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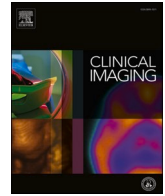
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Patients &amp; Practice, Policy &amp; Education



## Incidental imaging findings referred to a specialized sarcoma center: Frequency, determinants, and downstream healthcare costs

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### ABSTRACT

**Objective:** To determine the frequency and factors associated with incidental imaging findings (incidentalomas) that are referred to a specialized sarcoma center and that eventually turn out to be benign or of low-risk malignant potential, and to assess their downstream healthcare costs.

**Materials and methods:** This study included all consecutive new patients that were referred to a specialized sarcoma center within a 7-month period.

**Results:** Of 221 patients that were included, 28 had an incidentaloma. Of these 28 incidentalomas, 23 were benign ( $n = 11$ ) or of low-risk malignant potential ( $n = 12$ ), corresponding to a frequency of 10.4%. Utilization of conventional radiography (odds ratio [OR] = 6.538,  $P = 0.018$ ) and CT (OR = 8.167,  $P = 0.012$ ) was significantly more associated with the detection of benign or low-risk malignant potential incidentalomas than ultrasonography. The likelihood of detecting benign or low-risk malignant potential incidentalomas after MRI utilization was not significantly different from that after ultrasonography ( $P = 0.174$ ). All other variables (including patient age and gender, history of malignancy, specialty by whom the lesion was initially detected, and lesion location) were not significantly associated with these incidentalomas. The 23 cases with an incidentaloma that turned out to be benign or of low-risk malignant potential resulted in a total of €42,707 (\$49,552) downstream healthcare costs, with an average of €1857 (\$2155) per case.

**Conclusion:** Incidentalomas that are referred to a specialized sarcoma center and that eventually prove to be benign or of low-risk malignant potential are common, are more frequently detected on conventional radiographs and CT, and cause relevant subsequent healthcare costs.

### 1. Introduction

Sarcomas are a diverse group of cancers of mesenchymal origin.<sup>1</sup> The vast majority of sarcomas are soft tissue sarcomas, while malignant bone tumors comprise just over 10% of sarcomas.<sup>2</sup> Sarcomas are rare, with most occurring in fewer than 5 per 1,000,000.<sup>3</sup> Survival is poorer for those with more advanced grade, stage, and age at diagnosis.<sup>3</sup>

The diagnosis of sarcoma may be suspected based on clinical grounds and/or medical imaging findings. Once a sarcoma is suspected, patients are usually referred to a specialized sarcoma center, because early diagnosis and prompt (multimodality) treatment in a specialized sarcoma center are considered essential to improve patient outcome.<sup>4</sup> However, not all patients who are referred to a specialized sarcoma center are eventually diagnosed with this disease. Alternative diagnoses

include other malignancies than sarcoma, benign lesions, and biologically indeterminate lesions with low-risk malignant potential.

Over the past decades, the use of medical imaging, and in particular the use of CT and MRI in adults, has continued to rise.<sup>5</sup> Although medical imaging may improve patient outcomes by providing earlier and more accurate diagnoses, overutilization of imaging services may lead to the detection of incidentalomas. Incidentalomas are defined as incidental imaging findings serendipitously diagnosed in an asymptomatic patient or symptomatic patient undergoing imaging for an unrelated reason.<sup>6</sup> Some incidentalomas that eventually turn out to be benign or of low-risk malignant potential may initially be mistaken for sarcoma (even after review of imaging data by radiologists with expertise in sarcomas<sup>7</sup>), as a result of which these patients may be unnecessarily subjected to subsequent medical procedures such as additional

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imaging, biopsy, and/or surgery. This, in turn, may give patients psychological distress, lead to complications when invasive procedures are embarked on, and increases healthcare costs.

At present, there is a lack of data on which proportion of referrals to a specialized sarcoma center concerns incidentalomas that eventually prove to be benign or of low-risk malignant potential. It is also unknown which factors are associated with the referral of such cases, and how they impact subsequent healthcare expenses. This information would be useful to understand whether or not there is an overdiagnosis problem in this setting, and to identify potential solutions. Based on experience, it is expected that incidentalomas that eventually prove to be benign or of low-risk malignant potential comprise 1–5% of all cases in a specialized sarcoma center. It is also hypothesized that patient characteristics, requesting specialty, utilization of cross-sectional imaging modalities, and lesion location are associated with such incidentalomas, and that the subsequent healthcare costs are nonnegligible.

