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Post-treatment follow-up in common solid malignancies: expert panel recommendations

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Post-treatment follow-up is an essential component of comprehensive cancer care. Determining optimal follow-up schedules is crucial on clinical, organisational and economic grounds. Owing to the scarcity of prospective clinical follow-up trials, most recommendations are based on retrospective studies and expert opinions. In 2014, the first post-treatment follow-up recommendations in the most common solid malignancies was published by Polish oncology and family medicine experts. In this article, we present an update of this document that takes into account the current literature and the quality of the available scientific evidence.

Key words: cancer, post-treatment follow-up, recommendations

Introduction

Post-treatment follow-up is an essential part of comprehensive care for cancer patients. Its aim is to detect cancer relapse or secondary tumours, to allow early initiation of potentially effective retreatment, detection and treatment of late complications, psychological and social support, and assessment of late treatment outcomes. Other essential aspects of follow-up include physical and mental rehabilitation and reestablishment of the patient's social and familial roles. The most important objective of follow-up after palliative treatment is to provide

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the best possible quality of life. Follow-up after cancer therapy should be a reasonable compromise between the expectations of patients and their families and the actual value and cost of particular procedures.

Increasing public expectations, frequently combined with entitled attitudes, drive doctors to perform many unnecessary diagnostic procedures. Besides, the lack of unequivocal and widely accepted follow-up standards creates a gap in medical knowledge and exposes physicians to accusations of failure to maintain due diligence. In Poland, there have been no general or uniformly structured recommendations for cancer follow-up. This made it difficult for clinicians to conduct their daily practice, caused much arbitrariness and prohibited the development of clear financing rules.

Defining optimal follow-up schedules is not easy, as high-level evidence from prospective clinical trials for most malignancies is lacking. Even if such trials have been performed, the rapid progress of diagnostics and treatment does not allow the simple implementation of their results in contemporary clinical practice.

In 2014, the Polish Cancer Society developed national guidelines on post-treatment follow-up in the most common malignancies [1]. After eight years, it is necessary to update this document. The current version additionally describes the quality of the scientific evidence and the strength of particular recommendations (tab. I–II) [2].

Table I. Quality of scientific evidences

Grade	Evidence quality
I	evidence from at least one large controlled randomised clinical trial (RCT) of high methodological quality (low risk of bias) or a meta-analysis of well-designed RCTs without significant heterogeneity
II	small RCTs or large RCTs at risk of bias (lower methodological quality), meta-analyses of such studies or RCTs with significant heterogeneity
III	prospective cohort studies
IV	retrospective cohort studies or case-control studies
V	studies without a control group, case reports or expert opinions

Table II. Strength of recommendations

Grade	Recommendation strength
1	recommendation based on high-quality evidence about which the expert team has reached unanimity or a high level of agreement
2A	recommendation based on lower-quality evidence about which the expert team has reached unanimity or a high level of agreement
2B	recommendation based on lower-quality evidence about which the expert team has reached a moderate level of agreement
3	recommendation based on any evidence about which the expert team has not reached agreement

Head and neck cancer

The risks of failure to cure or recurrence in early-stage and advanced head and neck cancer (HNC) are 20%–30% and 60%–70%, respectively [3]. Additionally, patients with HNC carry an increased risk (3%–5% per year) of developing a second independent cancer of the chest or upper gastrointestinal tract [4].

The leading cause of HNC is active exposure to tobacco smoke. The continuation of smoking after a cancer diagnosis significantly worsens treatment outcomes and increases the risk of secondary tobacco-dependent malignancies [5]. Hence, smoking addiction should be recorded at each follow-up visit, and continuing smokers, irrespective of the malignancy, should be provided with evidence-based cessation support [6].

After treatment, patients require close observation because early detection of relapse or progression increases the chance of effective salvage treatment. In patients with locoregional recurrence or radiotherapy-induced second head and neck cancer, the treatment of choice is salvage surgery or, less frequently, reirradiation. However, curative retreatment is possible in only about 20% of patients; others are managed with systemic palliative or symptomatic therapies [7].

