12 923)	214 (–38 to 497)	66 504 (45 718 to 141 489)	65 703 (44 808 to 140 540)	800 (67 to 1783)
Total: 2022–30	22 549 (20 015 to 26 001)	21 680 (19 557 to 24 839)	869 (418 to 1301)	6562 (4255 to 11 884)	6391 (4174 to 11 625)	171 (–61 to 450)	61 591 (40 747 to 136 218)	60 202 (39 681 to 134 809)	1389 (364 to 2567)

Data are mean deaths (95% uncertainty interval).

Table 3: **Estimated number of breast cancer, cervical cancer, and colorectal cancer deaths, 2020–30**

(3299 deaths [2151–4431]; appendix 3 p 19) are projected to occur between 2022 and 2024 (tables 3, 4). Among the five modelled cancers, cancer deaths are estimated to be 10·8% higher compared with the no COVID-19 scenario in 2022–24, with differences by cancer site: 10·4% for breast cancer, 10·6% for cervical cancer, 12·4% for colorectal cancer, 17·2% for prostate cancer, and 6·0% for stomach cancer (tables 3, 4; appendix 3 p 19).

Discussion

Using a novel microsimulation model that fits well to the reported data, we find a projected short-term surge in diagnosed cancer cases due to delays in diagnosis from the COVID-19 pandemic, suggesting that the Chilean health system will need to ensure adequate capacity to detect and care for increased cancer cases in the coming years. Our findings show that among the five cancers responsible for an estimated 45% of Chilean cancer mortality,[16] Chile will face an estimated 3300 excess cancer deaths between 2022 and 2025, rising to more than 3500 by 2030 as a result of delays in diagnosis. These estimates do not consider treatment delays or the potential adverse impact of COVID-19 on the quality of the cancer care provided.

These results can help the Ministry of Health and other relevant agencies to inform surge capacity planning in Chile, during and after the COVID-19 pandemic in the ensuing 2–3 years, highlighting the need for health system flexibility to ensure a timely response to the impending wave of cancer cases while maintaining pre-COVID-19 levels of quality of care. Indeed, our estimates of excess cancer deaths assume that cancer treatment will be delivered at the same level of availability and quality as before the pandemic—a challenging task given the large backlog of cases. Delays in treatment or reduced quality of care would be likely to further contribute to poor survival outcomes and result in an even higher number of excess cancer deaths than our modelling has estimated. These findings also have important implications for cancer palliative care planning, which is guaranteed by GES, especially given the poorer survival outcomes due to the projected stage migration.

The impact of the COVID-19 pandemic is likely to differ by cancer type. For example, we find that stomach cancers are less likely to be affected due to a higher likelihood of emergency stage IV presentation before the pandemic, compared with breast and cervical cancers, which are more often diagnosed at earlier stages. The large proportion of stomach cancers typically diagnosed at advanced stages (III–IV) also means that the prognosis for these cases is affected to a much smaller degree than for cancers usually diagnosed at an earlier stage.