The purpose of this study was therefore to determine the frequency and factors associated with incidentalomas that are referred to a specialized sarcoma center and that eventually turn out to be benign or of low-risk malignant potential, and to assess their downstream healthcare costs.

## 2. Materials and methods

### 2.1. Study design

This retrospective study was approved by the institutional review board, and the requirement for informed consent was waived. The University Medical Center Groningen provides tertiary care to a region with more than 3 million inhabitants in the Netherlands. It has a specialized sarcoma center with a weekly multidisciplinary meeting that is attended by representatives from the departments of medical oncology, neurosurgery, oncologic surgery, orthopedics, pathology, plastic surgery, radiology, and radiation therapy. All new patients who were discussed in any of the weekly multidisciplinary sarcoma meetings between November 2018 and May 2019 were potentially eligible for inclusion in this study. All initial imaging was interpreted by a radiologist. Cases were excluded when they did not involve new patients, when no final diagnosis could be made (based on all available imaging, biopsies, and surgical procedures within a follow-up of at least 24 months), or when medical records were missing.

### 2.2. Data extraction

A researcher (M.Y.A.A.) reviewed the medical records of all included patients to retrieve the following variables: patient age and gender, history of malignancy, specialty by whom the lesion was initially detected, imaging modality on which the lesion was initially found, clinical signs or symptoms related to the lesion the patient was referred for to the sarcoma center (absence of clinical signs and symptoms signifies an incidentaloma), lesion location, final diagnosis (sarcoma, other malignancy than sarcoma, benign lesion, or lesion of low-risk malignant potential), and reference standard for the final diagnosis. All tumors were classified according to the WHO Classification of Tumors.<sup>8</sup> In all cases with an incidentaloma of benign nature or low-risk malignant potential the subsequent medical investigations after initial lesion detection (e.g. additional imaging, biopsy, or surgery) were also recorded. Minimum follow-up in all patients was 24 months.

### 2.3. Data analysis

Basic patient characteristics were descriptively analyzed. The frequency of incidentalomas of benign nature or low-risk malignant potential was calculated as a proportion of the total number of cases that were referred to the sarcoma center in the aforementioned inclusion period. Logistic regression analyses were performed to determine the

association between incidentalomas eventually turning out to be benign or of low-risk malignant potential (vs. all other tumors that were referred to the specialized sarcoma center), with the following variables: patient age (years) and gender (male or female), history of malignancy (yes or no), specialty by whom the lesion was initially detected (general practitioner, non-surgical specialty, or surgical specialty), imaging modality on which the lesion was initially detected (conventional radiography, ultrasonography, CT, MRI, or nuclear medicine imaging), and lesion location (head-neck, torso, or extremities). Variables or categories with less than 10 observations were excluded from logistic regression analysis. The category with the highest number of observations was used as reference for any nominal variable. For all incidentalomas that were finally diagnosed as benign or of low-risk malignant potential, the total costs of all subsequent medical procedures directed on the incidentaloma after its initial detection were determined, using the 2021 local hospital tariffs for diagnostic procedures<sup>9</sup> and the 2021 average contracted tariffs in the Netherlands for surgical procedures.<sup>10</sup> The average costs of subsequent medical procedures per incidentaloma that turned out to be benign or of low-risk malignant potential were also calculated. *P*-values <0.05 were considered statistically significant. All statistical analyses were executed using MedCalc version 19.1.6 software (MedCalc, Mariakerke, Belgium).

## 3. Results

### 3.1. Patient characteristics

A total of 305 consecutive patients were potentially eligible for inclusion. After applying the exclusion criteria, 221 individual patients remained (Fig. 1). These patients consisted of 124 males and 97 females with a median age of 55 years (range: 1–93 years). One hundred patients were eventually diagnosed with a sarcoma, 81 with a benign lesion, 28 with a lesion of low-risk malignant potential, and 11 with a malignancy other than sarcoma. Other patient characteristics are displayed in Table 1.

