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Cardio-oncology (MG Fradley, Section Editor)

The Importance of Primary Care in Cardio-Oncology

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Opinion statement

There is significant interplay between cancer and cardiovascular disease involving shared risk factors, cross disease communication where cardiovascular events can influence cancer recurrence, and mortality rates and cardiotoxicity from cancer treatments with resultant increased cardiovascular mortality and morbidity in cancer patients. This is a major cause of death in many long-term cancer survivors. As a result, cardio-oncology, which involves the prevention, early detection, and optimal treatment of cardiovascular disease in patients treated for cancer, is expanding globally. However, there is still limited awareness of its importance and limited application of the lessons already learnt. Primary care physicians, and their clinical teams, especially nursing colleagues, have a foundation role in the management of all patients, and this paper outlines areas where they can lead in the cardio-oncology management of cancer patients. Although there is currently a lack of an adequate clinical framework or shared care plan, primary care physicians have a role to play in the various phases of cancer treatment: pre-therapy, during therapy, and survivorship.

Introduction

There is increasing incidence of cancer globally as a result of an enhanced life expectancy interplaying with changing rates of individual and environmental risk factors [1, 2] and increased screening and detection [3]. It is estimated there were 19.3 million new cases of cancer globally in 2020 [4] and the 5-year prevalence was estimated by the World Health Organisation in 2018 to be 43.8 million [5].

Cancer treatments are expanding and include surgery, chemotherapy, radiotherapy, targeted therapies, immunotherapy, and theranostics. Many of these therapies, however, can have significant cardiovascular effects (Table 1), by being either directly cardiotoxic and/or indirectly via complex interactions with traditional cardiovascular risk factors, such as hypertension and hypercholesterolemia, and magnifying their significance [6–16]. In the general population we have seen a decline in cardiac mortality rates over many decades, but this decline has plateaued, particularly in some high-income countries, often because of a resurgence of cardiac risk factors which have the potential to interact with cancer therapies [17].

In cancer patients, cardiovascular disease is usually the major competing cause of death. Recent evidence reviewing 32,000 people with cancer in Australia has shown that by 13 years post diagnosis, cardiovascular disease was the most common cause of death and exceeded cancer cause-specific death [18•]. There is a 2 to 6 times increased rate of cardiovascular disease mortality in people with cancer compared to the noncancer population, which arises within the first year from diagnosis and exists for life [19, 20]. This is likely contributed to by reduced rates of guideline-directed cardiovascular therapy being applied to people with cancer [21] highlighting a potential treatment bias. Hence, there is a need to focus on the cardiovascular health of people diagnosed with cancer, those about to start therapy, undergoing therapy, or after therapy has finished in an effort to prevent premature and avoidable morbidity and mortality from cardiovascular causes. The care of a person with cancer is complex and requires multidisciplinary involvement and coordination. The role of primary care in this approach needs to be emphasised, as a large proportion of cardiovascular disease primary and secondary prevention and diagnosis occurs in this setting.

Table 1 Cardiotoxicity of specific cancer therapies

Cancer therapy class/type	Predominant cardiotoxicity	Postulated mechanisms	Reported incidence of cardiotoxicity
Anthracyclines[50, 51] (e.g. doxorubicin, epirubicin)	Left ventricular dysfunction/heart failure	• Redox stress leading to cellular damage • Disruption of topoisomerase 2β function leading to impaired DNA repair	Dose-dependent toxicity 3–57%
HER2-targetted therapies[50, 52] (e.g. trastuzumab, pertuzumab)	Left ventricular dysfunction/heart failure	• Redox stress leading to cellular damage • Impaired cellular repair pathways	Varies widely, higher when follows anthracyclines: 5–45%
Small molecule tyrosine kinase inhibitors (TKI)[51–54]: (e.g. sunitinib, lapatinib, neratinib, regorafenib, ibrutinib)	Left ventricular dysfunction/heart failure Hypertension Arrhythmias (esp. atrial fibrillation)	Multiple mechanisms depending on specific drug. Generally: • impaired vascular growth (VEGF inhibitors) • impaired cardiac energetics via AMPK inhibition • inhibition of cardiac PI3K-Akt signalling, leading to AF (Ibrutinib) • multiple off-target effects	Dependent on the agent and type of toxicity: 1–40%
Antimetabolites[50, 55] (e.g. 5-fluorouracil, capecitabine)	Coronary spasm	Not fully understood. Active metabolites may cause endothelial damage leading to coronary vasospasm and myocardial ischemia	1–35%
Immune checkpoint inhibitors[50, 56] (e.g. nivolumab, ipilimumab)	Myocarditis Left ventricular dysfunction/heart failure	Not fully understood: likely immune activation-mediated myocardial damage	1–2%
Antimicrotubule agents[51, 57] (e.g. docetaxel, paclitaxel)	Arrhythmias Left ventricular dysfunction/heart failure	Interfere with cardiomyocyte calcium handling and modulate mitogen-activated protein kinase/extracellular signal-regulated kinase 1 and 2 (MAPK/Erk1/2)	1–13%
Androgen deprivation therapy[58, 59] (e.g. degarelix, leuprolide, abiraterone)	Coronary artery disease Metabolic syndrome Hypertension	Varies with class of agents, generally: • induction of insulin resistance • acceleration of atherosclerosis • endothelial dysfunction	Variable and inconsistent, up to 2.2-fold higher risk of cardiovascular events reported for some therapies (e.g. abiraterone)

