



The impact of the COVID-19 pandemic on the dispensing of systemic anti-cancer therapy (SACT) in Ireland: A population based study

Peter M. Barrett^{a,b,1}, Fionn P. Daly^{b,c,1}, Mengyang Zhang^d, Aislinn O'Reilly^e, Patricia Heckmann^f, Paula Tierney^g, Deirdre Murray^{b,g}, Maeve Mullooly^d, Kathleen Bennett^{d,*}

^a Department of Public Health HSE South-West, St. Finbarr's Hospital, Cork, Ireland

^b School of Public Health, University College Cork, Cork, Ireland

^c School of Medicine and Health, University College Cork, Cork, Ireland

^d School of Population Health, RCSI University of Medicine and Health Sciences, Dublin, Ireland

^e Waterford Regional Hospital, Waterford, Ireland

^f HSE National Cancer Control Programme, Kings Inn House, Dublin, Ireland

^g National Cancer Registry in Ireland, Cork, Ireland

ARTICLE INFO

Keywords:

COVID-19

Systemic anti-cancer treatment

Cancer care

Interrupted time series

ABSTRACT

Objectives: The COVID-19 pandemic had considerable implications for cancer related care. This study aimed to examine its impact on the dispensing of systemic anti-cancer therapy (SACT) in Ireland.

Study design: A repeated cross-sectional design was used which involved a quasi-experimental interrupted time series analysis (ITSA), and autoregressive integrated moving average (ARIMA) models.

Methods: This nationally representative study utilised monthly pharmacy claims (i.e. dispensing) data from community and hospital schemes. Dispensed items among individuals prescribed any SACT from January 2019 to April 2021 were included.

Results: During the study period, 641,273 SACT items were dispensed, including 57,199 chemotherapeutic agents (8.9 %), 15,970 immunotherapeutic agents (2.5 %), 87,813 targeted therapies (13.7 %), and 480,291 (74.9 %) endocrine therapies. There were on average 3.3 and 4.1 fewer immunotherapy and targeted therapy agents, respectively, dispensed per 100,000 population per month post-March 2020 (vs. expected), compared to the level prior to March 2020. For endocrine therapy, there was a significant slowing of the trend post-March 2020 compared to the pre-pandemic period (slope change = -1.72 , 95 % CI -2.9 to -0.5 ; $p < 0.01$).

Conclusion: There was a significant level decrease in the dispensing of immunotherapy and targeted therapy during the first year of the pandemic, and a slowing of the trend for endocrine therapies. However, no differences in the dispensing of other SACT were observed.

1. Introduction

The morbidity and mortality associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 or COVID-19) infection changed substantially over time, including among medically vulnerable groups due to the evolution of newer COVID-19 variants, and the acquisition of population immunity in Ireland as of October 2023 [1].

During the initial stages of the COVID-19 pandemic, healthcare services were severely disrupted as efforts were made to provide essential clinical care to COVID-19 patients, while reducing risk of transmission both in the community and in healthcare settings [2,3]. In

Ireland, prioritisation of COVID-19 prevention and continuation of clinical care resulted in considerable staff redeployment, disruption to cancer screening and diagnostics, as well as changes in treatment pathways [4]. Cancer patients were disproportionately impacted by reduced surgical activity at the time [5]. Delays in some surgical procedures and curtailed access to radiotherapy meant that cancer therapies were sometimes extended or dosing intervals changed. Patients with an active cancer diagnosis were considered to be at higher risk of morbidity and mortality from COVID-19 infection [6], and healthcare services for these patients were reconfigured in efforts to reduce their risk of exposure to COVID-19 [4], for example, shorter, more accelerated

* Corresponding author. School of Population Health, RCSI University of Medicine and Health Sciences, Dublin, Ireland.

E-mail address: kathleenebennett@rcsi.ie (K. Bennett).

¹ These authors contributed equally to this work.

fractionation regimens among breast cancer patients [7]. For some immunotherapeutic agents, dosing intervals were increased (from April 2020 onwards) in line with emerging evidence, as part of efforts to reduce hospital attendances and potential exposure to COVID-19 [8–10]. Prescriptions for medicines dispensed in the community may have also been extended to avoid contact with general practitioners [11], and some chemotherapeutic or other therapies initiated when surgeries or radiation therapies were delayed.

To date, few published studies have examined the impact that the COVID-19 pandemic had on dispensing of systemic anticancer therapy (SACT; i.e. chemotherapy, immunotherapy, targeted therapy, and endocrine therapy) [12,13]. Therefore, this study aimed to examine patterns of SACT dispensing during the first three waves of the pandemic in Ireland, i.e. March 2020 to April 2021 [14], and to determine whether dispensing patterns varied during the onset and initial stages of the pandemic.