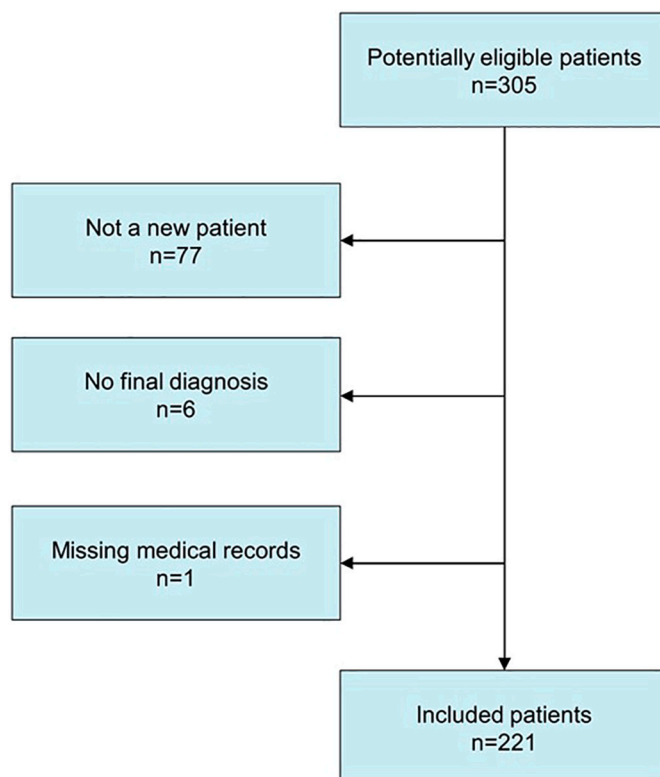


Fig. 1. Patient selection flowchart.

**Table 1**  
Patient characteristics.

Variable	No.	Percentage
Age (years)	55 <sup>a</sup>	1–93 <sup>b</sup>
Gender (male/female)		
-Male	124	56.1%
-Female	97	43.9%
History of malignancy		
-No	198	89.6%
-Yes	23	10.4%
Specialty by whom the lesion was initially found		
-Surgical specialty	168	76.0%
-Non-surgical specialty	39	17.6%
-General practitioner	14	6.3%
Imaging modality on which the lesion was initially visualized		
-Ultrasonography	65	29.4%
-Conventional radiography	64	29.0%
-MRI	54	24.4%
-CT	34	15.4%
-Nuclear medicine imaging	4	1.8%
Lesion location		
-Extremities	123	55.7%
-Torso	84	38.0%
-Head-neck	13	5.9%
-Combination <sup>c</sup>	1	0.5%
Incidentaloma		
-No	193	87.3%
-Yes	28	12.7%
Reference standard for final diagnosis (biopsy/surgery/follow-up)		
-Surgery	190	86.0%
-Biopsy	14	6.3%
-Clinical and imaging follow-up	12	5.4%
-Biopsy and clinical and imaging follow-up	5	2.3%
Final diagnosis		
-Sarcoma	100	45.2%
-Benign lesion	81	36.7%
-Biologically indeterminate lesion	28	12.7%
-Malignancy other than sarcoma	12	5.4%

## Notes:

<sup>a</sup> Median.<sup>b</sup> Range.<sup>c</sup> Combination of body regions.

### 3.2. Incidentalomas

Twenty-eight of 221 patients had an incidentaloma, which were all asymptomatic. Of these 28 incidentalomas, 23 were benign ( $n = 11$ ) or of low-risk malignant potential ( $n = 12$ ), corresponding to a frequency of 10.4%. Representative examples are shown in Figs. 2–4. Five incidentalomas were malignant. The final diagnoses of all incidentalomas are displayed in Table 2.