Table 1 (continued)

Cancer therapy class/type	Predominant cardiotoxicity	Postulated mechanisms	Reported incidence of cardiotoxicity
Proteasome inhibitors[60, 61] (e.g. bortezomib, carfilzomib)	Left ventricular dysfunction/heart failure	• Activation of pro-apoptotic signalling • off-target downregulation of autophagy • alterations of nitric oxide homeostasis	2–25%
Radiotherapy[62, 63]	Ischaemic heart disease Valvular dysfunction Pericarditis	• Redox stress leading to cellular damage • Direct DNA damage – strand breaks • Initiates inflammatory and profibrotic milieu leading to atherosclerosis, and myocardial fibrosis	Varies widely, depending on cardiac dose, type of toxicity and co-administered chemotherapy: 7–60%

Shared risk factors

There are a number of shared risk factors for cancer and cardiovascular disease that have been identified such as age, diet, alcohol intake, hormone replacement, obesity, physical inactivity, and tobacco [22]. It has been estimated that ~ 80% of cardiovascular disease and 30–50% of cancer deaths could be prevented through risk factor modification [22, 23]. The American Heart Association has recently re-framed a primary prevention approach to cardiovascular disease focusing on four health behaviours: smoking, diet, physical activity, body weight and three health factors: blood pressure, cholesterol, glucose. This has been referred to as the life's simple 7 formula (24). In oncology, there has been growing emphasis on risk factors also, and the following have been focused on: smoking, diet, physical activity, and body weight as well as infectious agents and ionising radiation [25]. Beyond shared risk factors there is now data to suggest that cardiovascular disease states and cancer also communicate. Immune-mediated cross-disease communication has been shown in a mouse model and in retrospective analyses of human disease. Myocardial infarction is an acute physiological stressor which results in a systemic response in an individual, reprogramming myeloid cells toward an immunosuppressed state and inducing monocytosis which increases the likelihood of tumor progression. In a recent publication of 1724 patients post early-stage breast cancer, the occurrence of a cardiovascular event increased the adjusted risk of recurrence of breast cancer by 59% and breast cancer–specific mortality by 60% [26••]. Attention to these risk factors and disease states are beneficial for primary and secondary prevention.

Why cardio-oncology?

Cardio-oncology is a comparatively new area of focus in medicine, variably defined. Hayek et al. eloquently describes it as involving the prevention, early detection, and optimal treatment of cardiovascular disease in patients treated for cancer, focused on balancing the cardiovascular and oncological needs of patients before, during, and after therapy [27]. Although rapidly growing throughout the world, there are still only limited numbers of cardio-oncology physicians, units, and training programs [28].

Despite cardio-oncology gaining prominence in many locales in recent times, there is still a significant gap between guideline-directed management of cardiovascular risk in cancer patients and physicians' perception of its importance and need for referral for cardiac assessment. Various oncological and cardiac consensus statements and guidelines recommend cardiovascular baseline evaluation, including with echocardiography, aggressive risk factor management, and longer-term follow-up [29–33, 34••, 35, 36], yet we know this frequently does not happen. In a recent survey of international healthcare providers involved with cardio-oncology, only 12% of oncologists felt

that cardiotoxicity should be monitored for in an asymptomatic patient and 50% stated cardiologists should only be involved when there is established cardiotoxicity. Only 46% of oncologists felt that cardio-oncology clinics would significantly improve patients' prognosis [37•]. This is a disappointing, although not surprising, stance given the limited outcome data in the field of cardio-oncology.