2. Methods

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used in the reporting of this research study [15], and can be found in [Appendix 1](#).

This study was based on a repeated cross-sectional design applying quasi-experimental interrupted time series analysis (ITSA). This approach can be used to evaluate the longitudinal effects of an intervention or interruption on a specified outcome over time [16]. In this present analysis the interruption here refers to the pandemic onset in March 2020 in Ireland.

In Ireland, the financial costs of SACT are covered by a number of different drug schemes. These schemes are administered through the Irish Health Service Executive Primary Care Reimbursement Services (HSE-PCRS), and national claims data are collated mainly for reimbursement purposes.

Prescriptions dispensed from community pharmacies are either fully funded (out of pocket) by the public, or partially funded through different community drugs schemes to reduce costs for the public. The community drug schemes include the General Medical Service (GMS) scheme, the Drug Payment (DP) scheme, and the Long-Term Illness (LTI) scheme [17]. The GMS scheme provides access to healthcare services, including drugs, for those unable to finance their prescriptions and/or other healthcare services without undue hardship. Through means-testing of total annual income and age, a medical card may be issued to those eligible under this scheme. The DP scheme covers individuals or families who are not eligible for a GMS medical card, and who instead must pay for their medicines up to a specific threshold amount per month per family. Currently, this threshold is €80 (since March 1, 2022), although it has previously been higher [18]. The LTI scheme covers persons with long-term medical illnesses or disabilities that require treatment. All medicines associated with these illnesses or disabilities are provided free of charge. Some examples of conditions covered include some haemato-oncological conditions such as leukaemia [19]. Further, medicines initiated or delivered in hospital settings may be covered through the High Tech Drug (HTD) scheme, which covers the cost of high-cost medicines typically initiated in hospital for specific clinical indications (e.g. imatinib), but subsequently available in the community via nominated pharmacies. Finally, the Oncology Drug Management System (ODMS) is for specific high-cost SACT drugs administered in hospitals.

Patterns of dispensed items were examined as data on the exact coverage of individuals eligible for the oncology medicines under the various drug schemes is largely unknown. Generally, data coverage of community schemes is most complete for the GMS scheme in Ireland and less complete for prescriptions which are dispensed within the LTI, private healthcare settings, or which fall below the monthly threshold of €80 per month. Data on drugs dispensed by hospital pharmacies under the ODMS, which are the more expensive medicines, are likely to have

more complete data. Since there is variable coverage across the drug payment schemes, and given that dispensing may occur across these different schemes, the focus herein is on overall trends, and thus results are not presented by scheme.

This study utilised monthly pharmacy claims (reimbursement) data from the Irish HSE-PCRS for SACT from January 2019 to April 2021. Importantly, “reimbursement” was used as a proxy for “dispensing”. SACT was defined as anti-neoplastic and endocrine drugs, outlined in more detail below. The monthly dispensing data included all those in receipt of SACT captured by the HSE-PCRS. The study period (January 2019 to April 2021) included a pre-pandemic timeframe, along with the timeframe covering the first three waves of the pandemic as defined by the Health Protection Surveillance Centre in Ireland [14]. For the third wave, analysis was conducted up to the end of April 2021 due to the occurrence of a national cyber-attack in May 2021, during which routine data management on all national health IT systems was severely interrupted for several months [20]. This study did not include anti-cancer medications delivered in private healthcare settings, or via exceptional compassionate access schemes in Ireland. Additionally, the cost of some SACT was funded directly via individual hospital base budgets, and these data were unavailable.

SACT can be administered in a variety of ways (e.g. intravenously/subcutaneously/orally) and delivered across different settings, including the outpatient/inpatient hospital setting, or in the community [21]. Oral SACT was typically dispensed in community pharmacies in order to facilitate the self-administration of medications at home [21].

Drugs were classified using the World Health Organisation’s (WHO’s) Anatomical Therapeutic Chemical (ATC) classification system, and included codes for individual drugs under the following classes: anti-neoplastic agents (L01) and endocrine therapies (L02A, L02B). The ATC codes for anti-neoplastic agents were classified further into three main groups for analysis: chemotherapeutic agents, immunotherapeutic agents, and targeted therapies. The full list of ATC codes which were used are available in [Appendix 2](#). Data on the specific indication for each dispensed drug were not available. Excluded medications are shown in [Appendix 3](#).

3. Statistical analysis

The number of items dispensed was used in the analysis to reflect the use of the medicines over time. The rates of dispensed items for each month, as well as for each specific type of SACT, were calculated from the total number of items dispensed (numerator) divided by the population estimates (per 100,000) for Ireland in each of the years 2019–2021 [22]. Population estimates were obtained from the Central Statistics Office (CSO) in Ireland [22], and the intervals used were yearly since the monthly estimates were not available.

