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Clinical activity in general practice prior to sarcoma diagnosis: Australian cohort study

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Author contributions

MR, JE and JL conceived the idea for the study. MR undertook the data management for the project. MR completed all of the data analysis. MR, JE, JL, JdB, JM, JD, SB, DG and CdB and GL were involved in interpretation of the findings. MR took the lead in writing the

manuscript. All authors provided critical feedback on the manuscript. JE and JL oversaw the project.

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Ethical approval

The protocol for this project was approved by the Melbourne Health Human Research Ethics committee (protocol number: 202002/2) and has MedicineInsight Data Governance approval (approval number 2016-014).

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This study is based on data from the Australian Comprehensive Cancer Outcomes and Research Database (ACCORD) sarcoma cancer subset using patient data from the Peter MacCallum Cancer Centre and supported by the Australia New Zealand Sarcoma Association (ANZSA); primary care data from Patron and MedicineInsight. This research used de-identified patient data from the Patron primary care data repository (extracted from consenting general practices), which has been created and is operated by the Department of General Practice, University of Melbourne (www.gp.unimelb.edu.au/datafordecisions). The data is provided by patients and collected by the organisations as part of their care and support. Damien McCarthy assisted with data management. The interpretation and conclusions contained in this study are those of the author/s alone.

Competing interests

None of the authors have any conflicts of interest to declare.

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Abstract

Background

Increased time-to-diagnosis in sarcoma is associated with poor prognosis and patient outcomes. Research is needed to identify if opportunities to expedite the diagnosis of sarcoma in general practice (GP) exist.

Aim

To examine pre-diagnostic GP clinical activity prior to sarcoma diagnosis.

Design and Setting

An Australian retrospective cohort study using hospital registry data (Australian Comprehensive Cancer Outcomes and Research Database) linked to two primary care datasets (Patron and MedicineInsight).

Method

The frequency of GP healthcare utilisation events (GP attendances, prescriptions, blood test and imaging requests) were compared in 377 soft tissue sarcoma (STS) and 64 bone sarcoma (BS) patients in the year pre-diagnosis. Poisson regression models were used to calculate monthly incidence rates and rate ratios (IRR) for the 24 months pre-diagnosis and estimate inflection points for when healthcare use starts to increase from baseline.

Results

In the six months pre-diagnosis sarcoma patients had a median of 3-4 GP attendances, a third had a GP imaging request (33% BS and 36% STS), and one in five had multiple imaging requests (19% BS and 21% STS). GP imaging requests progressively increased up to 8-fold from 6 months prior to sarcoma diagnosis (IRR 8.43 95%CI 3.92-18.15, p<0.001) and GP attendances increased from 3 months pre-diagnosis.

Conclusion

Sarcoma patients have increased GP clinical activity from 6 months pre-diagnosis, indicating a diagnostic window where potential opportunities exist for earlier diagnosis. Interventions to help identify patients and promote appropriate use of imaging and direct specialist centre referrals could improve earlier diagnosis and patient outcomes.

Keywords (six)

Sarcoma, general practice, diagnostic time window, imaging, consultations, diagnostic activity

How this fits in (4 sentences)

- Sarcoma is challenging to diagnose with delays associated with poor patient outcome and experience.
- This study shows that sarcoma patients often have multiple GP visits and imaging requests in the year prior to their diagnosis.

- Clinical activity in general practice increases from 6 months before sarcoma diagnosis, primarily in the form of imaging requests, indicating that opportunities for a more timely diagnosis may exist in some patients.
- Primary care interventions to increase awareness of sarcoma symptoms and streamline diagnostic pathways, including promoting and clarifying guidelines to optimise the use of appropriate imaging and direct specialist centre referrals, could improve earlier diagnosis and patient outcomes.

Introduction

Each year in Australia, approximately 2,500 new cases of sarcoma are diagnosed[1]. Sarcoma, although rare in adults, represents one of the most common forms of cancer among children and adolescents and young adults (AYA), accounting for about 10-20% of cancers within these groups[2]. Despite significant advances in the diagnosis and treatment of cancer broadly, outcomes in sarcoma remain disconcertingly low, with nearly 40% of patients dying within 5 years of diagnosis[1] and poorer outcomes for those with high-grade or metastatic disease[3 4]. The poor prognosis is partially attributed to the inherent challenges in diagnosing sarcoma, notably due to its rarity (represents <1% of all malignancies) and heterogenous symptoms[5 6]. As a result, many patients experience lengthy intervals between initial presentation and diagnosis[7-10]. This is particularly relevant in AYA, in whom the incidence of cancer is less frequent, placing it low on the list of differential diagnoses when new symptoms arise[6 11]. Delays in sarcoma diagnosis are associated with worse quality of life, poorer patient experience[12 13], and larger tumour size at diagnosis[14], which is an important prognostic factor in sarcoma[15]. Therefore, efforts to expedite the diagnosis of sarcoma are essential to improve patient outcomes and experience.

Almost all sarcoma patients are diagnosed after symptomatic presentation to their general practitioner (GP)[8 16]. Further research is needed to determine if there are opportunities to expedite the diagnosis of sarcoma in the primary care setting. UK studies have demonstrated that sarcoma patients often have multiple GP consultations before they are referred to a specialist[12 17]. Notably, patients with bone sarcoma (BS) experience one of the highest number of GP consultations pre-diagnosis among all rare cancer types[17]. It remains to be determined if similar pre-diagnostic increases in GP healthcare use occur in the Australian setting, where the healthcare structure, patient demographics and clinician/patient behaviors differ. In particular, GPs in Australia have direct access to a wide range of specialist investigations, few barriers to rapid investigation, referral autonomy (with the option of informal specialist referrals and formal managed referral pathways) and free movement of patients between public and private health systems [18]. This increased flexibility could present more / earlier opportunities for expediting diagnosis.