However, there are many studies that consistently show an increase in cardiovascular risk in various cancer therapies such as anthracyclines [38••, 39] and trastuzumab [40, 41], predominately centred around left ventricular dysfunction. Evidence that spans decades shows that exposure to therapeutic ionising radiation to the chest as well as occupational and environmental exposures [42–46] can adversely affect coronary arteries and valvular structures. Interventions, particularly with early detection and treatment of anthracycline and trastuzumab cardiotoxicity, have been shown to improve left ventricular dysfunction or result in less interruption of cancer therapy [47, 48]. Despite wide reaching cardiac effects, the major morbidity in the modern era of chest radiotherapy is an increase in rates of ischaemic heart disease with a mechanism that has been considered to be similar to that of standard atherosclerosis [49]. Although there is limited outcome data in this specific population, it is not unreasonable to assume that the very effective preventative strategies of controlling risk factors and treating specific disease states such as left ventricular dysfunction and coronary atherosclerosis that have led to a decrease in cardiovascular disease morbidity and mortality in the noncancer population would also be effective in reducing risk and therefore improving outcomes in this scenario.

The role of primary care

Primary care physicians are the foundation stone of clinical care in many countries, responsible for delivering and coordinating care across a spectrum of conditions including cardiology and oncology. Their activity in the care of patients has been linked to reductions in mortality, with a 2019 US-based epidemiological study showing that for every 10 additional primary care physicians per 100,000 population, there was an associated 51.5 day increase in life expectancy [64].

Oncologists have traditionally coordinated cancer care and follow-up. Interventions in terms of cardiovascular risk factor modification and disease assessment, monitoring, and management, however, are not "core business" for oncologists, yet is an area that forms a major part of primary care practice. What may be lacking is the awareness among primary care practitioners of the increased cardiovascular risk in patients with cancer.

There is a significant shortage of oncologists with data predicting a 2393 full-time equivalent shortage of oncologists in the USA by 2025 [65]. We have also seen that the acceptance of cardio-oncology is limited in this group at this stage, hence limiting referrals to cardio-oncology clinics, which currently would not be likely to cope with the volume of referrals if there was universal acceptance and implementation of guidelines and consensus statements.

It is important that we realise the importance of primary care physicians in clinical cardio-oncology care. Primary care physicians are crucial to the successful implementation of appropriate cardiovascular care in the cancer patient not only given their central role in care coordination and delivery but also because of the increasing burden of disease with rising cancer incidences and improving survivorship rates, workforce shortages in oncologists, and limited availability of cardio-oncologists and relatively poor acceptance of cardio-oncology by cancer physicians.

A recent systematic literature review of primary care physicians' perspectives of their role in cancer care concluded that the majority desired involvement in all aspects of care but only 55% reported broad involvement. A majority believed they should have been involved earlier in care and some expressed frustration at their lack of involvement with many reporting insufficient correspondence from the patients' treating specialist physicians [66].

A current barrier to primary care physician involvement seems to be a lack of a pathway of involvement in general cancer care and this extends to cardio-oncology. A shared care model of oncology management, akin to that seen in some locales with obstetric management, may be a solution for this issue. Such models outline the specific roles and responsibilities of differing health practitioners (usually in distinct physical settings) in their interactions with a patient. In the setting of cardio-oncology, a shared care model would, for example, involve oncological specialist teams having certain responsibilities involving cardiac evaluation and monitoring and primary care teams having others. This would not just involve assigning specific aspects of cardiac monitoring to be undertaken by specific teams, it would also outline at which point in the timeline of care each team is responsible for ensuring that appropriate follow-up occurs. Notwithstanding the current lack of such plans, a suggested protocol for cardiovascular monitoring is outlined in Table 2, and primary care physicians can play a role pre-, during, and post-cancer therapy anywhere, and most likely everywhere, along this continuum of care. It would be a matter of agreement among the distinct treating teams where the responsibility lies for each item.

Pre-, concurrent, and post-therapy care

Pre-therapy

Although there is often little time between diagnosis and commencing cancer therapies, with significant other factors competing for attention, such as psychological distress over a new diagnosis of cancer, there is still the opportunity for primary care to emphasise the importance of lifestyle and shared risk factor management.