An important aspect of follow-up after curative HNC treatment is the monitoring of late sequelae of disease and its treatment, potentially causing functional disorders and quality of life deterioration [8]. The first visit 2–3 months after the completion of treatment is crucial to assess its results. The frequency of subsequent follow-up visits and the type of diagnostics should consider the clinical situation (tab. III). Traditionally, a five-year active post-treatment follow-up has been practiced. However, although the risk of primary cancer progression after three years is relatively low, a proportion of HNC patients will develop a second primary cancer of the respiratory or upper gastrointestinal tract. Hence, the follow-up should extend beyond five years [9]. It should include detailed physical examination, upper respiratory tract endoscopy and evaluation of the patient's general condition. Assessment of treatment outcome usually necessitates computed tomography (CT) or, preferably, magnetic resonance imaging (MRI) of the head and neck 2–3 months after treatment completion. Thereafter, these studies are reasonable only for patients with symptoms or abnormalities in physical examinations.

Follow-up visits usually include an annual chest X-ray (CXR) or chest CT, although their usefulness in asymptomatic patients has not been proven [10]. Continued tobacco smokers, apart from cessation support, should undergo annual chest CT. Other imaging is reasonable only in case of symptoms or suspicion of cancer recurrence. In metastatic disease, curative treatment is rarely possible, and most patients are managed with palliative or symptomatic treatment. Detection of a second independent malignancy, e.g. lung cancer, requires the implementation of a new therapy, taking into consideration the tumour stage and general condition of the patient. There is no clinical use of tumour markers in HNC [11]. It is also unreasonable to regularly perform labora-

Table III. Recommended follow-up schedules for head and neck cancers (IV, 2B/3)

Treatment intent	Examinations	Frequency	Comments
curative	interview and physical examination with upper respiratory tract endoscopy	every 1–2 months for the first 6 months, every 2–3 months for the next 6 months, every 4 months in the 2nd year, every 6 months in years 3–5, then annually	necessary histopathological verification of all lesions suspected of tumour recurrence or progression TSH[a] every 6–12 months in patients irradiated in the thyroid area
	head and neck CT or MRI	2–3 months after treatment completion, then only in patients with symptoms or physical signs	cessation support and chest CT annually in smoking patients
	CXR	annually	
	neck USG with fine needle biopsy of suspicious nodes	in patients with signs of lymph node recurrence	
palliative treatment	interview and physical exam	1–2 months after treatment completion, then depending on the occurrence and severity of symptoms	observation and treatment by a palliative care team
	laboratory tests and imaging	as per individual indications	mainly to explain the causes of persistent complaints (especially pain)

[a] – TSH (*thyroid-stimulating hormone*) – thyrotropic hormone; USG – ultrasonography; CXR – chest X-ray

tory tests, except for thyroid function assessments in patients who underwent neck irradiation [9].

The consequences of radical surgery, apart from permanent, sometimes unavoidable complications, usually appear already in the postoperative period and decrease over time. However, late radiotherapy sequelae are difficult to reverse and may increase. Assessment of radiation reactions should particularly include a consideration of the patient's treatment history and evaluation of the irradiated area. The cumulative doses of cytotoxic drugs used concomitantly with radiotherapy are generally low; therefore, the risk of late toxicity after chemotherapy is relatively small.

The most important aim of follow-up in patients receiving palliative treatment is to maintain the best possible quality of life. To this end, patients' complaints should be carefully assessed and, if necessary, promptly managed. Imaging is used in particular situations – for example, to determine the cause of symptoms.

In HNC, there have been no high-quality prospective cohort studies or randomised controlled trials; therefore, follow-up schedules generally reflect the practices of individual centres and expert opinions. Since this group of malignancies is heterogeneous, their management should consider the individual patient's situation [10, 11].

Central nervous system malignancies

The largest group of primary central nervous system (CNS) malignancies are gliomas. In the new WHO classification published in 2021, an important role in determining individual types and grades of gliomas was attributed to molecular aberrations, such as isocitrate dehydrogenase mutations (favourable prognosis), 1p/19q co-deletions (favourable prognosis) or CDKN2A/B deletions (unfavourable prognosis) [12]. Grade 2 gliomas include astrocytomas, oligodendrogliomas and mixed gliomas; the Grade 3 group consists of astrocytomas or anaplastic oligodendromas, and Grade 4 includes glioblastoma.