This study aimed to examine trends in various GP clinical activities over time preceding a sarcoma diagnosis in the Australian context. This will help to identify when patients with as-yet-undetected sarcoma first start using primary healthcare more frequently, how far diagnosis could potentially be brought forward and where opportunities might exist within primary care to accelerate the diagnostic process.

Methods

Data sources

We conducted a retrospective cohort study using hospital cancer registry data from the Australian Comprehensive Cancer Outcomes and Research Database (ACCORD)[19], linked to two primary care databases[20], Patron[21 22] and MedicineInsight[23 24] (Supplementary Figure S1). The ACCORD sarcoma dataset used in this study contains clinician-recorded data on sarcoma patients who were seen at the Peter MacCallum Cancer Centre (PMCC) between 2009–2021[19], a tertiary referral service managing the majority of patients with sarcoma within the state of Victoria. This includes data from sarcoma patients diagnosed before 2009 who received care at PMCC after 2009. Patron and MedicineInsight are primary care electronic health record databases containing de-identified information from GP encounters. MedicineInsight covers a representative, nationwide sample of approximately 8% of general practices in Australia[24], with a subset of practices located in Victoria used in this study. A second source of general practice data came from the Patron primary care dataset, which contains data from over 130 GP clinics in Victoria[25].

Study population

All patients with a new soft tissue sarcoma (STS) or bone sarcoma (BS) diagnosed in ACCORD between 1st January 2002 and 31st July 2021 were identified and the earliest histologically confirmed diagnosis date selected. Patients who did not have linkage to at least one general practice dataset were excluded. In Australia, patients are not required to be registered at a single GP practice and can choose to receive care from multiple GP practices. As a result, individuals are often simultaneously registered to multiple practices, where they have consulted at some point in their life. To ensure only patients 'actively' registered with a linked GP practice were included, we excluded patients who did not have at least one GP

encounter in the year preceding sarcoma diagnosis. This criteria was selected as 90% of sarcoma patients will first present in primary care [8 16] and the vast majority of these presentations will be within the 12 months pre-diagnosis [8], so this approach should capture almost all sarcoma patients active in a linked practice. ACCORD data were extracted on referral route (GP or other), symptoms at the first hospital consultation (mass, pain, systemic symptoms), tumour characteristics (location, behaviour, grade, stage, depth, size), and occurrence of non-diagnostic biopsies pre-diagnosis.

Defining the exposures

Primary care data were extracted on patient demographics (age at diagnosis and sex) and instances of four types of GP clinical events: GP visits, radiological imaging requests, GP issued prescriptions (for any medication) and blood test requests. Imaging requests were included both as a composite measure, encompassing all x-ray, ultrasound (US), CT, MRI, and bone density scan (DXA) tests, and considering each modality individually. If patients were 'actively' registered (at least one encounter a year) at a linked GP practice for 2 or more years pre-diagnosis, clinical activity data were extracted from the 24 months pre-diagnosis. If patients were only 'actively' registered in the year pre-diagnosis, data were extracted from the 12 months pre-diagnosis.

Statistical analysis

Sensitivity analyses were conducted to compare patient and tumour characteristics between sarcoma patients in the final study cohort with all sarcoma patients in the ACCORD sarcoma registry and to compare sarcoma patients with and without linkage to a primary care dataset to ensure they were comparable. In the final study cohort, chi-squared analyses were then used to compare baseline and tumour characteristics of patients with STS to BS, and the proportion of patients receiving each type of GP event in the 6 and 12 months preceding sarcoma diagnosis. For each type of GP clinical activity, the proportion of STS and BS patients having the event in the 6 and 12 month periods pre-diagnosis was initially compared using a binary (any/none) classification, followed by comparison of the total number and average number of events (mean (standard deviation and range) and median (interquartile range)). GP imaging requests were initially analysed using the

composite measure, before repeating the analyses for each of the five imaging modalities separately.

Poisson regression models were used to examine trends in primary healthcare use and different types of clinical activity over time. For the four types of clinical events, monthly incidence rates (IR) were estimated and plotted for each of the 24 months before sarcoma diagnosis. Monthly rate ratios were then calculated, comparing monthly IRs to the baseline rate of each clinical activity in the study population at 24 months before diagnosis. Using previously described methods[26 27], the inflection point where the rate of each type of clinical activity first starts to increase from the baseline rate (at 24 months before diagnosis) was statistically estimated. This method involved conducting a series of Poisson regression models using different sequential monthly inflection points and using the maximum likelihood method to select the model with the highest log likelihood and therefore best fit for the data. Bootstrapping was used to provide confidence intervals for each inflection point and the earliest inflection point selected to define the diagnostic window. To take into account any trends in activity before the inflection point, incidence rate ratios (IRRs) were calculated comparing the periods pre and post the inflection point / diagnostic window.

To assess the extent of different types of primary care clinical activity among sarcoma patients over time, the monthly (incident and cumulative) percentage of patients experiencing each type of event was calculated and plotted for the 24 months pre-diagnosis.

Results

Patient characteristics

From the 3,741 patients with sarcoma in the ACCORD dataset, 1,250 (33%) were linked to primary care datasets and 441 (12%) had at least one recorded encounter in a linked general practice in the year before diagnosis. Of the 809 linked patients who were excluded: 200 only had a linked GP encounter after their sarcoma diagnosis, 436 only had historic linked GP encounters (>1 year before diagnosis), 53 patients had both and 120 had no linked GP encounter recorded between 1980 and 2020. Sensitivity analyses showed that no

substantial differences were found between patient and tumour characteristics in linked sarcoma patients when compared to those in the broader ACCORD dataset and that sarcoma patients with and without linkage to primary care were comparable (Supplementary Tables S1 and S2). Of the 441 linked patients, 377 patients were diagnosed with STS and 64 with BS. The sex distribution was similar in both groups, with males comprising 51% of STS patients and 63% of BS patients (p=0.08). BS patients were on average younger, with a mean age of 42 years compared to 54 years for STS patients. A higher proportion of BS patients were diagnosed during AYA years (23% of BS patients aged 15-25 years compared to 6% of STS patients (p<0.001))(Table 1).