### 3.3. Variables associated with benign or low-risk malignant potential incidentalomas

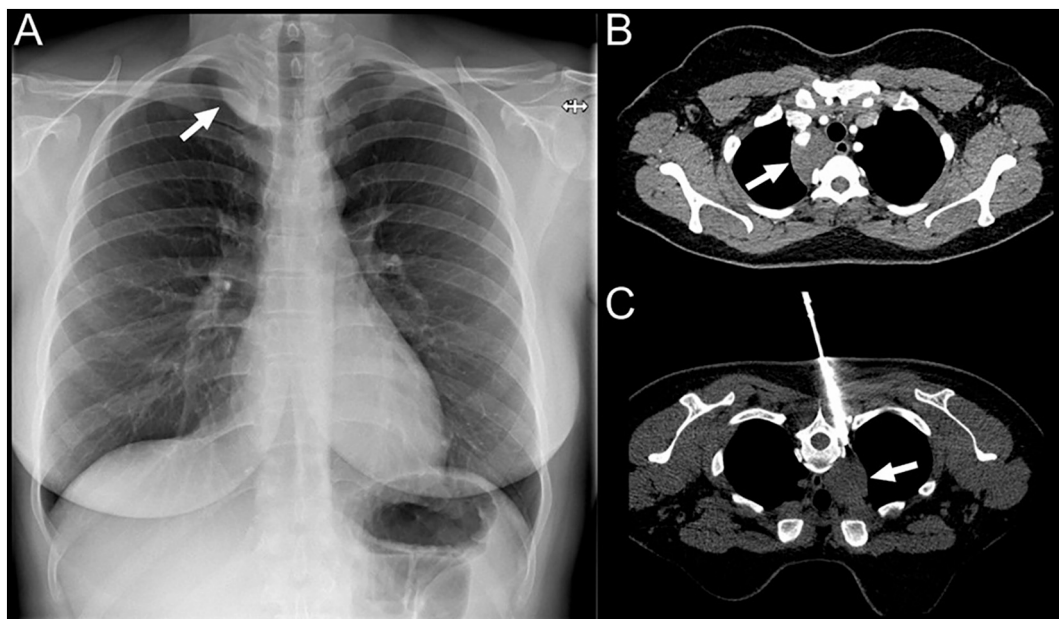
On univariate logistic regression analysis, the type of imaging modality on which the lesion was initially detected, was significantly associated with benign or low-risk malignant potential incidentalomas ( $P = 0.014$ ) (Table 3). Specifically, utilization of conventional radiography (odds ratio [OR] = 6.538,  $P = 0.018$ ) and CT (OR = 8.167,  $P = 0.012$ ) was significantly more associated with the detection of these incidentalomas than ultrasonography. The likelihood of detecting benign or low-risk malignant potential incidentalomas after MRI utilization was not significantly different from that after ultrasonography ( $P = 0.174$ ). All other variables (patient age and gender, history of malignancy, specialty by whom the lesion was initially detected, and lesion location) were not significantly associated with these incidentalomas (Table 3). Because only one variable was significant on univariate analysis, no multivariate logistic regression analysis was performed.

### 3.4. Downstream healthcare costs

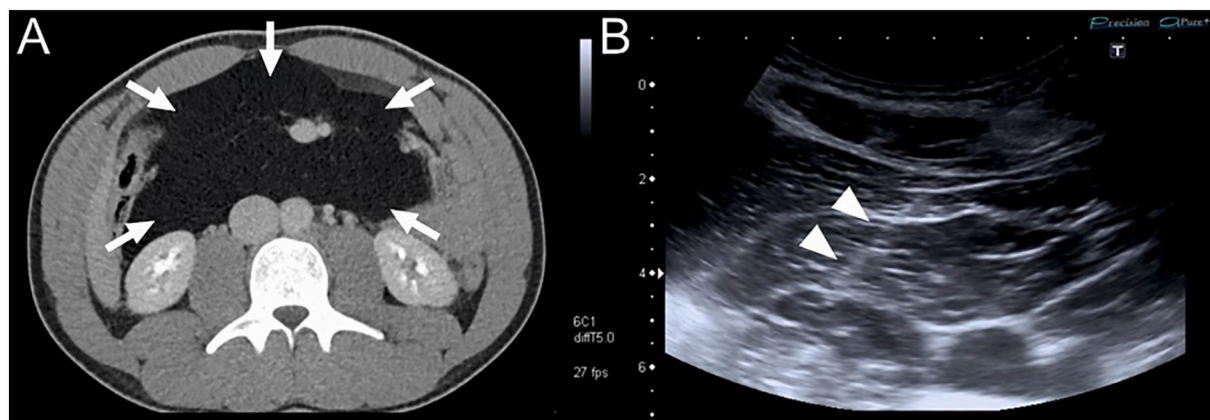
The 23 cases with an incidentaloma that turned out to be benign or of low-risk malignant potential underwent several medical procedures after initial lesion detection, with total costs of €42,707 (\$49,552) and average costs per case of €1857 (\$2155) (Table 4).