Follow-up schemes for patients with gliomas after curative treatment depend on the WHO grade (tab. IV). There is no evidence that regular follow-up improves prognosis in this group [13]. Generally accepted follow-up in malignant brain tumours includes regular visits in the treating centre, with assessment of neurological status and repeated MRI (V, 2B) [14]. Early diagnosis of limited recurrence or tumour progression allows in some patients secondary resection or radiotherapy. The frequency of imaging examinations depends on the histological tumour type, grade, molecular features and prognosis [15]. Notably, Grade 2 and 3 gliomas with favourable prognosis may undergo histological transformation and may progress even several years after primary treatment.

Early imaging of glioblastoma after neurosurgery and chemoradiotherapy may cause difficulties due to 'pseudo-progression', i.e., radiological post-treatment changes simulating cancer progression. Pseudo-progression usually occurs within a few months after treatment. Useful techniques for differentiating between pseudo-progression and genuine progression include diffusion and perfusion imaging, MRI spectroscopy [16] and positron emission tomography with computed tomography (PET-CT) using labelled tyrosine, choline, thymidine or methionine [16].

The second most common CNS malignancies are meningiomas. They are often detected incidentally and in asymptomatic patients, the preferred option is observation with periodical contrast-enhanced MRI. The post-treatment follow-up for a meningioma is long lasting and tailored to individual

Table IV. Recommended follow-up schedules for brain malignancies

Malignancy	Examinations	Frequency	Comments
grade 2 and 3 gliomas	interview and physical examination	every 3–6 months for 5 years, then every 6–12 months	glucocorticoids should be discontinued in a dose-reduced manner as soon as possible after treatment
	laboratory tests	according to clinical indications (e.g. monitoring of chemotherapy toxicity or anti-epileptic drugs)	
		MRI every 3–6 months for 5 years, then every 6–12 months	
grade 4 gliomas	interview and physical examination	every 3–4 months for 2–3 years, then less frequently	
	laboratory tests	according to clinical indications (e.g. monitoring of chemotherapy toxicity, glucocorticosteroids or anti-epileptic drugs)	
		MRI every 2–6 weeks after completion of radiotherapy, then every 3–4 months for 2–3 years, and then less frequently	
meningiomas	interview and physical examination	at 6 and 12 months post-treatment, every 6–12 months for 5 years and then every 2–3 years	follow up intensity considering recurrence risk
	laboratory tests	as clinically indicated	
	imaging	MRI scheme as detailed above	

patient's situation. In patients after surgery, the primary goal is to detect early tumour recurrence or progression. Within five years, this occurs rarely in patients after Simpson 0 surgery (total tumour resection with a margin of 2–3 cm) and in up to 80%–100% of patients after the Simpson 5 surgery (tumour biopsy). Early detection of the recurrence or progression of an unresected or irradiated tumour in many patients allows for salvage treatment. After definitive radiotherapy, an important goal of follow-up is to detect new neurological symptoms, which can be either treatment complications or tumour relapses. The mainstay of follow-up is contrast-enhanced MRI performed 3–6 months after treatment completion, every 6–12 months for five years and then every 2–3 years (V, 2B). However, there is no evidence that follow-up imaging alters therapeutic decisions in asymptomatic patients [17]. The intensity of follow-up should be adjusted to the risk of progression, age and comorbidities [18]. Because meningioma recurrences may occur even beyond ten years, the duration of observation is difficult to determine.

Similar recommendations apply to patients with less common and benign CNS malignancies. Therefore, post-treatment follow-up for CNS malignancies should be conducted in the treating centre that has access to the documentation, including the radiotherapy plan. The frequency of follow-up visits should consider the patient's situation, initial treatment outcome, tumour location and histology.

Thoracic malignancies

Follow-up in patients with primary thoracic malignancies (lung cancer, carcinoids, pleural mesothelioma and thymic malignancies) aims to detect recurrence and manage treatment-related complications [19]. Its most important aspect is tobacco prevention and the provision of cessation support [5, 20]. Follow-up in lung cancer patients should also include a search for secondary smoking-related tumours [20].