To examine changes in the rates of dispensed items for oncology drugs, we used ITSA with autoregressive integrated moving average (ARIMA) models. ARIMA models adjusted for pre-existing trends and autocorrelation (and seasonality) in time-series data, thereby providing unbiased estimates [23]. Autocorrelation (lag-1) was removed if non-significant. For the post-interruption period, the following time periods were considered (associated with each COVID-19 wave): March 2020 to July 2020, August 2020 to November 2020, and December 2020 to April 2021.

Variables were included to represent temporary changes for the months of March 2020, August 2020, and December 2020, and sustained level (step or average) and trend (slope, β) changes in the month-to-month rate of dispensed items per 100,000 eligible population for each oncology drug group before and during the waves of the COVID-19 pandemic from March 1, 2020. Level changes (temporary and step changes in rates following the interruption) and the trend change in the rate of dispensed items post-March 2020 were compared to the pre-pandemic time-period preceding these time points (baseline trend, January 2019 to February 2020). Level changes from March 2020 until

April 2021 were able to capture longer-term effects of changes in patterns over time. Where all month and level terms were non-significant (e.g. no significant changes from March 2020), we included only the pre-March 2020 trend. Separate analysis of each classification of SACT was also undertaken. Analyses were performed using Stata (v17.0) and significance at $p < 0.05$ was assumed.

4. Results

Between January 2019 and April 2021, there were 641,273 SACT prescriptions dispensed, including 57,199 chemotherapeutic agents (8.9 %), 15,970 immunotherapeutic agents (2.5 %), 87,813 targeted therapies (13.7 %), and 480,291 (74.9 %) endocrine therapies. Fig. 1 shows the overall trend for all SACT for the study period. Prior to the onset of the COVID-19 pandemic, the trend revealed increased dispensing of SACT over time (trend from January 2019 to February 2020; slope change (β) = 3.25 (95 % CI 1.55–4.94, $p < 0.01$); Fig. 1). Following the onset of the pandemic (March 2020 to April 2021), there was no overall significant level change in the dispensing of SACT in Ireland.

The most frequently dispensed anti-neoplastic medicines (ATC L01) between January 2019 and April 2021 included mercaptopurine (21,804; 13.6 %), capecitabine (16,657; 10.4 %), and palbociclib (13,261; 8.3 %). The most frequently dispensed endocrine therapies were tamoxifen (109,389; 22.8 %), letrozole (98,979; 20.6 %), and anastrozole (88,483; 18.4 %).

The rate of items dispensed for chemotherapeutic agents is summarised in Fig. 2A. While modest fluctuations in dispensing trends were observed, ITSA found no significant temporary or overall level change in the dispensing of chemotherapy agents (Table 1).

The rate of items dispensed for immunotherapy agents prior to, and after, the onset of the pandemic is summarised in Fig. 2B. ITSA found no change immediately post-March 2020 (onset of wave 1), August 2020 (onset of wave 2) or December 2020 (onset wave 3). However, a significant overall level change in the dispensing of immunotherapy agents over the entire post-March 2020 period (compared to the entire pre-pandemic period, January 2019 to February 2020) was observed (Table 1). The level change resulted in, on average, 3.3 fewer items dispensed per 100,000 per month compared to the level prior to March

2020, after adjusting for the underlying pre-pandemic trend.

Trends in the rates of items dispensed for targeted therapy prior to and after the onset of the pandemic are shown in Fig. 2C. No statistically significant temporary change immediately upon pandemic onset (post-March 2020), upon the onset of wave 2 (August 2020) or wave 3 (December 2020), was observed. A significant overall level change in the dispensing of targeted therapy agents over the period post-March 2020 compared to the pre-pandemic period (January 2019 to February 2020; Table 1) was observed. There was an average of 4.1 fewer items dispensed per 100,000 per month compared to expected pre-pandemic levels (prior to March 2020), after adjusting for the underlying pre-pandemic trend (Table 1).

The rate of items dispensed for endocrine therapy prior to and after the onset of the pandemic is summarised in Fig. 2D. No temporary or overall level change in the dispensing of endocrine therapy agents was observed (Table 1). There was, however, a slowing of the trend following the onset of the pandemic (post-March 2020) compared to the period January 2019 to February 2020 (see Table 2).

5. Discussion

Throughout the study period, the COVID-19 pandemic did not appear to have an overall significant impact on the dispensing of SACT in Ireland. Among the four groups of SACT examined, neither chemotherapeutic agents nor endocrine therapies showed any temporary or overall changes in their rates of dispensing. However, a reduction in rates of dispensing for immunotherapeutic agents and targeted therapies was observed over the study period (January 2019 to April 2021) relative to pre-pandemic trends.