Table 1: Baseline characteristics of sarcoma patients with linked data

P value from chi squared test *time from being active in a linked GP practice to diagnosis (max 2 years)

Characteristics	Soft Tissue Sarcoma (n=377)	Bone Sarcoma (n=64)	P value
Male sex	192 (51%)	40 (63%)	0.08
Age at diagnosis (years)			<0.001
15–25	24 (6%)	15 (23%)	
26–35	46 (12%)	12 (19%)	
36–45	54 (14%)	9 (14%)	
46–55	74 (20%)	12 (19%)	
56–65	60 (16%)	11 (17%)	
66–75	70 (19%)	1 (2%)	
76 and over	49 (13%)	4 (6%)	
Mean (SD, range)	54 (18, 17-95)	42 (18, 15-83)	<0.001
Year of diagnosis			0.054
2002–2006	4 (1%)	2 (3%)	
2007–2011	70 (19%)	20 (31%)	
2012–2016	173 (46%)	25 (39%)	
2017–2021	130 (34%)	17 (27%)	
Lookback period (days)*			0.10
<12 months	109 (29%)	25 (39%)	
12-24 months	268 (71%)	39 (61%)	
Median (IQR)	731 (307-731)	693 (152-731)	
GP clinical activity in 6 months pre-diagnosis			
GP visit	316 (84%)	55 (86%)	0.67
Imaging request (any)	134 (36%)	21 (33%)	0.67
Ultrasound request	101 (27%)	10 (16%)	0.06
X-ray request	35 (9%)	12 (19%)	0.02
CT request	52 (14%)	14 (22%)	0.09
MRI request	26 (7%)	3 (5%)	0.51
Bone Density request	7 (2%)	5 (8%)	0.007
Prescription	163 (43%)	27 (42%)	0.88
Blood request	103 (27%)	14 (22%)	0.36

Tumour characteristics

High-grade disease was common in both groups, comprising 70% of BS and 47% of STS diagnoses, where reported. Late-stage diagnosis (stage 3 and 4) was more prevalent among

STS patients (59% of STS patients vs 22% of BS patients, p<0.001). A considerable proportion of tumours in both groups were ≥5cm in diameter at diagnosis (59% of STS and 54% of BS), with STSs being larger on average than BSs at diagnosis (mean 7.4cm, range 0.3-34.5 in STS vs mean 5.3cm, range 0.6-14.6 in BS, P=0.009) (Table 2).

Presentation and referral

STS patients were more likely than BS patients to present with a painless mass (68% vs 34%, p<0.001), while BS patients were more likely to present with pain (70% vs 36%, p<0.001). Approximately half of sarcoma patients in both groups were referred to a specialist by their GP (55% of STS and 48% of BS), with about 1 in 10 having a non-diagnostic biopsy (9% of STS and 5% of BS) (Table 2).

Table 2: Baseline characteristics of sarcoma patients at first consult in specialist centre.

P value from chi squared test; SD, standard deviation, *Centralised tumour location is defined as soft tissue sarcomas of intraabdominal, intrapelvic, intrathoracic, mediastinal, retroperitoneal or gynaecological origin

Characteristics	Soft Tissue Sarcoma (n=377)	Bone Sarcoma (n=64)	P value
Tumour location			
Extremities	249 (66%)	–	–
Centralised*	96 (25%)	–	–
Both	27 (7%)	–	–
Missing	5 (1%)	–	–
Tumour behaviour			0.26
Malignant	212 (56%)	43 (67%)	
Intermediate	75 (20%)	10 (16%)	
Benign	76 (20%)	9 (14%)	
Missing	14 (4%)	2 (3%)	
Pre-diagnosis biopsy			0.38
Yes	34 (9%)	3 (5%)	
No	235 (62%)	36 (56%)	
Missing	108 (29%)	25 (39%)	
Grade			0.008
High	104 (28%)	28 (44%)	
Low	116 (31%)	12 (19%)	
Missing	157 (42%)	24 (38%)	
Stage			<0.001
Early (Stage I or II)	85 (23%)	28 (44%)	
Late (Stage III or IV)	123 (33%)	8 (13%)	
Missing	169 (45%)	28 (44%)	
Depth			0.006
Deep	220 (58%)	64 (100%)	
Superficial	39 (10%)	0 (0%)	
Missing	118 (31%)	0 (0%)	
≥5cm diameter			0.54
Yes	198 (53%)	27 (42%)	
No	140 (37%)	23 (36%)	
Missing	39 (10%)	14 (22%)	
Largest dimension (cm)			
Mean (SD, range)	7.4 (6.1, 0.3 – 34.5)	5.3 (35.1, 0.6 – 14.6)	0.009

Symptom present at 1st specialist consult			
Mass			<0.001
Yes	258 (68%)	22 (34%)	
No	95 (25%)	34 (53%)	
Missing	24 (6%)	8 (13%)	
Pain			<0.001
Yes	137 (36%)	45 (70%)	
No	194 (51%)	10 (16%)	
Missing	46 (12%)	9 (14%)	
Systemic symptoms			0.55
Yes	51 (14%)	7 (11%)	
No	282 (75%)	50 (78%)	
Missing	44 (12%)	7 (11%)	
Referred by GP			0.64
Yes	206 (55%)	31 (48%)	
No	115 (31%)	20 (31%)	
Missing	56 (15%)	13 (20%)	

