Acta Biomed 2023; Vol. 94, Supplement 3: e2023161 DOI: 10.23750/abm.v94iS3.14513

Short report

Delays in cancer diagnosis: challenges and opportunities in Europe

Cristina Renzi[1,2], Stefano Odelli[1], Federica Morani[1], Sara Benitez Majano[3], Carlo Signorelli[1]

[1]Faculty of Medicine, University Vita-Salute San Raffaele, Milan, Italy; [2]Epidemiology of Cancer Healthcare & Outcomes (ECHO) Research Group, Department of Behavioural Science and Health, Institute of Epidemiology & Health Care, University College London, London, UK; [3]Inequalities in Cancer Outcomes Network (ICON) Group, Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, Keppel St, Bloomsbury, London, UK

Abstract. *Background and aim:* Early cancer diagnosis is a public health priority, but large proportions of patients are diagnosed with advanced disease or as an emergency, even in countries with universal healthcare coverage. The study aimed at examining factors contributing to diagnostic delays and inequalities in cancer care, discussing challenges and opportunities for improving the diagnosis of cancer. *Methods:* We performed a critical review of the literature examining factors contributing to delays and inequalities in cancer diagnosis, published between 2019-2023, in Europe with a specific focus on Italy. *Results:* Disparities in screening, cancer diagnosis and treatment have been reported in many European countries, with poorer outcomes for some population sub-groups. For example, some Northern regions in Italy have six-times higher screening participation versus Southern regions. In 2019 36% of the Italian population aged 50-74 reported colorectal cancer screening, higher than the EU average (33%), but lower than in countries like Denmark (>60%). In Italy, the EU country with the largest percentage of people aged 65+, incident cancers are expected to rise by 19.6% over two decades. Older age is also associated with multimorbidity, with physical and mental health morbidities possibly affecting cancer diagnostic pathways. For example, colon cancer patients with pre-existing mental health conditions were 28% less likely to have a prompt colonoscopy when presenting with red-flag symptoms, according to recent UK research. COVID-19 has exacerbated pre-existing inequalities, with reductions in scheduled surgery and oncological treatments, especially affecting women, older and less educated individuals. *Conclusions:* For ensuring appropriate care, it is crucial to better understand how different factors, including physical and mental health morbidities, impact cancer diagnosis. The "NextGenerationEU" program and the "National Recovery and Resilience Plan" (PNNR in Italy) following the COVID-19 pandemic offer opportunities for reducing inequalities, improving cancer care and chronic disease management for ageing populations. (www.actabiomedica.it)

Key words: cancer, diagnosis, chronic disease, mental health, COVID-19, Italy, Europe

Timely cancer diagnosis is essential for improving cancer survival and patients' quality of life. Whilst early cancer diagnosis has long been regarded as a key public health priority, large proportions of cancer patients are still diagnosed with metastatic disease and/or following emergency presentations, even in settings with universal healthcare coverage. For example, colorectal cancer (CRC) is diagnosed at advanced stage in 30% of cases in Italy and in more than 50% of cases in England, despite the availability of national screening programmes, as well as clinical protocols and guidelines for investigating symptomatic patients (1-3). According to the European Cancer Information System (ECIS) 5-year relative survival for CRC ranges from

58% to 75% across European countries, with consistently better outcomes for early stage and screening-detected cancer patients (4). In particular, 5-year CRC survival in Europe is as high as 89.1% and 81.2% for patients diagnosed at stage I and II, respectively, while it is 69.4% for stage III and as low as 15.4% for stage IV cancers (5). According to population-based surveys, in 2019 36% of the Italian population aged 50-74 reported having participated in CRC screening in the previous two years, slightly higher than the EU average (33%), but lower than in countries like Denmark, which reached more than 60% CRC screening participation (6). Disparities in screening, timely cancer diagnosis and treatment have been reported in many countries, with poorer health outcomes for some sub-groups (including older individuals, people affected by mental health problems and those with lower educational level) (7). Similar to other EU countries, wide regional and socio-economic variations are seen in Italy, with some Northern regions having six-times higher screening participation compared to some Southern regions (8). While cancer survival is relatively high in Italy overall, notable and unacceptable disparities by region and patient characteristics persist. Increasing our understanding on factors contributing to diagnostic delays and disparities in cancer care is crucial for informing health policies and improving the quality of care and health outcomes for all patients.