In relation to immunotherapy, treatment cycle intervals were extended for some patients during the early waves of the pandemic as part of efforts to mitigate potential nosocomial transmission of COVID-19 [24]. Initially, multiple immunotherapy agents were approved for administration at either two-week or three-week intervals (e.g. nivolumab, atezolizumab, and pembrolizumab). However, extended dosing intervals of these agents was authorised during the pandemic [8–10], and has remained in place in Ireland. This may have partly contributed to the relative decrease in rates of dispensing for immunotherapeutic agents.

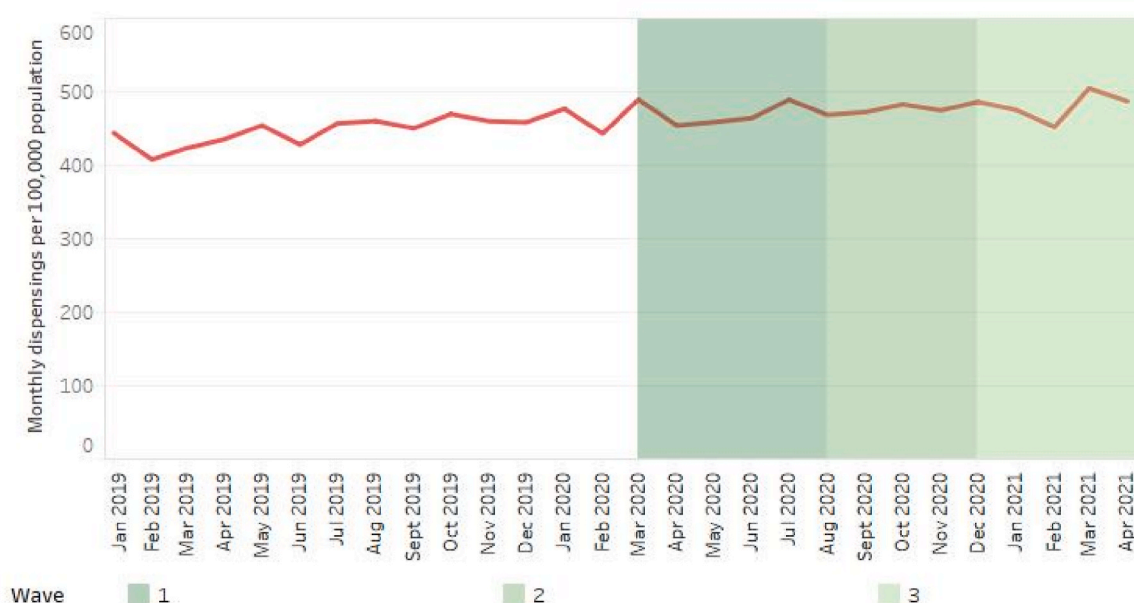


Fig. 1. Rate of monthly items dispensed per 100,000 population for the SACTs examined (anti-neoplastic (L01) and endocrine therapies (L02B, L02B)) in Ireland between January 2019 and April 2021. Vertical shaded areas represent the period of each pandemic wave in Ireland [1–3].



Fig. 2. Rate of monthly items dispensed per 100,000 population for chemotherapeutic agents (A), immunotherapeutic agents (B), targeted therapies (C), and endocrine therapies (D) in Ireland between January 2019 and April 2021. Vertical shaded areas represent the period of each pandemic wave [1–3].

Table 1

Estimated temporary and level changes in rates of monthly dispensings (per 100,000 population) of chemotherapy, immunotherapy, targeted therapy and endocrine therapies between March 2020 and April 2021. Temporary change in the month compared to all other months and level change to Jan 2019–Feb 2020.

	Temporary change pre-post March 2020 (95 % CI) ^a	Temporary change pre-post August 2020 (95 % CI) ^a	Temporary change pre-post December 2020 (95 % CI) ^a	Level (step) change March 2020–April 2021 (95 % CI) ^a
Chemotherapy	1.7 (−5.4, 8.8)	−1.7 (−4.1, 0.6)	1.4 (−1.6, 4.3)	0.1 (−1.47, 1.64)
Immunotherapy	0.30 (−3.0, 3.6) ^b	−0.05 (−3.4, 3.3)	−1.78 (−5.1, 1.6) ^b	−3.27 (−4.6, −1.9) ^c
Targeted therapy	5.1 (−1.2, 11.5)	−0.84 (−6.0, 4.3) ^b	−1.04 (−6.3, 4.2) ^b	−4.10 (−8.0, −0.2) ^c
Endocrine therapy	8.41 (−70.5, 87.4)	3.31 (−281.3, 288.0)	9.41 (−14.9, 33.7) ^b	−0.47 (−13.2, 12.2)

^a Adjusted for pre and post-March 2020 slopes over time if significant.