Due to the scarcity of controlled clinical trials, recommendations for primary thoracic malignancies are based on relatively weak scientific evidence. Follow-up schedules depend on the aim of primary treatment. In patients treated with curative intent, observation should be based on structured schedules, whereas in patients treated palliatively, the type and frequency of follow-up examinations depend on the individual clinical situation; in both cases, there is no reason to actively search for asymptomatic extrathoracic disease [19, 21].

Non-small cell lung cancer

Most non-small cell lung cancer (NSCLC) recurrences after complete pulmonary resection with or without adjuvant chemotherapy or radiotherapy occur within the first two years, which justifies more intensive follow-up during this period [20, 22] (tab. V). A standard component of follow-up after curative surgery is contrast-enhanced chest CT (II, A). CT allows detection of recurrence or secondary thoracic malignancy earlier than CRX, but its impact on survival is questionable [19, 21, 23–26]. Performing CT more often than every six months does not improve treatment outcomes [27]. After two years, depending on the recurrence risk, follow-up with low-dose, non-contrast-enhanced CT may be considered. There is no evidence based reason to perform PET-CT as a part of follow-up after curative treatment. Follow-up schedules after definitive chemoradiotherapy follow the same principles and are the extrapolation of schedules used in surgically treated patients (IV, 2A).

Table V. Recommended follow-up schedules for thoracic malignancies

Malignancy and treatment intent	Examinations	Frequency	Comments
NSCLC			
curative intent	interview and physical examination (considering symptoms suggesting cancer recurrence and treatment complications)	every 3 months for the first 2 years, then every 6 months or as clinically indicated	follow-up based on electronically reported symptoms may be more effective; no reason to search for asymptomatic extrathoracic disease; increased CT frequency in cases with residual disease
	contrast-enhanced chest CT	every 6 months for the first 2 years, then annually[a]	
palliative intent	based on the individual clinical situation		follow-up based on electronically reported symptoms may be more effective
SCLC			
stage I–III	as in NSCLC after curative treatment		
stage IV	as in advanced NSCLC		
carcinoids	as in lung cancer, depending on the treatment intent		
pleural mesothelioma	as in lung cancer, depending on treatment intent		
thymic malignancies			
stage I–II, curative treatment	interview and physical examination	every 3 months	
	chest CT	after 3 months, then annually	
stage III–IV	chest CT	every 6 months for 2 years, then annually	

NSCLC – non-small cell lung cancer; SCLC – small cell lung cancer; [a] – after two years, consider further follow-up with low-dose CT

The follow-up of NSCLC patients after palliative treatment depends on the individual clinical situation. The type and frequency of check-ups should mainly consider possible treatment options. Most important are interviews and physical examinations performed every three months and, in patients who respond to treatment, imaging (mainly CRX and, in doubtful situations, CT) (III, 2A). A randomised controlled trial showed that follow-up based on symptoms reported electronically by patients allows for earlier detection of tumour progression, provides more treatment possibilities and prolongs overall survival compared to the traditional system [28].

Longer survival of NSCLC patients associated with the widespread use of molecular targeted therapies and immunotherapy justifies a more active observation of selected patients. Monitoring of specific complications is also essential (e.g. early and late toxicity of immune checkpoint inhibitors).

Small cell lung cancer

Follow-up in stage I–III small cell lung cancer (SCLC) patients is similar to that recommended for NSCLC after curative treatment (tab. V). However, these recommendations are based only on the results of observational studies (III, B). The follow-up benefits may apply particularly to patients with a complete response after chemoradiotherapy, fit and without persistent complications, who might benefit from salvage treatments [29].

Follow-up in stage IV SCLC is similar to that in advanced NSCLC (III, B). In patients who did not receive elective brain irradiation as part of their primary treatment, brain MRI may be considered every three months in the first year and then every six months [30] (I, 2A).

Carcinoids

Follow-up of patients with respiratory carcinoids is similar to that in lung cancer (IV, 2A), depending on the histological type (typical or atypical carcinoids) and treatment intent (curative or palliative) [31].

Pleural mesothelioma

Depending on the treatment intent (curative or palliative), follow-up of patients with pleural mesothelioma includes an interview, physical examination and chest CT (IV, 2A) [32].