Primary care utilisation prior to diagnosis

Among the study cohort, who had ≥1 encounter in a linked GP practice in the year pre-diagnosis, approximately four in five sarcoma patients visited a GP in the six months leading up to diagnosis (84% of STS and 86% of BS) (Table 1). Repeat GP visits were common, with half of STS (50%) and BS (47%) patients visiting their GP ≥4 times in the six months pre-diagnosis (Table 3). Patients had a median of 3-4 GP visits in the six months pre-diagnosis (Table 3) and six GP visits in the year pre-diagnosis (Supplementary Table S3). Pre-diagnostic imaging was ordered by GPs for around a third of patients (33% of BS and 36% of STS) in the six months before diagnosis. STS patients were most likely to be referred for an USS (27% vs 16%, p=0.06), and BS patients were more likely to be referred for an x-ray (19% vs 9%, p=0.02) (Table 1 and Supplementary Table S4). In the six months pre-diagnosis, multiple imaging (≥2 scans) was requested in 21% of STS and 19% of BS patients (Table 3). Repeat USS were requested in 5% of BS and 7% of STS patients, and repeat CT and DXA scan were requested in 5 and 8% of BS patients, respectively (Table 3).

Trends in primary care utilisation

The monthly rate of GP imaging requests progressively increased from six months before sarcoma diagnosis (the statistically determined inflection point and estimated diagnostic window), peaking at eight times the baseline rate immediately before diagnosis (Figure 1, Supplementary Tables S5-S6). This increase was initially gradual, followed by a more rapid rise in the three months preceding cancer diagnosis. This trend was accompanied by much smaller increases in the rate of GP visits (from -3 months), prescriptions (-2 months) and

blood test requests (-4 months). Comparison of rates during the periods pre (-24 to -7 months) and post (-6 to 0 months) the diagnostic window inflection point found a 3-fold increase in imaging requests (IRR 2.87, 95%CI 2.39-3.46) with only marginal increases in all other events (IRRs <1.4) (Figure 1, Supplementary Tables S5 and S6).

On examining the proportion of sarcoma patients experiencing GP events over time, the monthly percentage of patients with a GP imaging request progressively increased from four months pre-diagnosis, from a baseline of 3% up to 18% in the month immediately preceding sarcoma diagnosis (Figure 2, Supplementary Table S7). The monthly proportion of patients with a GP visit increased steadily over the same period from a baseline of around 40% of patients to 55% in the month pre-diagnosis. The proportion of patients receiving prescriptions or blood test requests remained stable over the 24 months pre-diagnosis (Figure 2, Supplementary Table S7).

Table 3: Number of GP clinical events in the 6 months before sarcoma diagnosis among the study cohort of 441 sarcoma patients who had ≥1 linked GP encounter in the year pre-diagnosis.

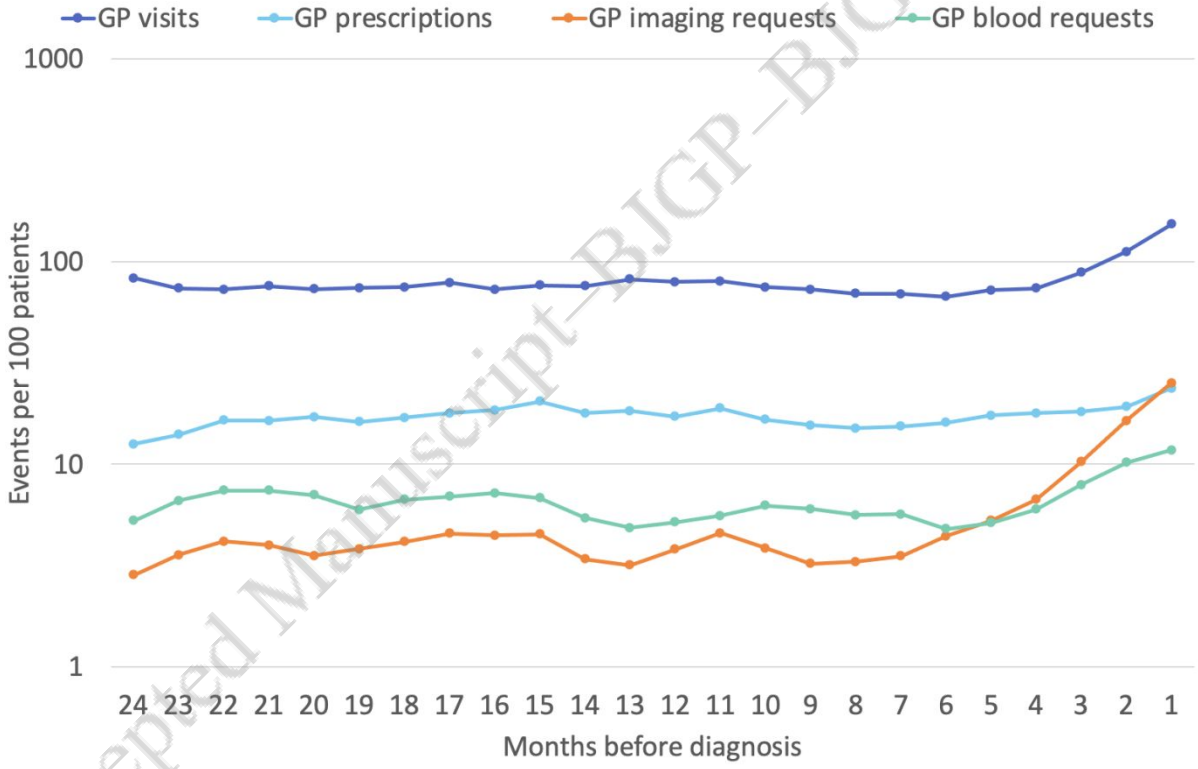
P value from chi squared test; SD, standard deviation, IQR, interquartile range, maximum one event counted per day