^b Without lag term in ARIMA model (regression).

^c $p < 0.05$.

It is plausible that reduced or delayed diagnoses of new cancer cases occurred during the pandemic period and this may have impacted on some categories of SACT dispensing [25]. Although the overall incidence of cancer is increasing both in Ireland and around the world [26, 27], the National Cancer Registry Ireland (NCRI) estimated that 8 % fewer diagnoses of cancer (vs. projected) were made during 2020 and 2021 [28]. This was likely due to curtailed access to healthcare services in both community and hospital settings, such as cancer screening services (breast, colorectal, and cervical cancer), reduced referrals for suspected cancer diagnoses [29], and patient hesitancy to attend GP and/or diagnostic appointments due to fear of contracting COVID-19 infection [4].

No significant change was observed for chemotherapeutic agents or endocrine therapy during the study period. Some chemotherapy drugs (e.g. capecitabine) and common endocrine medicines (e.g. triptorelin or bicalutamide) are dispensed from community pharmacies [21]. Hence, these medications are typically taken at home. Only a smaller proportion would arise as new or acute prescriptions, which may have been more vulnerable to sudden changes in acute healthcare delivery. Moreover, in Ireland, legislative and policy amendments led to a significant increase

in home delivery of drugs in the early waves of the pandemic and prescriptions for medicines dispensed in the community were extended in some cases to avoid contact with general practitioners [30]. Thus, patients accessing treatment in community pharmacies may have been less susceptible to the immediate impact of the COVID-19 pandemic

Table 2

Estimated trend change in rates of monthly dispensings (per 100,000 population) of chemotherapy, immunotherapy, targeted therapy and endocrine therapies between March 2020 and April 2021 compared to pre-March 2020.

	Pre-March 2020 slope ^a (95 % CI)	Post-March 2020 slope change ^a (95 % CI)
Chemotherapy	0.13 (0.03, 0.24) ^b	–
Immunotherapy	0.20 (0.13, 0.27) ^c	–
Targeted therapy	1.20 (0.97, 1.44) ^c	–
Endocrine therapy	1.85 (1.02, 2.68) ^c	−1.72 (−2.90, −0.55) ^c

All models include ARIMA (1,0,0) term.

^a Model with level change and slope included.

^b $p < 0.05$.

^c $p < 0.01$.

(compared with those accessing treatment in acute hospitals). Since three-quarters of all dispensed drugs were classified as endocrine therapies, this may have also attenuated the overall study findings (for combined SACT) towards null.

In contrast, immunotherapy and targeted therapy, particularly parenteral formulations, are typically administered in hospitals or specialised centres [21]. We observed a significant overall level change in dispensing relative to pre-pandemic trends, likely to be influenced, in part, by the impact of the pandemic on acute oncology services. Over recent years, significant progress has been made in the development of new targeted therapies [31]. Over time, targeted therapies may slowly begin replacing chemotherapy as the mainstay of cancer treatment [32]. Targeted therapies are often initiated on the basis of specific molecular markers necessitating clinical biopsies or surgical procedures. During the early waves of the COVID-19 pandemic, more stringent infection control precautions within Irish hospitals may have limited the number of surgical/biopsy slots, impacting the timeliness of targeted therapy initiation for new patients. However, it may take several years before the ramifications of delayed presentations, delayed diagnoses, and restricted in-patient activity on patient outcomes have been fully determined [25].

A population-based cohort study conducted in Australia examined variations in SACT dispensing among 51,515 participants from January 2017 to December 2020 [13]. The authors demonstrated that the initial impact of the pandemic on SACT dispensing was minimal. Overall, antineoplastic (i.e. chemotherapy, immunotherapy, and targeted therapy) dispensing did not change between March and December 2020, possibly reflective of public health measures introduced in Australia to mitigate the spread of COVID-19 throughout the country. In New Zealand, nationwide intravenous chemotherapy attendance rates throughout the height of the pandemic were mostly unaffected [33]. However, by international standards, the incidence of COVID-19 was also particularly low in New Zealand during the initial years of the pandemic, and thus it is difficult to draw any direct comparisons in terms of healthcare impact. To date, two national technical reports have been published which detailed the negative impact that COVID-19 had on patient attendance levels for day-case SACT in Ireland [34,35]. The day-case attendance rate for SACT in public hospitals reached its lowest in April 2020, with a 32 % reduction in activity levels relative to 2019 [35]. A return to baseline began in May 2020, and by the following month, levels of day-case attendance in public hospitals were at a comparable level to 2019. Despite this, the overall attendance throughout 2020 was 90 % of the overall level achieved in 2019. Given the overall increasing incidence of cancer at the population level in Ireland, attendance levels for SACT would be expected to grow every year. Of note, some hospitals relocated their SACT services offsite when COVID-19 cases began to surge during the first pandemic wave. Many subsequently returned to their original locations over time [34,35]. From a service planning and resilience perspective, it is imperative that health systems worldwide robustly prepare for, and adapt to, major disruptions or emergency scenarios, which may threaten future continuity of cancer care.