	Prostate			Stomach			Total		
	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess	COVID–19	No COVID–19	Excess
2020	788 (693 to 898)	919 (813 to 1037)	–131 (–193 to –74)	2139 (1965 to 2278)	2279 (2116 to 2453)	–140 (–300 to –29)	7303 (7026 to 7536)	8072 (7775 to 8408)	–769 (–1026 to –572)
2021	916 (697 to 1188)	986 (888 to 1114)	–70 (–295 to 256)	2071 (1869 to 2343)	2401 (2240 to 2617)	–330 (–662 to –41)	7990 (7298 to 9118)	8671 (8272 to 9101)	–680 (–1365 to 125)
2022	1472 (1215 to 1944)	1060 (912 to 1234)	412 (136 to 757)	2673 (2100 to 3415)	2544 (2317 to 2814)	129 (–486 to 631)	11328 (10162 to 12964)	9369 (8841 to 10103)	1959 (994 to 3246)
2023	1288 (1082 to 1639)	1141 (1001 to 1384)	147 (–9 to 314)	2929 (2603 to 3331)	2677 (2404 to 3046)	251 (13 to 510)	11070 (10263 to 12269)	10134 (9467 to 11389)	936 (442 to 1506)
2024	1269 (1087 to 1648)	1237 (1065 to 1491)	32 (–81 to 166)	2960 (2546 to 3594)	2852 (2506 to 3412)	107 (–88 to 362)	11521 (10391 to 13385)	11117 (10110 to 13098)	404 (21 to 819)
2025	1368 (1167 to 1867)	1342 (1136 to 1747)	26 (–87 to 140)	3068 (2595 to 3950)	3058 (2643 to 3844)	11 (–172 to 215)	12427 (10869 to 15473)	12252 (10740 to 15304)	175 (–187 to 535)
2026	1490 (1208 to 2199)	1471 (1204 to 2109)	19 (–109 to 126)	3279 (2693 to 4483)	3278 (2747 to 4496)	1 (–157 to 170)	13711 (11580 to 18543)	13613 (11511 to 18484)	98 (–242 to 462)
2027	1600 (1264 to 2606)	1605 (1284 to 2580)	–6 (–122 to 110)	3533 (2810 to 5220)	3538 (2842 to 5188)	–5 (–236 to 167)	15316 (12409 to 22594)	15304 (12391 to 22559)	12 (–349 to 303)
2028	1776 (1354 to 3256)	1780 (1347 to 3186)	–4 (–123 to 110)	3847 (2881 to 5999)	3856 (2954 to 6262)	–9 (–212 to 179)	17394 (13368 to 28628)	17424 (13277 to 28773)	–30 (–467 to 360)
2029	1995 (1432 to 4122)	1973 (1414 to 4016)	23 (–104 to 148)	4210 (3044 to 7053)	4221 (3013 to 7215)	–11 (–217 to 181)	20087 (14540 to 37262)	20072 (14501 to 37396)	15 (–342 to 383)
2030	2244 (1500 to 5324)	2231 (1494 to 5299)	14 (–102 to 172)	4650 (3138 to 8478)	4675 (3192 to 8505)	–25 (–221 to 180)	23501 (15654 to 49699)	23526 (15680 to 50005)	–26 (–457 to 444)
Total: 2020–30	16207 (13190 to 25636)	15744 (12726 to 24933)	463 (–81 to 1122)	35359 (29347 to 49661)	35380 (29434 to 49947)	–20 (–561 to 447)	151648 (125100 to 224075)	149555 (122624 to 222480)	2093 (856 to 3227)
Total: 2022–30	14503 (11590 to 23973)	13839 (10937 to 22893)	664 (193 to 1293)	31150 (25108 to 45189)	30700 (24890 to 44942)	450 (–69 to 1073)	136354 (109623 to 208462)	132812 (106300 to 205324)	3542 (2236 to 4816)

Data are mean deaths (95% uncertainty interval).

Table 4: **Estimated number of prostate cancer, stomach cancer, and total cancer deaths, 2020–30**

In addition to the backlog of diagnosed cancer cases, our modelling also shows a delay in deaths due to cancer, with fewer cancer deaths in 2020–21 than previously expected due to high competing mortality from COVID-19 (ie, with some patients who would have died from cancer dying from COVID-19 instead). These findings are consistent with recent empirical data on cancer mortality rates reported by the Ministry of Health of Chile.[22]

However, from 2022 to 2026, longer-term cancer deaths are projected to increase due to stage migration before reverting to pre-pandemic trends, even after accounting for competing mortality risks that (differentially) affect older adults who have higher risks of developing cancer, as well as pre-symptomatic patients who die before being diagnosed with cancer.

Timely application of efficacious cancer treatments in Chile is strongly dependent on early diagnosis and prompt referral to specialised and centralised centres. Consequently, the dramatic decrease in cancer notifications seen during 2020 and the start of 2021 is alarming. The likely reasons behind these trends are multiple and shared worldwide. First, delayed care, because patients with initial cancer symptoms might have chosen to wait for the pandemic to subside before asking for medical advice due to fear of exposure to the virus or of difficulties in accessing medical attention. Second, foregone care, as patients with initial cancer symptoms might have chosen not to access services, even when available. Third, inability to access care, due to the unprecedented overload of the health system, with human and monetary resources being reallocated for COVID-19 purposes, plus the shutdown of all but emergency surgeries during the most critical months of the pandemic, all of which have reduced and delayed diagnostic procedures. Mandatory and centralised cancer notifications and referrals to specialists for confirmation and future treatment heavily rely on general practitioners or family physicians working in primary health-care centres. These medical staff have been overwhelmed by the large number of patients with respiratory symptoms and other health problems that are not being addressed in tertiary centres. Consequently, the entry point for patients with cancer has narrowed substantially. Finally, the public health system in Chile has long been overstretched, with long waiting lists and delays in cancer treatment present even before the COVID-19 pandemic, reducing the ability of the country's health system to cope with the pandemic due to capacity constraints and the inability to create surge capacity.