Type of clinical activity	Soft Tissue Sarcoma (n=377)	Bone Sarcoma (n=64)	P value
GP visits			0.76
0	61 (16%)	9 (14%)	
1–3	119 (32%)	25 (39%)	
4–6	82 (22%)	11 (17%)	
7–9	60 (16%)	11 (17%)	
≥10	55 (15%)	8 (13%)	
Mean (SD, range)	5 (5.7, 0-34)	5 (4.4, 0-19)	
Median (IQR)	4 (1-7)	3 (1-7)	
Imaging requests (any type)			0.045
0	243 (64%)	43 (67%)	
1	54 (14%)	9 (14%)	
2	42 (11%)	1 (2%)	
3	28 (7%)	6 (9%)	
≥4	10 (3%)	5 (8%)	
Mean (SD, range)	1 (1.1, 0-6)	1 (1.4, 0-5)	
Median (IQR)	0 (0-1)	0 (0-1)	
Prescriptions			0.32
0	214 (57%)	37 (58%)	
1	80 (21%)	11 (17%)	
2	29 (8%)	4 (6%)	
3	28 (7%)	3 (5%)	
≥4	26 (7%)	9 (14%)	
Mean (SD, range)	1 (1.6, 0-9)	1 (2.0, 0-9)	
Median (IQR)	0 (0-1)	0 (0-2)	
Blood requests			0.47
0	274 (73%)	50 (78%)	
1	64 (17%)	11 (17%)	
2	24 (6%)	1 (2%)	
3	9 (2%)	2 (3%)	
≥4	6 (2%)	0 (0%)	
Mean (SD, range)	0 (0.9, 0-5)	0 (0.7, 0-3)	
Median (IQR)	0 (0-1)	0 (0-0)	
Ultrasound requests			0.16

0	276 (73%)	54 (84%)	
1	74 (20%)	7 (11%)	
≥2	27 (7%)	3 (5%)	
X-ray requests			0.03
0	342 (91%)	52 (81%)	
1	32 (8%)	12 (19%)	
≥2	3 (1%)	0 (0%)	
CT scan requests			0.20
0	325 (86%)	50 (78%)	
1	44 (12%)	11 (17%)	
≥2	8 (2%)	3 (5%)	
MRI scan requests			0.73
0	351 (93%)	61 (95%)	
1	24 (6%)	3 (5%)	
≥2	2 (1%)	0 (0%)	
Number of bone density requests in 6m pre-diagnosis			0.007
0	370 (98%)	59 (92%)	
1	7 (2%)	5 (8%)	

Figure 1: Monthly rate and rate ratio of different types of GP clinical activity in the 24 months before sarcoma diagnosis.

Top panel show incident rates (3 month moving average, log scale) bottom panel shows rate ratios compared to baseline rate at 24 months pre-diagnosis