International evidence has proposed that patients with an active diagnosis of malignancy were at a greater risk of morbidity and mortality from COVID-19 infection [6]. In response to the pandemic, the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) both published guidelines to inform treatment strategies during these unprecedented times, as decisions around balancing risks and benefits of treatment interruptions became clearer over time [36,37]. The specific type of cancer that a patient had been diagnosed with, in addition to their predicted response to treatment and/or overall prognosis, had considerable implications for clinical care pathways. Strengths of this study include the utilisation of a national population-based dataset, which increases the generalisability of our findings, given that the costs of many types, but not all, SACT in Ireland are covered by the schemes included in this analysis. Secondly, the large

number of dispensed items adds statistical power to our findings. Thirdly, few studies have been published to date which relate to the relationship between COVID-19 and the dispensing rates of SACT. Previous literature has mainly reported on SACT attendance levels [33,38–40].

A number of limitations to this study must be acknowledged. Firstly, it is possible that some of the medicines were prescribed for reasons other than cancer. Where possible, drugs were entirely excluded from the analysis if cancer treatment was more likely to be a secondary or tertiary indication (e.g. methotrexate). Further, it was not possible to determine the individual-level indication for use. Moreover, only data pertaining to dispensing of drugs was available, and we were unable to gain any insight into adherence or discontinuations. Further, we were unable to determine if the data were obtained from newly initiated or existing prescriptions during the study period. Additionally, our study only included SACT that was covered through the various schemes administered through the HSE-PCRS. These data did not capture SACT available through other routes. Data may have been missing for those who access their medicines through the DP scheme, which may have resulted in an under-estimation of dispensing for certain medicines e.g. endocrine therapy which is less expensive. As outlined in the methods, only dispensings which exceeded the monthly threshold was reimbursed by the HSE-PCRS [18]. Finally, for the third wave of the pandemic, our analysis only covers up until April 30, 2021 due to the onset of a nationwide cyber-attack on health system IT servers in May 2021 [20].

In conclusion, these findings suggest that the COVID-19 pandemic did not appear to significantly impact the dispensing of chemotherapeutic agents or endocrine therapies overall. However, reductions in the dispensing of both immunotherapeutic agents and targeted therapies were observed relative to pre-pandemic trends. This may be partly due to their customary administration in the acute hospital setting, as well as reduced eligibility for these drugs due to delayed diagnoses during the early stages of the pandemic. Future strategies must be developed and implemented to mitigate the impact of any further unprecedented disruptions on SACT administration. These findings may inform future healthcare services' preparedness plans to ensure they are optimally equipped for unanticipated disruptions or future pandemics.

Ethical approval

Ethical approval was not required as the analysis was conducted using anonymised aggregated data provided by the HSE-PCRS for the purpose of the research. The study was performed in accordance with the Declaration of Helsinki.

Authors contributions

All authors contributed to the writing of the manuscript. All authors reviewed the manuscript.

Concept and design: PB, MZ, PT, DM, MM, KB.

Generation, collection, and assembly of manuscript: PB, FD, MZ, AOR, DM, MM, KB.

Manuscript writing: PB, FD, PH, DM, MM, KB.

Funding statement

This work is supported by the Irish Cancer Society through the Research Grant CMP21BEMU. The opinions, findings and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the view of the Irish Cancer Society. MM is supported by the Health Research Board.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank the HSE-PCRS for supplying the data on which this study was based. The authors would like to thank the COVID-19 and Cancer Working Group and project Advisory Group for providing valuable support for the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhp.2024.100557>.