## 4. Discussion

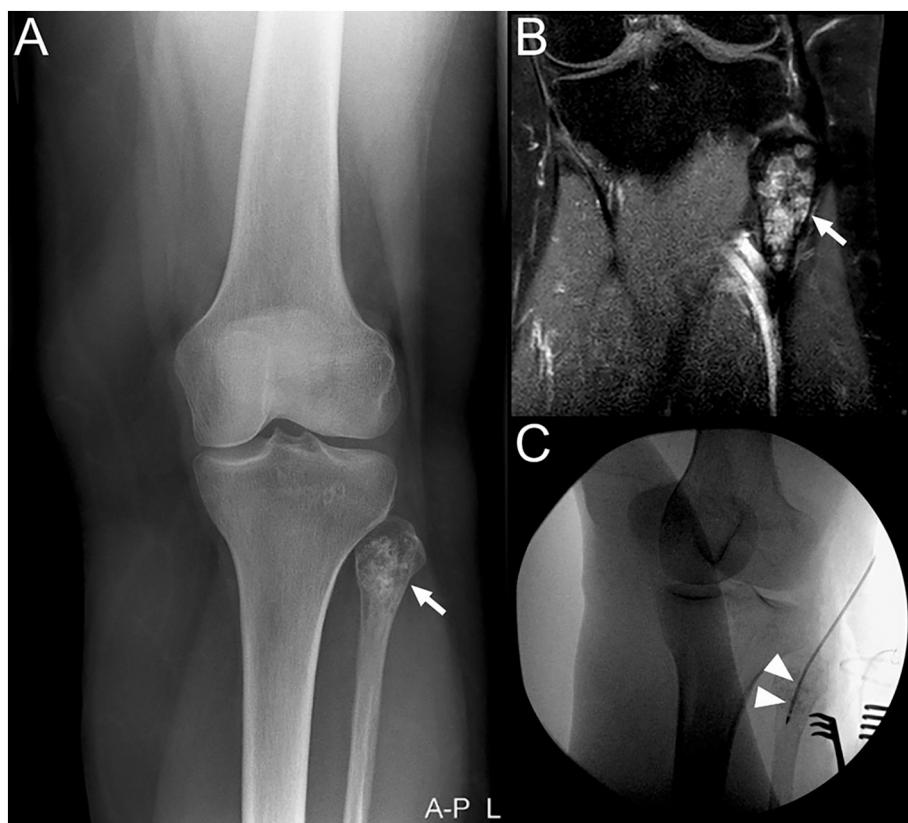
The results of this study show that incidentalomas that eventually prove to be benign or of low-risk malignant potential comprise a



**Fig. 2.** Incidentaloma that eventually turned out to be benign in a 32-year-old woman who was referred to a specialized sarcoma center. Chest radiography, which was performed because of fatigue, showed a right paratracheal lesion (A, arrow). The lesion is also shown on subsequent axial chest CT (B, arrow). CT-guided biopsy was performed (C) and pathological examination demonstrated a ganglioneuroma.



**Fig. 3.** Incidentaloma that eventually turned out to be benign in a 21-year-old man who was referred to a specialized sarcoma center. Abdominal CT, which was performed because of suspicion of appendicitis, showed a lipomatous mass in the mesentery (A, arrows), without any gross non-lipomatous components. The mass surrounds the superior mesenteric artery and vein. Subsequently, ultrasonography-guided biopsy was performed (B, with arrowheads indicating the biopsy needle traversing the mass). Pathologic examination showed mature fat tissue without any histological abnormalities (i.e. no signs of malignancy or atypia). The mass remained unchanged on 2-year follow-up imaging. Findings are compatible with a (mesenteric) lipoma.