There has been increasing awareness of the importance of cardiometabolic changes induced by the cancer itself and cancer therapies [67, 68] and their relationship to increased cardiovascular event rates and overall survival. Pre-existing risk factors can deteriorate early in the cancer journey, or become present where they were not before, with increased risk of physical

Table 2 Cardiovascular primary prevention and surveillance protocol

Stage of treatment	Lifestyle and risk factors	Assessment of cardiac structures (myocardium, valves, conducting system)	Assessment of coronary arteries
Pre-cancer therapy commencement	Emphasise lifestyle factors: - Diet especially alcohol - Tobacco use - Exercise Psychological health Monitor and treat risk factors: - Weight - Blood pressure - Cholesterol - Glucose	All patients that are due to have potentially cardiotoxic cancer therapies should have a baseline echo and ECG	No routine investigation
During cancer therapy	Emphasise lifestyle factors: - Diet especially alcohol - Tobacco use - Exercise - Psychological health Monitor and treat risk factors: - Weight - Blood pressure - Cholesterol Glucose	Usually performed by oncologists as necessary but if not done consider: - 3 monthly echo if on trastuzumab (or equivalent) for ejection fraction +/− global longitudinal strain assessment	Review incidental CT imaging for evidence of atherosclerotic disease of vasculature
Post-cancer therapy	Emphasise lifestyle factors: - Diet especially alcohol - Tobacco use - Exercise - Psychological health Monitor and treat risk factors: - Weight - Blood pressure - Cholesterol Glucose	Echo (if potentially cardiotoxic cancer therapies): - 6–12 months post-conclusion of therapy - 2 years post-conclusion of therapy - Consider periodically thereafter Echo (if anthracyclines) - 6–12 months post-conclusion of therapy - Yearly for 10 years - Consider periodically thereafter Echo (if thoracic radiotherapy with cardiac exposure) - 5 yearly echo	Review any CT imaging performed for evidence of atherosclerotic disease of vasculature If thoracic radiotherapy with cardiac exposure and not already on maximal coronary preventative therapies: - 5 yearly assessment of coronary atherosclerosis – consider use of Coronary Artery Calcium score

Note: If specific abnormalities are found, further surveillance should occur based on the specific condition and current guidelines

deconditioning and obesity developing during the treatment phases of cancer [69]. Hence, with the rest of the treating team being focused on the cancer and its therapy, a consistent message on the importance of management of risk factors by primary care physicians is an important contribution.

During therapy

Cancer therapies can have a multitude of effects on longer-term cardiovascular risk. Anthracyclines and trastuzumab have long been known to affect myocardial function directly as can ionising radiation; the latter more importantly affects coronary arteries and promotes atherosclerosis [51]. Newer, targeted agents such as tyrosine kinase inhibitors, BRAF/MEK inhibitors, immune checkpoint inhibitors, and VEGF-inhibitors also increase risks of cardiovascular events; in some cases due to a direct effect on the vasculature or myocardium, or perpetuating effects of other CV risk factors such as arterial hypertension, however, the precise mechanisms for the adverse effects have not been fully elucidated [11, 70, 71]. Various hormonal therapies for breast cancer, such as letrozole, have been implicated in worsening low-density lipoprotein levels and hence increasing cardiovascular event rates, although there has been some inconsistency in the data to date [72]. Androgen deprivation therapy for prostate cancer likewise appears to be associated with increased cardiovascular events, again with inconsistency in the data but metabolic changes have been suggested to be involved [73]. There is increasing awareness of the importance of hormone therapy in breast and prostate cancer and the interplay with cardiac disease leading to a recent scientific statement from the American Heart Association, highlighting its importance and stressing the importance of multidisciplinary care in these patients [74].

Therefore, the aggressive management of cardiovascular risk factors during therapy becomes even more important, although clearly more difficult than in a "stable" patient not undergoing various therapeutic interventions. Primary care, particularly in a shared care type of arrangement, could certainly play an important role in this management.

Of increasing relevance is the use of incidental information that arises from medical imaging. Radiological imaging is a mainstay of cancer management and often the heart and other vascular structures such as the carotid arteries and aorta are in the imaging field. Cardiovascular risk has been primarily determined by various risk equations in the last couple of decades [75] but it has become increasingly well recognised that there are significant limitations with this approach, including the failure to account for increased cardiovascular risk induced by cancer therapies. Information obtained on the presence or absence of coronary and arterial calcification better selects patients that are at risk of future cardiovascular events and thus enables an enhanced focus on cardiovascular prevention, particularly assisting in the decision making regarding medication therapy for lipid lowering [76].