Thymic malignancies

Follow-up in stage I and II thymomas undergoing curative treatment includes an interview, physical examination (every three months) and chest CT (after three months and then annually). For more advanced thymomas, imaging should be performed every six months for two years and then annually (IV, B) [33].

Gastrointestinal malignancies

Follow-up after curative treatment of gastrointestinal (GI) malignancies generally lasts for five years (tab. VI). However, follow-up schedules are based on recommendations of scientific societies, expert opinions and clinical practice, and not on randomised clinical trials. Therefore, the quality of scientific evidence and the strength of the recommendations for all items listed in table VI should be set at V, 2A at best. Notably, no improved prognosis associated with regular follow-up has been demonstrated at any GI malignancy. This indicates the need for individualisation of follow-up procedures that accounts for the risk of recurrence, organisational conditions and patient expectations.

The management of patients with colorectal cancer (CRC) needs more extensive discussion, mainly due to results of randomised trials and the established role of surgery in metastatic disease. CRC is characterised by a high incidence of relapses potentially eligible for curative treatment (limited hepatic spread and local recurrences). This suggests that regular follow-up (in particular, imaging) of patients after curative treatment may translate into earlier detection of relapse, increasing the use of salvage surgery and improving prognosis.

The results of consecutive meta-analyses of randomised controlled trials published in the Cochrane database, which evaluated the value of intensive regular observation compared to so-called minimal observation in CRC patients after local curative treatment, led to surprising conclusions. Reviews published in 2002 and 2007 indicated that regular follow-up and additional check-ups were associated with lower overall mortality but did not significantly impact cancer-related mortality. This was attributed, among other causes, to the positive impact of intensive follow-up on more effective general health awareness, more frequent detection and treatment of late adverse symptoms and more effective detection and treatment of comorbidities, including secondary malignancies. The prolongation of overall survival has historically provided strong argument in favour of intensive surveillance in CRC patients. However, the heterogeneity of the studies included in the meta-analysis did not allow for defining the optimal pattern and duration of follow-up. However, since 2016, updates to this publication, including additional studies, have not confirmed the benefit of intensive follow-up. The latest Cochrane meta-analysis of 16 clinical trials, including 15 (with over 12,500 patients) with an analysis of overall survival, was published in 2019 [34]. As in previous publications, patients undergoing more intensive follow-up were subjected almost twice more often to salvage surgery and interval relapses (i.e. those diagnosed due to symptoms between scheduled follow-up visits) occurred almost twice less frequently. Nevertheless, the hazard ratio (HR) of death in patients undergoing more intensive follow-up was 0.91 (95% CI: 0.80–1.04) compared to minimal follow-up, which proves with the highest degree of scientific credibility that it does not significantly reduce overall mortality. As before, there was also no reduction in CRC-related mortality (HR 0.93, 95% CI: 0.81–1.07). None of the evaluated interventions: more frequent follow-up, carcinoembryonic antigen (CEA) monitoring and imaging had any effect on overall survival compared to their absence. Despite such strong evidence, the latest recommendations of scientific societies have not changed significantly.

Some light on the type of follow-up that has an impact on the frequency of surgery at relapse may be shed by the results of a prospective randomised study FACS (follow-up after colorectal surgery) published in 2014 [35]. This study included 1,202 CRC patients who had undergone curative treatment, and compared four follow-up strategies:

1. monitoring of serum CEA every three months for two years and then every six months for three years,
2. performing CT of the abdomen, pelvis and chest every six months for two years and then annually for three years,
3. CEA monitoring and CT imaging combined,
4. minimal observation, during which tests were performed only in the case of symptoms.

In groups 1 and 4, a single CT scan of the abdomen, pelvis and chest between 12th and 18th month of follow-up was possible at the physician's request as expressed at the study outset. In all patients, colonoscopy was performed at one year and repeated after five years; in patients from groups 2 and 3, colonoscopy was also performed after two years. After almost five years, the incidence of salvage surgery for relapses was higher in groups 1–3 compared to group 4 (6.7%, 8% and 6.7% *vs.* 2.3%, respectively); however, there was no significant difference in mortality. The results of this study contradict the recommendations for intensive surveillance and, in particular, for combining regular imaging with CEA monitoring. Most likely, a single CT scan between 12th and 18th month combined with CEA monitoring every three months for two years and then every six months for three years can well replace multiple CT imaging.