**Fig. 4.** Incidentaloma with low-risk malignant potential in a 51-year-old woman who was referred to a specialized sarcoma center. Knee radiography, which was performed because of stiffness, showed a lesion with cartilaginous calcifications in the proximal fibula (A, arrow). Subsequent (coronal gadolinium chelate-enhanced fat-suppressed T1-weighted) MRI showed a relatively well-circumscribed, lobulated, contrast-enhancing lesion in the proximal fibula (B, arrow), without any signs of aggressive growth (i.e. no endosteal scalloping, cortical destruction, or extraosseous expansion). Findings are compatible with an atypical cartilaginous tumor. The lesion was biopsied (which confirmed a cartilaginous tumor) and underwent subsequent radiofrequency ablation (C, with arrowheads showing the radiofrequency electrode tip).

considerable proportion of cases (1 out of 10) that are referred to a specialized sarcoma center. This proportion is higher than we expected before starting this investigation. This finding is probably due to the relatively high degree of medical imaging utilization in the Western world,<sup>5</sup> including the Netherlands.<sup>11,12</sup>

Our results also indicate that the use of conventional radiography and the use of CT more frequently lead to the detection of benign or low-risk malignant potential incidentalomas that are referred to a specialized sarcoma center. The main reason why conventional radiography emerged as a culprit of overdiagnosis is the fact that 7 (30.4%) out of 23 of such incidentalomas in our series concerned atypical cartilaginous

tumors that were detected with conventional radiography. Although the exact frequency of atypical cartilaginous tumors is unknown, they are perhaps the most commonly incidentally detected type of primary bone tumor, with reported prevalence rates of around 2–3%.<sup>13–15</sup> They are most frequently located in the extremities,<sup>13</sup> where conventional radiography is often the first-line imaging modality. The reason why CT utilization was identified as another cause of overdiagnosis, is probably due to the fact that modern CT systems, which are able to visualize the entire human body in just a few seconds, are often used to image large anatomic volumes. Applied anatomic volumes in CT are frequently larger than those in other cross-sectional imaging modalities such as

**Table 2**  
Nature and final diagnosis of 28 incidentalomas.

Nature	Final diagnosis
Benign (n = 11)	Fibrous dysplasia (n = 2)
	Lipoma (n = 2)
	Cystic lesion in the upper abdomen (n = 1)
	Ganglioneuroma (n = 1)
	Hemangioma (n = 1)
	Insufficiency or stress fracture (n = 1)
	Pseudotumor with fat necrosis (n = 1)
	Schwannoma (n = 1)
	Tenosynovial giant cell tumor (n = 1)
	Atypical cartilaginous tumor (n = 9)
Low-risk malignant potential (n = 12)	Lipomatous tumor not otherwise specifiable (n = 1)
	Osteochondroma (n = 1)
	Osteofibrous dysplasia-like adamantinoma (n = 1)
	Well-differentiated liposarcoma (n = 2)
	Chronic myeloproliferative lesion (n = 1)
Malignant (n = 5)	High-grade pleomorphic sarcoma (n = 1)
	Thymoma (n = 1)

**Table 3**  
Univariate logistic regression analysis on the association of several variables with incidentalomas eventually turning out to be benign or of low-risk malignant potential (vs. all other tumors that were referred to the specialized sarcoma center).

Variable	Odds ratio	95% CI	p-value
Patient age	0.986 <sup>a</sup>	0.966–1.006	0.174
Patient gender	2.155	0.891–5.216	0.084
History of malignancy	1.335	0.364–4.892	0.671
Specialty by whom the lesion was initially detected			
-General practitioner	0.683 <sup>b</sup>	0.084–5.551	0.722
-Non-surgical specialty	1.306 <sup>b</sup>	0.451–3.787	0.623
Initial imaging modality on which the lesion was found <sup>c</sup>			
-Conventional radiography	6.538 <sup>d</sup>	1.387–30.812	0.018
-CT	8.167 <sup>d</sup>	1.592–41.886	0.012
-MRI	3.214 <sup>d</sup>	0.598–17.278	0.174
Lesion location <sup>e</sup>			
-Head-neck	NC	NC	0.994
-Torso	0.820 <sup>f</sup>	0.328–2.050	0.671

Abbreviations: CI: confidence interval; NC: not calculable due to a lack of incidentalomas in this category.