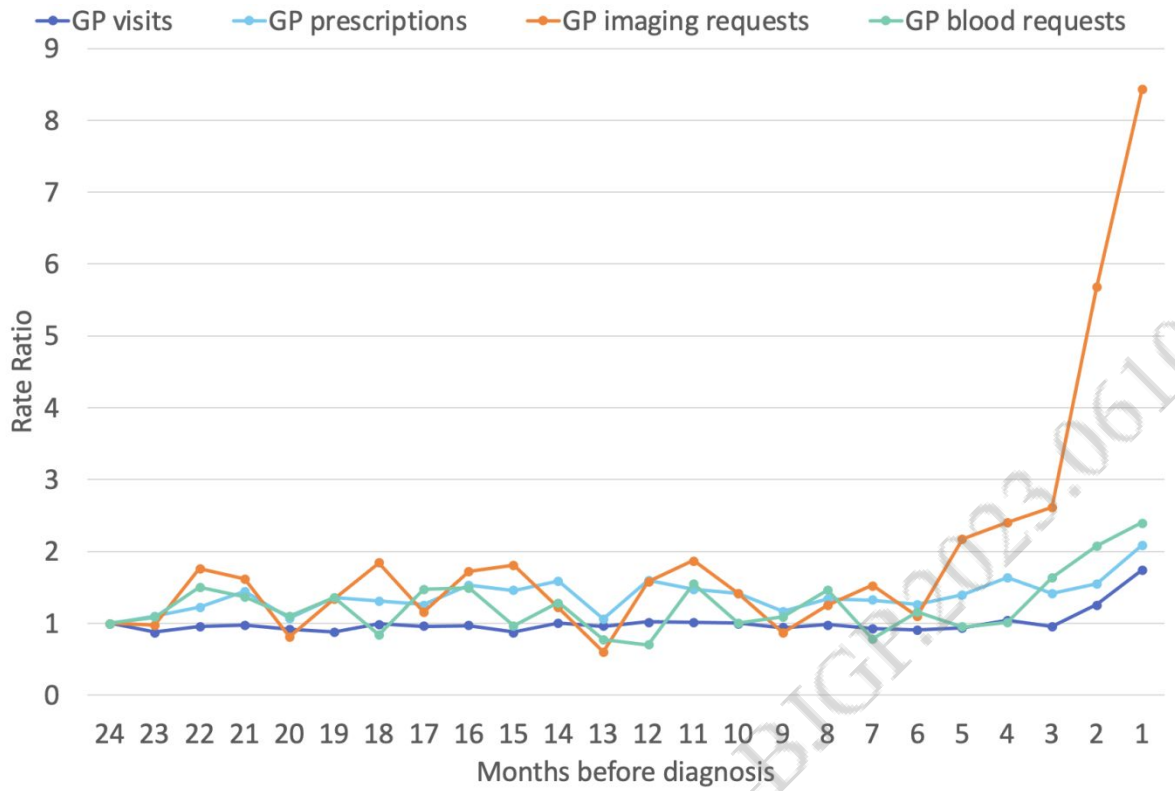
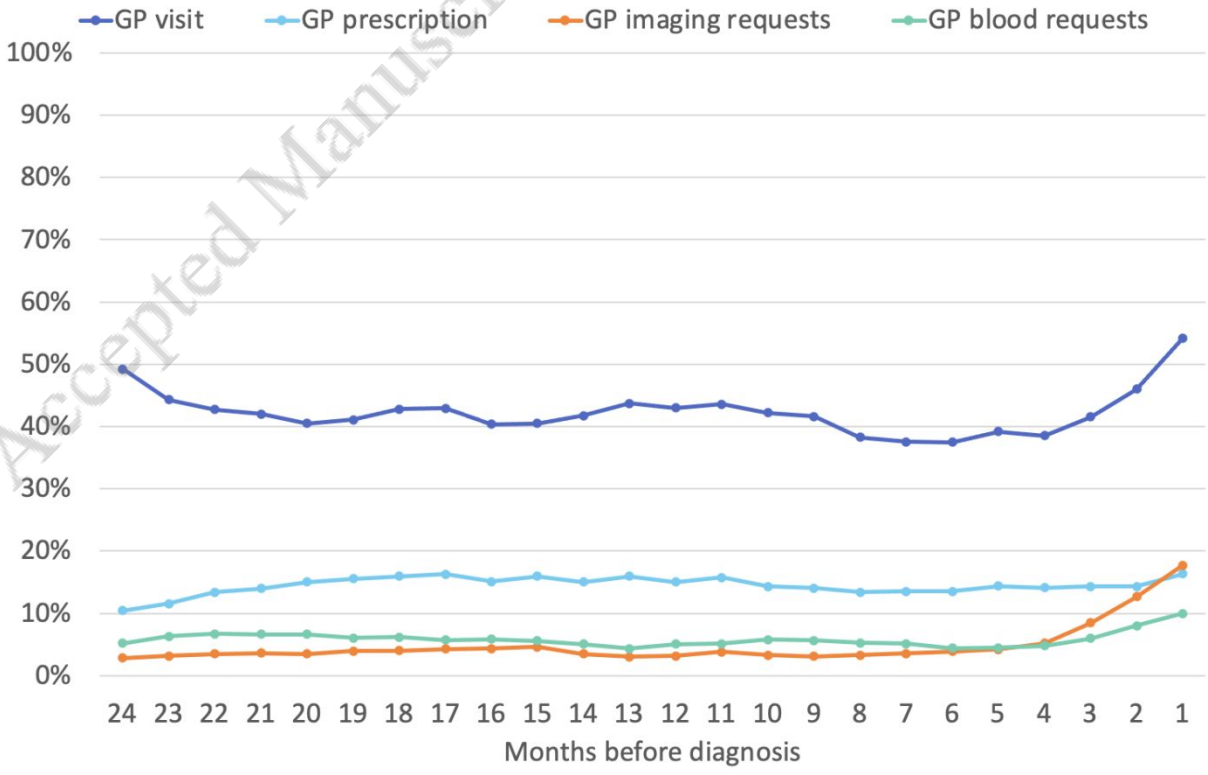
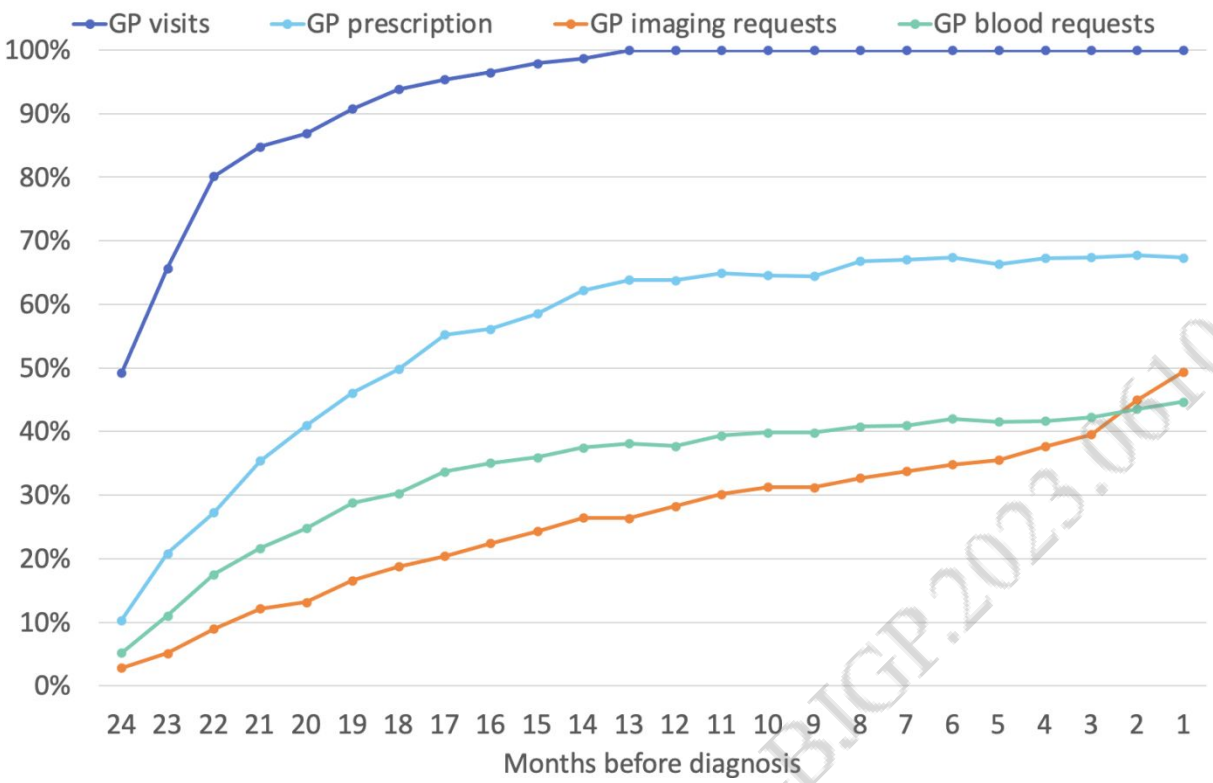