References

- [1] COVID-19 Ireland, Ireland's COVID-19 data hub – confirmed headline figures, May 16th [Internet] [cited May 11th 2023]. Available at: <https://covid19ireland-geohive.hub.arcgis.com>, 2023.
- [2] B. Kennelly, M. O'Callaghan, D. Coughlan, J. Cullinan, E. Doherty, L. Glynn, et al., The COVID-19 pandemic in Ireland: an overview of the health service and economic policy response, *Health Policy Technol* 9 (4) (2020) 419–429.
- [3] A. Huggins, M. Husaini, F. Wang, R.J. Waken, A.M. Epstein, E.J. Orav, et al., Care disruption during COVID-19: a national survey of hospital leaders, *J. Gen. Intern. Med.* 38 (5) (2023) 1232–1238.
- [4] S. O'Reilly, H. Kathryn Carroll, D. Murray, L. Burke, T. McCarthy, R. O'Connor, et al., Impact of the COVID-19 pandemic on cancer care in Ireland - perspectives from a COVID-19 and cancer working group, *J Cancer Policy* 36 (2023) 100414.
- [5] M. Zhang, C. Kelly, T. McCarthy, P. Tierney, A. Brennan, L. Burke, et al., Examining the COVID-19 impact on cancer surgery in Ireland using three national data sources, *Glob Epidemiol* 8 (2024) 100159.
- [6] N.M. Kuderer, T.K. Choueiri, D.P. Shah, Y. Shyr, S.M. Rubinstein, D.R. Rivera, et al., Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study, *Lancet* 395 (10241) (2020) 1907–1918.
- [7] A. Murray Brunt, J.S. Haviland, D.A. Wheatley, M.A. Sydenham, A. Alhasso, D. J. Bloomfield, et al., Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial, *Lancet* 395 (10237) (2020) 1613–1626.
- [8] G.V. Long, S.S. Tykodi, J.G. Schneider, C. Garbe, G. Gravis, M. Rashford, et al., Assessment of nivolumab exposure and clinical safety of 480 mg every 4 weeks flat-dosing schedule in patients with cancer, *Ann. Oncol.* 29 (11) (2018) 2208–2213.
- [9] K.M. Morrissey, M. Marchand, H. Patel, R. Zhang, B. Wu, H. Phyllis Chan, et al., Alternative dosing regimens for atezolizumab: an example of model-informed drug development in the postmarketing setting, *Cancer Chemother. Pharmacol.* 84 (6) (2019) 1257–1267.
- [10] U.S. Food and Drug Administration, FDA approves new dosing regimen for pembrolizumab, Available at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-new-dosing-regimen-pembrolizumab>, 2020.
- [11] Health Service Executive, Community Pharmacy Contractors Frequently Asked Questions COVID-19 (Coronavirus), 2020.
- [12] C.J. Bright, S. Lawton, S. Benson, M. Bomb, D. Dodwell, K.E. Henson, et al., Data resource profile: the systemic anti-cancer therapy (SACT) dataset, *Int. J. Epidemiol.* 49 (1) (2020), 15–1.
- [13] M. Tang, B. Daniels, M. Aslam, A. Schaffer, S.A. Pearson, Changes in systemic cancer therapy in Australia during the COVID-19 pandemic: a population-based study, *Lancet Reg Health West Pac* 14 (2021) 100226.
- [14] Health Protection Surveillance Centre, Epidemiology of COVID-19 outbreaks/clusters in Ireland, Available at: <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/covid-19outbreakclustersinireland/covid-19outbreakclustersinirelandweeklyreports2022/COVID-19/20Weekly/20Outbreak/20Report/20Week/2016/202022/20v.1.0.pdf>, 2022.
- [15] E. von Elm, D.G. Altman, M. Egger, S.J. Pocock, P.C. Gøtzsche, J. P. Vandenbroucke, The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies, *J. Clin. Epidemiol.* 61 (4) (2008) 344–349.
- [16] A.K. Wagner, S.B. Soumerai, F. Zhang, D. Ross-Degnan, Segmented regression analysis of interrupted time series studies in medication use research, *J. Clin. Pharm. Therapeut.* 27 (4) (2002) 299–309.
- [17] S.J. Sinnott, K. Bennett, C. Cahir, Pharmacoepidemiology resources in Ireland—an introduction to pharmacy claims data, *Eur. J. Clin. Pharmacol.* 73 (11) (2017) 1449–1455.
- [18] Irish Pharmaceutical Healthcare Association, Supply and reimbursement [cited May 20th 2023] [Internet]. Available at: <https://www.ipha.ie/supply-and-reimbursement/>, 2022.
- [19] Health Service Executive, Long-term illness scheme, Available at: <https://www2.hse.ie/services/schemes-allowances/ti/about/>, 2022.
- [20] Conti Cyber Attack on the HSE. Independent post incident review. Commissioned by the HSE board in conjunction with the CEO and executive management team. Available at: <https://www.hse.ie/eng/services/publications/conti-cyber-attack-on-the-hse-full-report.pdf>.