However, the results of the FACS study have been ignored, and the European Society for Medical Oncology, United States National Comprehensive Cancer Network and American Society of Clinical Oncology all recommend performing both regular CEA and imaging in CRC patients, which is reflected in the current document (tab. VI) [36–40].

Breast cancer

The main aims of post-treatment follow-up in breast cancer include early detection of local and regional recurrence and secondary cancers, managing late complications (e.g. related to

Table VI. Recommended follow-up schedules for gastrointestinal malignancies (V, 2A)

Cancer	Examinations	Frequency	Comments
oesophageal cancer	interview and physical examination	every 3–6 months for 2 years, then annually	patients eligible for curative treatment of local recurrence (e.g. after chemoradiotherapy) may benefit from regular endoscopy and imaging; in other patients, the follow-up should primarily be focused on treatment complications and nutritional status
	laboratory tests, imaging and endoscopy	as indicated clinically	
gastric cancer	interview and physical examination, blood counts	every 3–6 months for 2 years, then annually	assessment should evaluate treatment consequences, including nutritional status; vitamin B_{12} deficiencies should be supplemented
	other laboratory tests, imaging and endoscopy	as indicated clinically	
pancreatic cancer	interview and physical examination	every 3–6 months for 2 years, then annually	mainly for diagnosis and consequences of curative treatment (e.g. diabetes, pancreatic enzyme deficiency)
	laboratory tests and imaging	as indicated clinically	
liver cancer	interview and physical examination, liver function tests, CT or MRI of the abdomen	every 3–6 months for 2 years, then every 6–12 months	regular imaging is reasonable, as it frequently allows for salvage local treatment of recurrent disease. Hepatic function should be assessed in all patients. Patients who underwent liver transplant due to immunosuppressive therapy should be observed in transplantation centres
cholangiocarcinoma	interview and physical examination	every 3–6 months for 2 years, then every 6–12 months	ESMO[a] recommends regular laboratory tests and imaging
	laboratory tests (including CA 19.9 in patients with baseline elevated concentration) and imaging	as indicated clinically	
colon cancer	interview and physical examination	every 3–6 months for 3 years, then every 6–12 months for 2 years	possible modifications considering the risk of relapse. Controversies are presented in the text
	laboratory tests, imaging and colonoscopy	serum CEA[b] every 3–6 months for 3 years, then every 6–12 months for 2 years; CT of the abdomen, pelvis and chest every 6–12 months for 3 years, then annually for 2 years; colonoscopy[c] at 1 year, then every 3–5 years; other imaging (including PET-CT) – as clinically indicated	
rectal cancer	interview and physical examination	every 3–6 months for 3 years, then every 6–12 months for 2 years	possible modifications considering the risk of relapse. Controversies are presented in the text. The value of intensive follow-up is even more controversial than in colon cancer, as local recurrence is more frequently accompanied by clinical symptoms; in patients undergoing endoscopic surgery or managed without surgery after complete clinical remission following induction chemoradiotherapy, close endoscopic and imaging supervision is carried out in specialised centres
	laboratory tests, imaging and colonoscopy	serum CEA[b] every 3–6 months for 3 years, then every 6–12 months for 2 years; CT scan of the abdomen, pelvis (or MRI of the pelvis) and chest every 6–12 months for 3 years, then annually for 2 years; colonoscopy[c] at 3–5 years; other examinations (including PET-CT) – as clinically indicated	
anal cancer	interview and physical examination	first assessment 2 months after chemoradiotherapy completion, then every 3 months for 3 years and every 6 months for the next 2 years (always including *per rectum* examination); in women, annual cytological examination of cervical swab	finding a residual tumour on the first follow-up visit does not allow for a diagnosis of treatment failure
	laboratory tests and imaging	as indicated clinically	

[a] – European Society for Medical Oncology; [b] – *carcinoembryonic antigen;* [c] – if a full colonoscopy was not performed prior to curative treatment, it should be performed within a few months after the surgery to detect possible synchronous tumours

early menopause or osteoporosis), psychological and social counselling (including recommendations of physical activity and maintenance of proper body weight), and the assessment of late treatment results. The active search for asymptomatic distant metastases is less important because detecting them through more intensive follow-up does not significantly impact on overall survival and quality of life (I, 1) [41–44].