Figure 2: Monthly proportion of sarcoma patients receiving different types of GP clinical activity in the 24 months before diagnosis

Top panel: monthly incident percentage using 3 month moving average, bottom panel: cumulative percentage from 24 months pre-diagnosis





Discussion

Summary

To our knowledge, this is the first study to examine GP healthcare utilisation over time before a sarcoma diagnosis. Patients with as-yet-undetected sarcoma who visited a GP in the year pre-diagnosis experience increased clinical activity in primary care from 6 months before diagnosis, predominantly in the form of imaging requests. This indicates that many sarcoma patients present to their GP several months pre-diagnosis with symptoms prompting imaging investigation. During this 6-month period sarcoma patients on average visit their GP 3-4 times, a third are referred for imaging (predominantly USS and x-rays) and one in five have multiple scans requested. This period represents a 'diagnostic window' where potential opportunities exist for expediting sarcoma diagnosis in some patients, if supported by interventions to help identify these patients, optimise their investigation and overcome barriers to timely diagnosis.

Comparison with existing literature

European studies have reported average diagnostic intervals[28] (time from first clinical presentation to sarcoma diagnosis) ranging from 2-6 months[7-10 16]. These studies involved

<200 patients, used retrospectively collected survey data, and showed wide variation between countries. Our study estimates the diagnostic *window* length in 441 Australian sarcoma patients. Rather than a single estimate of average time-to-diagnosis, this measure collates data from multiple pre-diagnostic events in a population of sarcoma patients to identify when clinical activity first starts to increase[27 29-31]. This inflection point indicates the start of the 'diagnostic window', within which potential opportunities exist for expediting diagnosis in some patients, with longer diagnostic windows signaling that earlier action could potentially be taken. The diagnostic window therefore represents the maximum time that diagnosis could potentially be brought forward in some patients, if supported by diagnostic advances to help identify them. Consistent with previous diagnostic interval estimates, we found a diagnostic window of up to 6 months before sarcoma diagnosis where there are increased GP visits and imaging requests and potential opportunities for earlier diagnosis in some patients.

UK studies of GP consultations before sarcoma diagnosis found that 41%-50% of BS patients and 25-32% of STS patients had ≥3 GP consultations pre-referral and 15% and 10%, respectively, had ≥5 consultations[12 17]. In both studies, consultations could occur at any point from first relevant GP presentation. We are not aware of previous evidence examining the timing of GP consultations pre-diagnosis, or using Australian data. We show that around half of sarcoma patients have ≥4 GP visits in the 6 months pre-diagnosis, suggesting more potential opportunities to expedite diagnosis exist and in a larger proportion of patients than previously described. Furthermore, we determined that increases in GP visits and imaging requests were concentrated in the 3–6 months before sarcoma diagnosis.

Regarding pre-diagnostic imaging, a Swedish study found 64% of sarcoma patients had imaging requested at their first medical presentation (to primary care or emergency department)[32]. An Australian study of 21 clinicians and 22 sarcoma patients reported prolonged intervals in after tests referral, with some patients having several scans pre-diagnosis[5]. Our study builds on these findings by longitudinally examining GP requests for five imaging modalities, showing that GP imaging requests increase 6 months before sarcoma diagnosis, and in this period a third of sarcoma patients have imaging and many experience multiple/repeat scans. Unlike many other healthcare settings, there are not long waiting times for imaging or specialist care in the Australian system. Potential causes of

delay may therefore exist after patients undergo imaging, including due to false negative results from using modalities with poor diagnostic accuracy for sarcoma or from onward referrals to non-sarcoma specialists.

Strengths and limitations

Using linked primary care data is an important strength of this study as almost all sarcoma patients first present in this setting[8 16]. Using two GP datasets, with broad coverage of Victoria and a representative sample of the Australian population, enabled a sample size large enough to longitudinally examine several GP clinical events. Statistical estimation of inflection points increased reliability of findings[27]. Data on GP encounters, prescriptions and investigations are automatically recorded and time stamped, increasing accuracy and completeness. The ACCORD dataset captures the majority of sarcoma in Victoria and ensured access to accurate tumour-related data.

Some information was not available, including indications for investigations, imaging results and referral details. Future research into these factors and reasons for consultations could help understand causes of diagnostic delays. Some tumour characteristics were partially missing, but data on the primary outcomes (diagnosis date and tumour site) were complete. The small increases in GP events (apart from imaging) when comparing periods pre and post the estimated diagnostic window inflection point could reflect regression to the mean.

In Australia, patients are not restricted to visiting a single GP practice and can be simultaneously registered with multiple practices, even if they have not consulted there for several years. To ensure only data from patients 'actively' registered at a GP practice were included, we excluded any patients who had not attended a linked practice in the year pre-diagnosis. This could introduce selection bias, as these patients may have higher levels of primary healthcare utilisation than those who did not see a GP in this period. However, the effects of this are likely to be minimal as studies have shown that almost all sarcoma patients (87-90%) will present in primary care [8 16] in the 12 months before diagnosis (median time of first GP presentation = 65 days before diagnosis, range 42-133 days) [8]. Additionally, sensitivity analyses showed that our study cohort were similar to all sarcoma patients in the broader ACCORD dataset across a range of patient and tumour characteristics. The results

are therefore likely to be generalisable to the vast majority of sarcoma patients who will see a GP at least once in the year pre-diagnosis. If we included all sarcoma patients who had attended a linked GP practice, we would capture many 'inactive' patients who were receiving primary care elsewhere, which would underestimate primary care activity pre-diagnosis. Due to the structure of Australian primary care, patient activity occurring at GP practices outside our datasets will not be captured, however, this is likely to be minimal in our 'actively' registered sarcoma cohort as 90% of Australians visit a regular general practice[33].