Ageing populations and the challenge of physical and mental health morbidities

Cancer is among the leading causes of death globally, with population ageing substantially contributing to the rising number of new cancer cases worldwide. In Italy, the European country with the largest percentage of people aged 65 or older (23% of the Italian population) (9), there were 390,700 new cancer cases in 2022, including 205,000 cases in men and 185,700 cases in women (compared with 199,500 and 183,200 cases in men and women, respectively, in 2020, with an estimated increase of 2.8% and 1.4%, respectively, during this time period) (10). While the lower number of cancer cases in 2020 is partially related to the disruptions of non-urgent healthcare during the COVID-19 pandemic, in the next two decades cancer cases are expected to rise by 19.6% in Italy, with 457,824 projected new cases by 2040 (6,11). Among people aged 65 or older, the expected increase is as high as 40% by 2040, similar to the European average. In addition to being associated with increasing cancer incidence, older age is also associated with a higher prevalence of chronic morbidities and multimorbidity, which may contribute to delays in cancer diagnosis. According to the Italian National Institute of Statistics, about one-third of the Italian population is affected by one or more chronic conditions, with cardiovascular diseases and diabetes being the most common. Among people aged 65-74 years about one-in-two have chronic morbidities, while they affect more than three-in-four people aged 85 or more. Pre-existing physical and mental health conditions can influence the time to cancer diagnosis through different mechanisms (12): patients may attribute possible cancer symptoms to their pre-existing morbidity, delaying help-seeking (also known as the 'alternative explanation' mechanism). Some pre-existing conditions requiring urgent medical care may be prioritised by patients and doctors, postponing cancer screening and/or investigations for symptoms suggestive of cancer (also known as the 'competing demands' mechanism). For example, a patient experiencing change in bowel habit and having a pre-existing cardiovascular condition might not be promptly investigated with a colonoscopy due to the risk of complications associated with invasive diagnostic procedures, possibly delaying the diagnosis of an underlying colorectal cancer (12). By contrast, some medical consultations or tests performed for a chronic disease might sometimes enable an earlier diagnosis of cancer (surveillance effect). Chronic conditions can affect the diagnostic process at different levels of cancer pathways, influencing both patients and healthcare providers.

Mental health conditions can also affect diagnostic pathways and timely cancer diagnosis, as shown by a recent UK study (13). Examining a cohort of 3,766 colon cancer patients revealed that individuals with pre-existing mental health conditions and an as-yet undiagnosed cancer were 28% less likely to be promptly investigated with colonoscopy even when presenting in primary care with red-flag cancer symptoms, such

as rectal bleeding or change in bowel habit. Patients with pre-existing diagnoses of anxiety or depression experienced more than two times longer intervals before cancer diagnosis compared to individuals without mental health morbidity, and they had 63% higher odds of emergency cancer diagnosis. Mental health morbidity has also been shown to be associated with lower screening participation and higher cancer mortality rates in various countries (14,15). There is a critical need for enhanced diagnostic and follow-up strategies to limit possible inequalities in cancer care for the non-negligible group of individuals with mental health morbidities. Additionally to mental and physical morbidities, other factors, such as age, gender, educational and socioeconomic levels also play a role in influencing disparities in cancer screening, access to investigations, treatment, palliative and supportive care (6,7).

Cancer pathways and the COVID-19 pandemic

The COVID-19 pandemic has exacerbated pre-existing health inequalities, as also shown by a recent Italian study comparing the pandemic period with 2018–2019 (16): reductions in hospitalisations for acute conditions, scheduled surgery and oncological treatments have especially affected women, older individuals and those with lower educational level. Possible explanations include greater fear of infections for older individuals, preventing them from accessing hospitals; women, especially if more socioeconomically disadvantaged, might have experienced greater disparities in accessing care due to their caring responsibilities, often prioritising needs of family members over their own, as well as due to a greater compliance with activity-restraining policies (16). The COVID-19 emergency has put healthcare systems under great pressure, decreasing resources available for cancer screening and early diagnosis, increasing waiting times for specialist referrals and consultations, and discouraging patients from seeking healthcare due to fear, and to avoid overburdening the healthcare system (16-18). Italy, similarly to other countries, faced the pandemic in a situation of lack of preparedness, inadequate territorial healthcare organisation, undersized intensive care units, and insufficient number of health workers (19-21).