- [21] Health Service Executive, National Cancer Control Programme (NCCP), Systemic Anti-Cancer Therapy Model of Care, 2023.
- [22] Central Statistics Office, Population, Available at: <https://www.cso.ie/en/statistics/population/>, 2023.
- [23] A.L. Schaffer, T.A. Dobbins, S.-A. Pearson, Interrupted time series analysis using autoregressive integrated moving average (ARIMA) models: a guide for evaluating large-scale health interventions, *BMC Med. Res. Methodol.* 21 (1) (2021) 58.
- [24] M. Bersanelli, Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors, *Immunotherapy* 12 (5) (2020) 269–273.
- [25] L. Burke, R. O' Laoide, M. Lawler, D. Murray, A. Galvin, T. McCarthy, et al., Cancer care in Ireland in 2020 – the impact of the COVID-19 pandemic. Faculty of Pathology, Royal College of Physicians of Ireland (RCPI), National Cancer Control Programme (NCCP), National Histopathology Quality Improvement (NHQI) Programme, National GI Endoscopy Quality Improvement (NEQI) Programme, National Radiology Quality Improvement (NRQI) Programme, DATA-CAN: the UK's Health Data Research Hub for Cancer, Queen's University Belfast, Northern Ireland Cancer Registry (NICR), National Cancer Registry Ireland (NCRI), 2021.
- [26] National Cancer Registry, Cancer incidence projections for Ireland 2020–2045, Available at: https://www.ncri.ie/sites/ncri/files/pubs/CancerIncidenceProjections_NCRI_fullreport_09042019_final.pdf, 2019.
- [27] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA A Cancer J. Clin.* 71 (3) (2021) 209–249.
- [28] P. Tierney, J. McDevitt, A. Brennan, P.M. Walsh, COVID-19 Impact on Cancer Incidence in Ireland in 2021: a Preliminary Analysis, 2023.
- [29] N. Bambury, M. Zhang, T. McCarthy, I. Dawkins, L. Burke, P. Tierney, et al., Impact of the COVID-19 pandemic on electronic referrals to rapid access clinics for suspected breast, lung and prostate cancers in Ireland, *Eur. J. Publ. Health* 34 (5) (2024) 908–913.
- [30] Pharmaceutical Society of Ireland, Health Service Executive, Medical Council, Guidance for Prescribers and Pharmacists on Legislation Changes to Facilitate the Safe Supply of Medicines during the COVID-19 Pandemic, 2020.
- [31] L.K. Smith, K.E. Sheppard, G.A. McArthur, Is resistance to targeted therapy in cancer inevitable? *Cancer Cell* 39 (8) (2021) 1047–1049.
- [32] W.D. Joo, I. Visintin, G. Mor, Targeted cancer therapy—are the days of systemic chemotherapy numbered? *Maturitas* 76 (4) (2013) 308–314.
- [33] J.K. Gurney, E. Millar, A. Dunn, R. Pirie, M. Mako, J. Manderson, et al., The impact of the COVID-19 pandemic on cancer diagnosis and service access in New Zealand—a country pursuing COVID-19 elimination, *Lancet Reg Health West Pac* 10 (2021) 100127.
- [34] Royal College of Physicians of Ireland, Faculty of Pathology, Deploying Data Driven Intelligence to measure the impact of COVID-19 on cancer care and cancer patients, Available from: <https://rcpi-live-cdn.s3.amazonaws.com/wp-content/uploads/2021/01/Cancer-Care-and-COVID19-Report.pdf>, 2020.
- [35] Royal College of Physicians of Ireland, Faculty of Pathology, Cancer care in Ireland in 2020: the impact of the COVID-19 pandemic, Available from: https://rcpi.acces.preservica.com/uncategorized/IO_ec89e5fa-3e55-471f-944e-423b56720e8e/, 2021.
- [36] American Society of Clinical Oncology, COVID-19 patient care information, Available at: <https://old-prod.asco.org/covid-resources/patient-care-info>, 2023.
- [37] European Society for Medical Oncology, Cancer patient management during the COVID-19 pandemic, Available at: <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic>, 2023.
- [38] J.J. Clark, D. Dwyer, N. Pinwill, P. Clark, P. Johnson, A. Hackshaw, The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: a retrospective analysis, *Lancet Oncol.* 22 (1) (2021) 66–73.
- [39] A.G. Lai, L. Pasea, A. Banerjee, G. Hall, S. Denaxas, W.H. Chang, et al., Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study, *BMJ Open* 10 (11) (2020) e043828.
- [40] M.A. Baxter, J. Murphy, D. Cameron, J. Jordan, C. Crearie, C. Lilley, et al., The impact of COVID-19 on systemic anticancer treatment delivery in Scotland, *Br. J. Cancer* 124 (8) (2021) 1353–1356.