A number of large trials have shown that coronary artery calcification is associated with cardiovascular risk and a much better predictor of event rates than traditionally used risk factors [76, 77]. Silverman

et al., for example, demonstrated the cardiovascular event rates can alter by a factor of > 10 × with the same traditional risk factors dependent on the absence or presence, and degree, of coronary artery calcification [78]. Importantly, data has now emerged that intervening on coronary artery calcification results, with appropriate statin therapy, can lead to changes in clinical outcomes with reductions in major adverse cardiovascular events such as myocardial infarction, stroke, or cardiovascular death [79•].

Historically, the presence or absence of coronary artery calcification has not been routinely reported by radiologists when it is an incidental finding. Coronary artery calcium scoring is usually performed by ECG-gated non-contrast CT scans and is a dedicated and specific test for this abnormality, although unfortunately in many jurisdictions this is an unfunded investigation with significant financial toxicity to patients. There is now evidence to show that the presence or absence of coronary artery calcification can often be determined on incidental scans with a high degree of accuracy [80]. This has led to a change in guidelines for radiologists with the British Society of Cardiac Computed Tomography, British Society of Cardiovascular Imaging, and British Society of Thoracic Imaging recommending the reporting of findings of coronary artery calcification and aortic calcification in non-gated thoracic CTs [81••]. The primary care provider can use this information to assist in their determination of commencement of lipid lowering therapy in these patients, as it is often not done by oncologists.

Various organisations such as the National Comprehensive Cancer Network (NCCN), Clinical Oncology Society of Australia, and the American College of Sports Medicine all recommend exercise during, and after, cancer therapies [82–84]. A recent review of meta-analyses showed that of 140 included studies, 139 suggested a beneficial effect of exercise. The effect was statistically significant in 75% of those studies, with most effect sizes small for cancer-related fatigue, health-related quality of life, and depression but moderate for cardiovascular fitness and muscle strength. It was concluded that exercise likely has an important role to play in cancer management [85]. Although often in the realm of exercise physiologists, primary care teams play an important role in informing patients of the benefits of exercise, reassuring patients as to the safety of exercise and encouraging them to attend to exercise at a time that they may not inherently feel inclined to do so.

A high proportion of cancer patients develop mental health symptoms after their cancer diagnosis and during treatment. A recent review concluded that anxiety, irritable mood, demoralisation, major depression, and post-traumatic stress disorder have all been documented in cancer patients [86]. It has shown to be beneficial to provide psychosocial care to cancer patients [87], particularly so in the community and within primary care [88]. Although there are disparate findings in terms of the relevance of stress and cardiovascular disease, a number of reviews have suggested a link, although causation has not been proven [89, 90]. Nonetheless, it

is appropriate to consider psychological care as part of the extended and broader care of the heart in a cancer patient.

Post-therapy

Primary care physicians play an important role post cancer therapy in assessing and managing risk factors, surveillance, empowering the patient, and supporting them with self-management.

The importance of primary care follow-up with reduction in oncologist follow-up

It has previously been shown that whereas medical input from primary care remains high in adult cancer patient cohorts, after 5 years of survival only approximately one-third of patients still obtain care from physicians whose speciality is related to their original cancer [91]. Although there is slightly better follow-up of survivors of childhood cancer, up to 50% do not follow-up with oncological specialists after 10 years of survival [92]. Hence the opportunity for primary care to guide patients through appropriate post cancer treatment cardiac surveillance is significant and should be encouraged and supported with creating of appropriate frameworks and education materials [93].

Risk factor modification and education/secondary prevention

Continuing with aggressive management of all cardiovascular risk factors as previously outlined including lifestyle factors, blood sugar, cholesterol, and blood pressure as well as psychological health on a regular basis is important in all patients. This could occur in a primary care setting for visits related to cancer follow-up and incidental visits for other reasons. Ideally this would occur within the context of a clinical framework and shared care environment.

Patients with cancer are not always aware of the significance of the symptoms and signs of cardiovascular disease and tend to attribute them to cancer itself. It is therefore important to ensure patients' awareness of symptoms and signs of cardiovascular disease such as dyspnoea, peripheral oedema, and chest pains and the need to seek medical attention for those. Cajita et al. recently conducted a systematic review of health literacy and found that for heart failure, for example, 39% of patients had low health literacy in regard to this condition including lack of understanding of symptoms and signs [94].