During 2020, compared to the previous year, in Italy there has been a significant reduction (29%) in newly diagnosed colorectal cancers, with smaller proportions of cancers diagnosed at non-metastatic stages (63% in 2020 vs 78% in 2019) (18). At the same time, the number of emergency cancer diagnoses has increased (about 15% of cancer diagnoses during the pandemic, compared to 13.9% during the pre-pandemic period. There was also a significant reduction in the multidisciplinary management of cancer patients (18). A recent study, involving 17,938 CRC patients treated in 81 Italian centres between 2018 and 2021, examined the stage at cancer diagnosis before and during the COVID-19 pandemic. The results confirmed that patients who underwent surgery for CRC during the pandemic had higher risks of being diagnosed with cancer at an advanced-stage, with aggressive biology, and requiring urgent surgery, which may lead to poorer survival (19). The suspension of screening activity in Italy disrupted the regular schedule of about 6 million FIT (faecal immunochemical test) invitations annually. A 2-month delay may result delays of around 1 million invitations, leading to a 50% reduction in tested individuals. This screening reduction will likely result in a significant decrease in screen-detected CRC. It has been estimated that reductions in screening and investigations in symptomatic individuals and diagnostic delays will significantly increase advanced CRC diagnoses: an estimated 26% increase in advanced cases following a 0-3 months delay, 29% increase following a 7-12 months delay, and 33% increase for a delay of >12 months (17). A significant mortality increase has also been estimated for screening and diagnostic delays of >12 months (17). While eight Italian oncology centres reported a shorter time between symptom onset and first oncological appointment during the pandemic (69 vs 79 days in the pre-pandemic year) and between histological diagnosis and first oncological appointment (34 vs 42 days in the pre-pandemic year), this is unlikely caused by improvements in diagnostic pathways during the pandemic, as suggested by some (18). Rather, this may be due to the presence of more severe symptoms, which contributed to more rapid specialist referrals and diagnosis.

Opportunities for improving diagnostic pathways and cancer care in Italy

The "NextGenerationEU" (NGEU) program is the EU's most important response to the pandemic. Implementation of the NGEU in Italy will take place through the "National Recovery and Resilience Plan" (NRRP, in Italian PNRR). Mission 6 of the Italian PNRR seeks to address the challenges faced by the healthcare system, including diagnostic delays, growing waiting lists, and increasing burden of chronic conditions, including mental and physical conditions and cancer. The Plan aims at strengthening preventive medicine, redesigning primary care, enhancing care coordination between hospital and community settings, and implementing digital technologies in public health (20). It includes two key strategies: 'Proximity networks, structures and telemedicine for territorial healthcare assistance' and 'Innovation, research and digitisation of the National Health System'. The first strategy has the objective of strengthening the Italian system of primary care and increasing the availability of telemedicine to decentralise hospital visits and provide more care through local health centres, doctor's offices, and patient homes (20,21). This could help decrease disparities in accessing healthcare services, for fragile patients and for people living in disadvantaged and remote areas. The second strategy allocates resources for the digital transition and the employment of innovative health technologies. It promotes a systematic use of Personal Electronic Health Records (EHR) and underlines the need to re-organise the national network of the Scientific Institutes for Research, Hospitalisation and Healthcare (IRCCS) and their governance. It also increases the resources dedicated to healthcare professionals' education. This deep transformation could not only directly benefit patient care, but it could also be a driving force for research thanks to a wealth of highly informative electronic health records. In order to exploit the full potential of EHR for research and healthcare quality improvements there is a pressing need for linked epidemiological data encompassing primary and secondary care, as well as cancer and other chronic diseases registration systems across all regions of the country. This might offer promising opportunities for improving cancer care, and for managing other chronic diseases.

The strict and frequent lockdowns enforced during 2020-2021 have been associated with an increase in mental health disorders across different countries, including Italy. While there is growing recognition of the influence of mental health issues on cancer diagnosis (13-15), there is a need for further research to better understand their impact on screening participation, timely diagnosis and cancer outcomes in Italy. Such studies could inform policies and interventions aimed at improving both mental health and cancer services. Targeted plans and strategies are needed to address these issues. Yet, The Italian National Recovery and Resilience Plan (PNRR) does not currently allocate resources specifically for mental health (21).

Conclusions

Timely cancer diagnosis is of primary importance not only because it is a prerequisite for improving survival and quality of life of individual patients, but also because it can reduce the economic and social burden of advanced cancers at population level. For developing appropriate strategies that ensure timely and appropriate cancer care, it is crucial to better understand how different factors, including physical and mental health morbidities and healthcare-related factors might impact diagnostic timeliness. The COVID-19 pandemic highlighted several critical areas in healthcare systems, emphasising the need of resilient health services for allowing timely diagnosis and care. In this context, resources offered by the PNRR are a great opportunity to improve healthcare provision according to needs across the country, reducing inequalities, renewing strategies and infrastructures for enhanced cancer care and chronic disease management for ageing populations. A re-organisation of the healthcare system is essential for offering equitable access to quality services and improve public health.

Funding: Cristina Renzi acknowledges funding from Cancer Research UK - Early Detection and Diagnosis Committee (grant number EDDCPJT\100018) since the initial planning of the work.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Ethic Committee: not applicable.

Authors Contribution: C. R.: conception and design of the study, interpretation of the data, original draft preparation, final approval of the version to be published. S. O.: conception of the study, interpretation of the data, original draft preparation, final approval of the version to be published. F. M.: conception of the study, interpretation of the data, original draft preparation, final approval of the version to be published. S. B. M.: design of the study, interpretation of the data, original draft preparation, revising the article, final approval of the version to be published. C. S.: design of the study, interpretation of the data, revising the article, final approval of the version to be published.