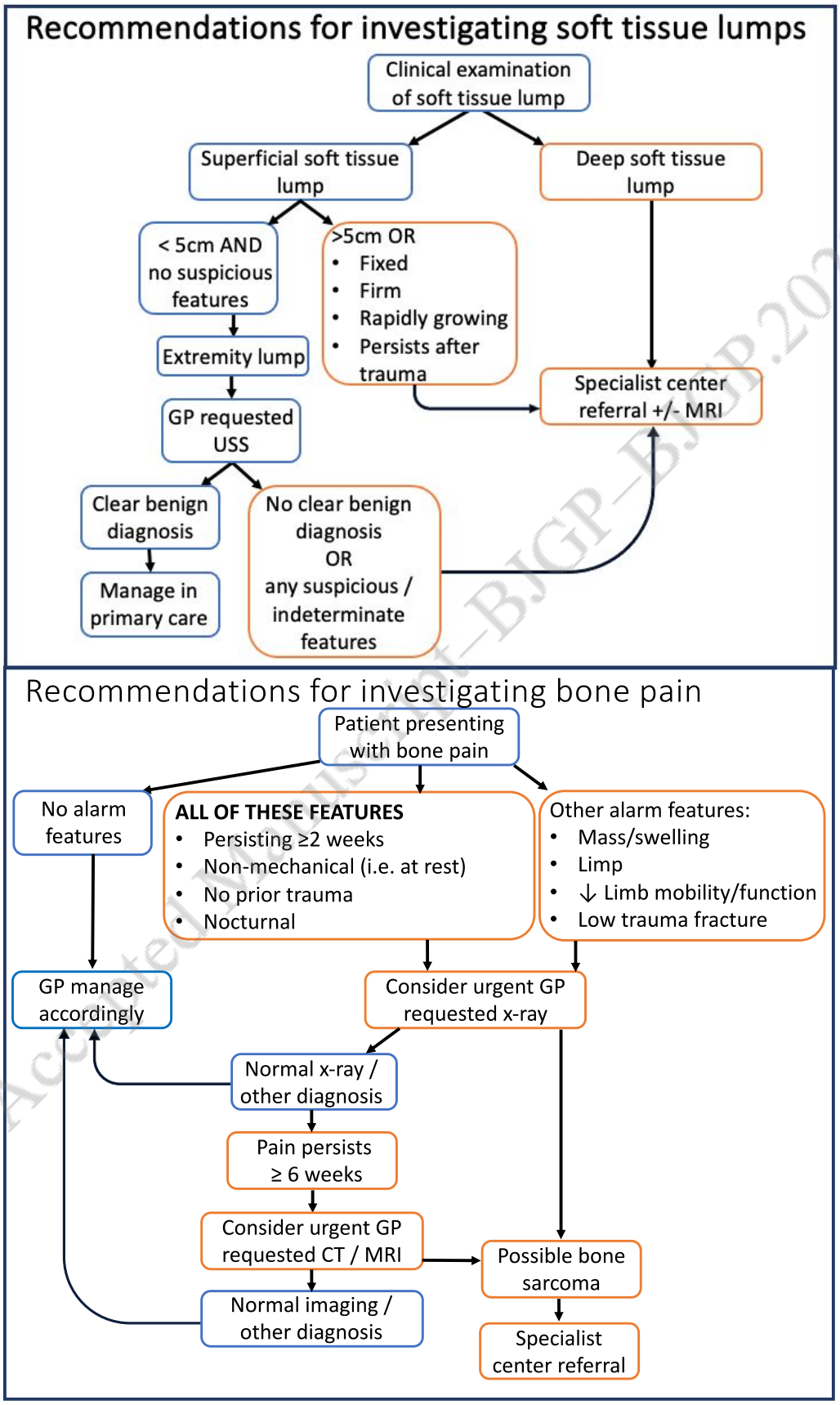
Implications

A window of opportunity exists where the diagnosis of sarcoma could potentially be accelerated in primary care by several months in some patients if supported by targeted interventions and diagnostic advancements. We identified the types of GP diagnostic activity that occur early in this window to inform development of future interventions, which could, in turn, improve the timeliness of diagnosis. During this window, many sarcoma patients report multiple GP visits and wide variability exists in clinical practice: one third have GP imaging, different imaging modalities are used, and many have multiple scans. Improving awareness, scope and consistency of guidelines to optimise investigation of bone pain and soft tissue lumps could improve timely diagnosis. Australia's Sarcoma Optimal Care Pathway (OCP)[34] recommends urgent x-ray in persistent, non-mechanical bone pain in the absence of prior trauma, lasting more than 6 weeks, however only 1 in 5 BS patients in this study had a GP x-ray request despite bone pain being the most common presenting feature. The OCP also recommends that all soft tissue lumps that are deep, growing, >5cm or not caused by trauma should be directly referred to a specialist for gold-standard MRI imaging. However, no guidance is given on the management of lumps outside these criteria. Other international guidelines (NICE and ESSR) recommend triage imaging with ultrasound to identify patients warranting specialist referral[35 36], with CT having a limited role, except for intra-thoracic or intra-abdominal lesions or where MRI is contraindicated[35 37]. Clear, high-quality reporting and avoiding downstream delays after abnormal imaging in BS and STS are also essential as GP imaging requests increased up to six months before sarcoma diagnosis. Only half of sarcoma patients were directly referred by their GP to specialised centres (recommended for optimal sarcoma outcomes[38 39]), revealing opportunities for strategic

interventions in patients with possible BS or STS to increase direct GP-to-specialist centre referrals and redirect referrals from other entry points. Based on these findings, we provide a summary guide to optimise investigation of bone pain and soft tissue lumps in primary care to support earlier diagnosis and improve patient outcomes (Figure 3).

Figure 3: Summary of recommendations for investigation of bone pain and soft tissue lumps in primary care.

Blue boxes represent primary care management; Orange boxes represent specialist center management; clear benign diagnosis refers to a confirmed reported diagnosis of a benign nature e.g. lipoma, with no additional suspicious or uncertain features.



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