The effectiveness of follow-up performed by oncology specialists and trained primary care physicians is comparable (I, 1) [41, 42, 45, 46]. Breast cancer relapses may occur even after many years, but their risk gradually decreases, whereas other ageing-associated health problems arise. Hence, after the period of greatest risk recurrence, the preferred option is a more comprehensive follow-up provided by a primary care physician [41, 42, 45].

Follow-up schemes for stage I–III ductal in situ and invasive breast cancer are presented in Tab. VII [47]. Follow-up visits are recommended every 3–4 months for the first two years, every 6–8 months between third and fifth year and then annually (II, 2A). This scheme has been developed empirically, as no prospective studies have defined the optimal frequency of follow-up in the entire breast cancer population and particular subgroups [41–44, 46, 48].

The most important elements in relapse detection are interview and physical examination [47]. The follow-up should also include the assessment of the patient's mental condition and the presence of endocrine symptoms (hot flushes, dyspareunia, vaginal dryness or sexual disorders). The only recommended imaging is annual mammography (MMG) (II, 2A), which, regardless of the patient's age, has been demonstrated to reduce breast cancer mortality [41–44, 48, 49]. In patients treated with breast-conserving approaches, the first MMG should be performed six months after the completion of postoperative radiotherapy. There is no indication for routine breast ultrasonography (USG) or MRI; both are reasonable only if MMG imaging proves difficult [50, 51]. MMG is of limited value and is not recommended in patients who have undergone breast reconstruction using endoprostheses. In these patients, a physical examination supplemented by MRI is more accurate in diagnosing recurrence in the subcutaneous tissue or chest muscles [52].

Laboratory tests (blood count or biochemistry), serum tumour markers (CA15-3, CA27.29 or CEA) or imaging other than MMG (e.g. USG, CXR, CT, MRI, PET or bone scintigraphy), do not impact survival and are not recommended in asymptomatic patients (I, 2A) [41–44]. Patients with preserved uterus who receive adjuvant tamoxifen have an increased risk of endometrial cancer, which justifies an annual gynaecological examination (I, 1) [41–43, 53]. The frequency of these examinations can be reduced in patients after hysterectomy and ovariectomy. There is no evidence justifying routine intravaginal USG [41–43].

Postmenopausal patients (following natural and pharmacologically or surgically induced menopause), particularly those receiving aromatase inhibitors, have an increased risk of osteoporosis [41, 42, 54, 55]. A higher risk of skeletal events also applies to patients over 65 years, with osteoporosis or a family history of osteoporosis, with a body mass index <18 kg m^2, with a history of smoking, alcohol abuse or low physical activity [56]. Therefore, regular densitometric evaluation of bone density and supplementation with calcium and vitamin D3 (I, 1) are recommended in these groups.

Patients with HER2-positive breast cancer after adjuvant trastuzumab treatment who have no symptoms of drug-related cardiotoxicity do not necessitate regular echography or electrocardiography (I, 1) [41–43].

In patients with a family history of cancer, genetic testing for hereditary *BRCA* mutations should be considered if not performed earlier. Patients should be encouraged to exercise (for at least four hours a week), avoid alcohol and smoking (II, 2A), and follow an appropriate diet to maintain a body mass index in the range of 20–25 (II, 2A) [57, 58].

Pregnancy after breast cancer treatment does not increase the risk of recurrence. The safe interval between treatment completion and pregnancy has not been established. Pregnancy is contraindicated during adjuvant endocrine treatment. Pregnancy should be prevented using mechanical measures (condoms or intrauterine devices), as there are scarce data on the safety of hormonal contraception in breast cancer survivors. Hormonal replacement therapy (HRT) containing oestrogen and progesterone increases the risk of tumour recurrence and is contraindicated (I, 1) [59]. The safety of oestrogen-only HRT requires further research [60]. In patients with dyspareunia or other vaginal menopausal symptoms, oestrogens applied in the form of creams or vaginal tablets may be considered, but the impact of such treatment on the risk of recurrence is unclear [61–64].