Although we synthesised data from multiple sources and calibrated our model to available empirical data, we faced several data limitations when developing the model.

For example, we did not have data on stage distribution shifts for diagnosed cancers during the pandemic with which to fit the model. However, recent data for patients diagnosed with breast cancer in Santiago at the Cancer Centre of Pontificia Universidad Católica de Chile and Dr Sótero del Río Hospital revealed an increase in patients with stage III–IV cancer in 2020 of more than 30%, compared with the average stage distribution of diagnosed cases between 1997 and 2018, similar to our model estimates. We also based our priors for cancer incidence trends on data from only one registry in Chile (Valdivia), for which publicly available data were available for 1999–2012. However, we calibrated the model to national GES data from 2015 onwards, so our estimated trends should be nationally representative and account for trends in risk factors such as human papillomavirus vaccination and obesity, which might have affected any trends in cancer incidence occurring after the observed registry data.

We also assumed that the survival impact of COVID-19 was only due to worse stage at diagnosis, and that risks of COVID-19-related mortality were independent of cancer status. Although having cancer might have made patients more likely to die from COVID-19, we did not have data to include this impact in the current analysis. However, further research on this point could be incorporated into future work. Because of a paucity of data, we also did not account for the potential survival impacts of treatment delays after diagnosis, or quality of care due to health system constraints for patients who would have been diagnosed at the same stage. Accounting for these factors would probably result in even higher numbers of excess cancer deaths than we estimated. Lastly, we were only able to model the five cancer sites for which GES data were available, which are estimated to comprise nearly half of diagnosed cancers and cancer deaths in Chile. For example, lung cancer was only included in GES in early 2019, so we did not have enough data on longer-term trends to include it in the model. This lack of data is especially unfortunate because lung cancer most closely resembles COVID-19 symptoms and comorbidities (eg, chronic obstructive pulmonary disease or smoking history) and might be associated with increased rates of COVID-19 complications and mortality.

For the **model results** see https://doi.org/10.7910/DVN/SQLO19

Our estimates of excess cancer deaths are thus likely to be conservative, accounting for only half of the total excess deaths, assuming a similar impact of the COVID-19 pandemic on cancers not included in the model. However, our model can be revised as more data become available, which might also reduce the (sometimes substantial) uncertainty around our projections.

Our current projections are based on the assumption that the acute adverse effects of the pandemic would be felt up to 2022 in Chile, when the post-COVID-19 era and recovery might begin. However, there is a risk that the start of the anticipated recovery period could be delayed, especially given the rapid spread of new COVID-19 variants.

Nevertheless, our findings provide timely information for policy makers in Chile who have to make decisions under uncertainty and a rapidly changing epidemiological context, and highlight the importance of accounting for diagnosis delays as well as competing mortality from COVID-19. A recent Position Paper that convened different cancer leaders of the Latin American region has proposed a series of measures to face the challenges posed by the post-pandemic scenario regarding cancer.[26] Our findings can help to inform such planning by providing regular estimates of both the short-term and long-term consequences of COVID-19 on cancer outcomes in Chile. Additionally, although we fitted the model to Chile-specific data for this analysis, the global nature of the pandemic and general similarity of policy responses means that the insights from our study are likely to be generalisable to other countries. The underlying conceptual model can also be adapted for different contexts to provide more precise estimates of the impact of the COVID-19 pandemic on cancer outcomes in other countries.

Our work also highlights the importance of collaborating with different stakeholders, such as the Ministry of Health, the National Health Fund, national cancer registries, and other nationally representative data sources to use modelling for present and future estimations, both during and after emergency situations such as an epidemic. Such model-based analyses can improve health system preparedness by helping to quantify necessary surge capacity under different scenarios, contributing to effective responses and resilience over time to ensure health system sustainability and mitigate future excess deaths from cancer.

Contributors

RA, BN, JJdlJ, MW, and BW conceived the study. MW, BW, MJG, and ZJW acquired the data. ZJW developed the model and did the analyses. ZJW, MW, and BW accessed and verified the data. All authors designed the study, interpreted the results, and contributed to the writing of the report. All authors had access to the data and the final responsibility to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Model results (means and 95% UIs) are available in a public data repository.

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