Notes:

<sup>a</sup> Per year of age increase.

<sup>b</sup> Surgical specialty as reference category.

<sup>c</sup> Nuclear medicine examinations were excluded because of only 4 observations in this category.

<sup>d</sup> Ultrasonography as reference category.

<sup>e</sup> One case with a combination of body regions was excluded.

<sup>f</sup> Extremities as reference category.

ultrasonography and MRI. The likelihood of incidental findings naturally increases along with the size of the anatomic volume that is visualized. Clinicians, radiologists, and patients should weigh the potential benefits of imaging against the risk of detecting an incidentaloma that ends up in a sarcoma workup, especially when requesting conventional radiography (particularly of the extremities) and CT examinations (particularly when large anatomic volumes are to be imaged).

Finally, our results demonstrate that incidentalomas that are referred to a specialized sarcoma center and that turn out to be benign or of low-risk malignant potential, pose a considerable financial burden to patients and the healthcare system. The average costs of additional medical procedures after initial lesion detection were €1857 (\$2155) per case. Note that the average healthcare insurance premium of a citizen in the the Netherlands is €1522 (\$1766) in the year 2022.<sup>16</sup> Because these

**Table 4**  
Medical procedures and costs after initial lesion detection, for incidentalomas that turned out to be benign, for incidentalomas that turned out to be of low-risk malignant potential, and for both groups combined (follow-up ranging between 24 and 31 months).

Medical procedure	Incidentalomas that proved to be benign (n = 11)	Incidentalomas that proved to be of low-risk malignant potential (n = 12)	Incidentalomas that proved to be benign or of low-risk malignant potential (n = 23)
Conventional radiography	4	5	9
Ultrasonography	1	0	1
CT	5	3	8
MRI	7	12	19
FDG-PET	1	1	2
Bone scintigraphy	2	3	5
Percutaneous image-guided biopsy	6	8	14
Surgery	4	4	8
Radiofrequency ablation	0	5	5
Total costs	€19,186 (\$22,261)	€23,521 (\$27,291)	€42,707 (\$49,552)
Costs per incidentaloma	€1744 (\$2023)	€1960 (\$2274)	€1857 (\$2155)

incidentalomas can be considered clinically irrelevant, we believe that there is no benefit in detecting them and that they only represent costs rather than benefits. Given the sharply increasing costs of healthcare in the Western world, including the Netherlands,<sup>17–19</sup> they should be a target for cost savings. Healthcare professionals should take responsibility to “image wisely”, reduce overutilization of imaging services, and avoid overdiagnosis. This may be accomplished by avoiding or minimizing the use of imaging when the probability of disease is very low (also known as the “rule out scan”) and applying probabilistic hypothetico-deductive reasoning before requesting imaging.<sup>20</sup> Furthermore, patients may have to be informed about the possibility and potential consequences of detecting an incidentaloma, and provide consent before imaging is done.<sup>21</sup> On another note, in their communication to referring clinicians, radiologists may assign less clinical relevance to some incidental findings whose nature is most likely indolent, such as atypical cartilaginous tumors. This may save unnecessary additional investigations and therapies. However, the difference between completely benign nature and malignant potential is often unclear, and downscaling incidental findings of ambiguous nature to “clinically irrelevant” may be complicated by legal and financial accountability issues that may only be solved by comprehensive healthcare reforms.

Some may argue that the detection of unrequested information on imaging may also be beneficial. In particular, it can be postulated that the incidental detection of malignancies at an earlier stage may potentially improve outcome. However, except for breast, colorectal, and lung cancer screening in specific populations in dedicated screening programs,<sup>22</sup> there is no evidence that imaging improves outcome and is cost-effective as a screening tool in other settings. This also applies to the 5 incidentalomas that were diagnosed as malignant in the present study (2 well-differentiated liposarcomas, 1 chronic myeloproliferative lesion, 1 high-grade pleomorphic sarcoma, and 1 thymoma). Whether or not the incidental discovery of malignant lesions justifies the costs in this setting, remains unclear. A longitudinal case-control study, with incidentally discovered malignancies as cases and symptomatically discovered malignancies as controls, may shed more light on this topic. On another note, it can also be postulated that incidentalomas that are benign or of low-risk malignant potential may become symptomatic on the longer term, and that prompt evaluation or treatment may be warranted despite the current lack of symptoms. However, this also remains speculative, and there are no scientific data that prove that preemptive

treatment of incidentalomas that are benign or of low-risk malignant potential is beneficial.