References

1. Piano Oncologico Nazionale: documento di pianificazione e indirizzo per la prevenzione e il contrasto del cancro 2023-2027
2. NHS screening UK, https://www.nhs.uk/conditions/nhs-screening/
3. NICE guidelines UK, https://www.nice.org.uk/guidance/published?ngt=NICE%20guidelines
4. ECIS - European Cancer Information System
5. The Lancet Regional Health - Europe 2022;21: 100458 Published online 6 July 2022
6. "Profili sul cancro per paese" European Cancer Inequalities Registry – Italy, OECD, https://www.quotidianosanita.it/allegati/allegato1675421077.pdf
7. "It Can Be Done – Beating Inequalities in Cancer Care." Action Report of the European Cancer Organisation; 10 November 2020
8. https://www.oecd-ilibrary.org/social-issues-migration-health/eu-country-cancer-profile-sweden-2023_7b5ff594-enItNor
9. Rapporto annuale 2022, ISTAT (Italian National Institute of Statistics)
10. "I numeri del cancro in Italia 2022" Report AIOM 2022
11. Armaroli P, Battagello J, Battisti F, et al, ONS (osservatorio nazionale screening): Rapporto sui ritardi accumulati alla fine di maggio 2020 dai programmi di screening Italiani e sulla velocità della ripartenza.
12. Renzi C, Kaushal A, Emery J, et al. Comorbid chronic diseases and cancer diagnosis: disease-specific effects and underlying mechanisms. Nat Rev Clin Oncol. 2019;16(12):746-761. doi:10.1038/s41571-019-0249-6
13. Benitez Majano S, Lyratzopoulos G, de Wit NJ, et al. Mental Health Morbidities and Time to Cancer Diagnosis Among Adults With Colon Cancer in England. JAMA Netw Open. 2022;5(10):e2238569. Published 2022 Oct 3. doi:10.1001/jamanetworkopen.2022.38569
14. Solmi M, Firth J, Miola A, et al. Disparities in cancer screening in people with mental illness across the world versus the general population: prevalence and comparative meta-analysis including 4 717 839 people. Lancet Psychiatry. 2020 Jan;7(1):52-63. doi: 10.1016/S2215-0366(19)30414-6.
15. Davis LE, Bogner E, Coburn NG, et al. Stage at diagnosis and survival in patients with cancer and a pre-existing mental illness: a meta-analysis. J Epidemiol Community Health. 2020 Jan;74(1):84-94. doi: 10.1136/jech-2019-212311.
16. Di Girolamo C, Gnavi R, Landriscina T, et al. Indirect impact of the COVID-19 pandemic and its containment measures on social inequalities in hospital utilisation in Italy [published online ahead of print, 2022 May 12]. J Epidemiol Community Health. 2022;jech-2021-218452. doi:10.1136/jech-2021-218452
17. Ricciardiello L, Ferrari C, Cameletti M, et al. Impact of SARS-CoV-2 Pandemic on Colorectal Cancer Screening Delay: Effect on Stage Shift and Increased Mortality. Clin Gastroenterol Hepatol. 2021;19(7):1410-1417.e9. doi:10.1016/j.cgh.2020.09.008
18. Mentrasti G, Cantini L, Zichi C, et al. Alarming Drop in Early Stage Colorectal Cancer Diagnoses After COVID-19 Outbreak: A Real-World Analysis from the Italian COVID-DELAY Study. Oncologist. 2022;27(9):e723-e730. doi:10.1093/oncolo/oyac129
19. Rottoli M, Gori A, Pellino G, et al. Colorectal Cancer Stage at Diagnosis Before vs During the COVID-19 Pandemic in Italy. JAMA Netw Open. 2022;5(11):e2243119. doi: 10.1001/jamanetworkopen.2022.43119
20. Tarricone R, Listorti E, Tozzi V, et al. Transformation of Cancer Care during and after the COVID Pandemic, a point of no return. The Experience of Italy. J Cancer Policy. 2021;29:100297. doi:10.1016/j.jcpo.2021.100297
21. Crispo A, Montagnese C, Perri F, et al. COVID-19 Emergency and Post-Emergency in Italian Cancer Patients: How Can Patients Be Assisted?. Front Oncol. 2020;10:1571. doi: 10.3389/fonc.2020.01571

Correspondence:
Received: 11 March 2023
Accepted: 11 April 2023
Stefano Odelli, MD
Public Health Resident,
University Vita-Salute San Raffaele,
Via Olgettina 58, Milan, 20132, Italy
E-mail: odelli.stefano@gmail.com
ORCiD: 0009-0007-9124-368X