Cardiac surveillance

The recommendation for the degree of cardio-oncology follow-up is dependent on the original cancer and subsequent treatment. Although there is no universal agreement on duration, frequency, and type of follow-up,

the authors believe it is reasonable to adopt a pragmatic approach, adopting the most recent guidelines and consensus statements from national and international cardio-oncology, cardiology, and oncology societies to guide follow-up. In addition, where those recommendations are lacking in the cancer population, it is considered reasonable to apply non-cancer cardiovascular guidelines to assist in decision making.

Periodic screening for the development of asymptomatic left ventricular dysfunction with echocardiography at 6–12 months and 2 years post-therapy and periodically thereafter should be considered for patients who received other potentially cardiotoxic cancer treatments according to the most recent European Society of Medical Oncology (ESMO) Consensus Recommendations [34••].

For patients who have had chemotherapy with anthracyclines, consideration of a yearly echocardiogram for up to 10 years is reasonable. This is supported by the findings of a recent study evaluating 56,338 newly diagnosed women with breast cancer given standard low-dose anthracycline chemotherapy, which showed that the risk of late heart failure was significantly higher than those not receiving chemotherapy and this increased incidence continued to up to 8 years after cancer therapy [38••]. In long-term survivors of adult lymphoma who received anthracyclines during treatment, there was a 6.6 × greater rate of cardiac dysfunction compared to matched controls. This risk was dose dependent and was present at a mean follow-up of 9.4 years after diagnosis [95].

In the authors' view this approach is reasonable given that echocardiography is a simple, painless, non-invasive investigation that does not involve exposure to ionising radiation. Importantly, it is established that clinical symptoms and signs of heart failure frequently occur after a period of asymptomatic left ventricular dysfunction [96], and that in anthracycline cardiotoxicity, the chance of recovery is improved with early institution of therapy [97].

Patients with cancer who have undergone radiotherapy are also recommended to undergo routine ongoing monitoring for cardiotoxicity. The basis for that is a known and early association with increased cardiovascular events such as myocardial ischaemia and infarction and late association with valvular disease in those with higher chest doses. ESMO recommends evaluation for ischaemic heart and valvular disease, even if asymptomatic, every 5 years post-therapy [34••].

It is the authors' experience that this level of follow-up is generally not adhered to by oncologists, even where they engage in longer-term follow-up. Although there are no adequate studies to evaluate the level of follow-up that is provided across all cancer patients, the medical literature is littered with evidence of patients not receiving appropriate care in medicine. A seminal paper by McGlynn et al. showed that only 55% of patients in the USA received therapy compliant with current recommendations across a range of conditions [98]. This finding was confirmed in Australia by Runciman et al., showing that compliance with guideline-recommended treatment in 1154 patients, assessed for 22 conditions at 9 years of follow-up, was on average 57% with a range of 13% to 90%, depending on condition [99]. In a Dutch study relating to Trastuzumab cardiac monitoring, one of the most definitely established and recommended surveillance protocols, it was found that of the

328 patients treated with trastuzumab, 24% had no left ventricular ejection fraction estimation prior to commencing therapy, and serial measurements at 3, 6, and 12 months were only done in 53%, 40%, and 30% of patients, respectively [100].

Conclusion

Primary care physicians and their clinical teams play a central and pivotal role in the management of patients, generally, and those with cardiovascular disease and cancer, specifically. This starts before the potential development of disease with management of psychological health, lifestyle, and risk factors such as diabetes, hypertension, and hyperlipidaemia. Once a malignancy is diagnosed, the ongoing involvement of primary care physicians is important as we have outlined. However, the expertise of primary care practitioners is often underutilised in people with cancer. There is an absence of widespread clinical pathways or formalised shared care arrangements in place and a general lack of awareness of the interplay between cancer and cardiovascular risk.

The authors would encourage more consideration of the role of cardio-oncology, in general, and the involvement of primary care physicians, in particular, in an effort to provide the best possible care for cancer patients. We would call on national and international primary care, oncological, and cardiological representative organisations to establish links and work together to form bridges over the voids that are currently present in the multidisciplinary care of cancer patients.

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Declarations

Conflict of Interest

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