Five of 28 incidentalomas in the present study were malignant. It can be argued that this proportion of malignant cases was relatively low, and that more incidentalomas could perhaps have been worked-up without referral. However, currently we do not support such an approach. More research is necessary to determine what number of incidental malignancies per every incidentaloma evaluated would justify the costs. First and foremost, we advocate to reduce overutilization of imaging services to reduce the incidence of incidentalomas. However, once an incidentaloma is detected, and sarcoma is suspected or in the differential diagnosis, we believe referring these cases to a specialized sarcoma center and pursuing additional investigations when deemed necessary to be the best practice, regardless of whether the incidentaloma turns out to be sarcoma or not. Accurate diagnosis of sarcoma (in terms of both ruling in and ruling out disease) is crucial, and management of sarcoma patients in a specialized center is considered essential to improve patient outcome.<sup>4</sup>

A systematic review found a mean frequency of incidental findings in imaging tests of 23.6% (95% confidence interval [CI]: 15.8–31.3%).<sup>23</sup> This frequency was higher in studies involving CT technology with a mean percentage of 31.1% (95% CI 20.1–41.9%).<sup>22</sup> The finding that CT usage increases the detection of incidentalomas is in line with the results of the present study. The costs of subsequent medical procedures after the detection of an incidentaloma have been reported to vary widely.<sup>23,24</sup> This depends on the differential diagnosis of the incidentaloma and whether or not the referring clinician decides to take action to track down the nature of a lesion according to established guidelines, when the latter are available.<sup>23,24</sup> In the present study, all incidentalomas that were analyzed had been referred to our specialized sarcoma center to undergo additional investigations to track down their nature. Therefore, it is not possible to meaningfully compare the downstream costs that were found in the present study to those of previous studies that also included incidentalomas that were either not suspected to be sarcomatous or that were not further investigated by clinicians.<sup>23,24</sup> The present study is unique because it provides insight into how much a multidisciplinary sarcoma team is occupied with the management of incidentalomas. It would be of interest to investigate how much time and resources are spent on incidentalomas by other multidisciplinary cancer teams in a hospital. This information would be useful to obtain a more comprehensive picture of how much healthcare systems are spending on incidentalomas.

The present study had several limitations. First, the results of this study apply to a sarcoma center in the Netherlands. The results may be different in other countries where medical imaging utilization is different. Note that medical imaging utilization is affected by several factors, including payment mechanisms and financial incentives in the healthcare system, the practice behavior of referring physicians, defensive medicine, and patient expectations.<sup>25</sup> Second, only a relatively limited 7-month time period (November 2018 to May 2019) was analyzed. Therefore, it remains unknown whether there are any long-term temporal trends in referrals of incidentalomas to a specialized sarcoma center that are eventually classified as benign or of low-risk malignant potential. With increasing use of cross-sectional imaging and CT in particular,<sup>5</sup> it is expected that the number of such incidentalomas that are referred to specialized sarcoma centers will only increase. This should be the topic of future studies. Third, whether or not there was a justified clinical indication to perform the initial imaging that led to the discovery of the incidentalomas in this study, remains unclear. However, this is a complex issue, as for the great majority of clinical imaging applications, evidence on whether or not they improve patient outcome and are cost-effective, is lacking.<sup>26</sup> Answering these questions require considerable future research efforts. Fourth, only the costs of subsequent medical procedures after initial detection were calculated for each incidentaloma that turned out to be benign or of low-risk malignant potential. However, other costs, such as those related to

psychological distress of patients and absence from work were not taken into account. Therefore, the overall costs per incidentaloma are probably higher.

In conclusion, incidentalomas that are referred to a specialized sarcoma center and that eventually prove to be benign or of low-risk malignant potential are common, are more frequently detected on conventional radiographs and CT, and cause relevant subsequent healthcare costs.

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## Declaration of competing interest

None (all authors).

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