There are no standard follow-up schedules for disseminated breast cancer. It is reasonable to adjust them to cancer location, symptoms and general patient condition.

Gynaecological malignancies

Data from prospective studies assessing the impact of follow-up on the survival of patients with gynaecological malignancies are scarce, and recommendations are based mainly on literature reviews and expert opinions [65–68]. In this group, a necessary component of post-treatment follow-up is gynaecological examination. In Poland, this examination is not routinely performed by general practitioners (GP), therefore, follow-up is carried out mainly by gynaecologists or oncologists. The follow-up of patients who underwent radiotherapy should involve a radiation oncologist, due to the possibility of late radiation reactions and increased risk of secondary malignancies. Follow-up of less common gynaecological ma-

Table VII. Follow-up of breast cancer patients after curative treatment, as recommended by the Polish Society of Clinical Oncology [47]

Examinations	Frequency	Quality, strength
self-examination	monthly	III, 1
physical examination	every 3–4 months for 2 years[a], every 6–8 months at years 3–5, then annually	III, 1
mammography[b]	annually; in patients who have undergone breast-conserving treatment, first examination after 6 months	I, 1
gynaecological examination	annually in women with preserved uteruses treated with tamoxifen[c]	III, 2B
laboratory tests and imaging	only as clinically indicated	V, 3
densitometry[d]	every 12–24 months	III, 2B
body mass	recommended maintenance of body mass index in the range of 20–25	III, 2A

[a] – in ductal *in situ* cancer, follow-up every 6 months for the first 2 years, then annually; [b] – MRI to be considered in carriers of *BRCA* mutations; [c] – no indications for intra-vaginal USG and endometrial biopsy in patients without genital symptoms; [d] – applies to patients at high risk of osteoporosis associated with aromatase inhibitor treatment or ovarian suppression

lignancies (uterine sarcomas, nonepithelial ovarian tumours, trophoblastic disease) should be carried out in specialised centres, and for patients managed with organ-sparing surgery, in the centre that provided the treatment.

The gynaecological examination should include a visual assessment of the perineum and vulva, a speculum assessment of the vagina and cervix, a two-handed vaginal examination, a rectal examination and an assessment of peripheral lymph nodes (tab. VIII). Transvaginal ultrasound, often performed in Poland, is not a part of international follow-up recommendations [65–67, 69–71], and the Society of Gynaecologic Oncologists even discourages its use [65].

Recurrences of gynaecological malignancies are most often detected by clinical symptoms or physical examinations. Therefore, it is essential to educate patients about recurrence symptoms and to explain the unreasonableness of imaging and laboratory tests in the absence of symptoms.

For low-risk gynaecological cancers, the British Gynaecological Cancer Society recommends on-telephone nurse follow-up supplemented by in-person patient visits in the event of symptoms (so-called 'patient-initiated follow-up') [72].

Endometrial cancer

Recurrences may affect 2%–15% of stage I endometrial cancer patients and up to 50% of patients with higher stages or unfavourable histologies [65]. Approximately 70%–100% of recurrences occur within the first three years [65, 71, 73]. In about half of patients, recurrence is accompanied by clinical symptoms, whereas in asymptomatic patients, physical examination detects 35%–70% of recurrences [65]. More than 80% of recurrences are accompanied by clinical symptoms or abnormalities in physical examination [65]. A prospective study comparing less and more intensive follow-up, even in patients with increased recurrence risk, did not demonstrate increased survival with more intensive follow-up, including additional examinations [74]. Cytology, CXR and CA125 monitoring, as well as intravaginal USG are not recommended in asymptomatic patients [65]. Imaging, such as CT, MRI or PET-CT, is used to verify possible recurrence and to select treatment in recurring patients [65, 71].

Cervical cancer

Approximately 75% of cervical cancer recurrences occur within the first 2–3 years after treatment completion [75]. Typical symptoms of recurrence include abdominal or pelvic pain, vaginal bleeding or pain, lymphatic leg oedema, urinary symptoms, cough and weight loss. Only 26%–36% of relapses are detected at follow-up visits. Physical examination, including vaginal and rectal examination, allows the detection of asymptomatic recurrences in 29%–75% of cases [76]. Cytology may mainly detect new vaginal lesions and should be performed annually (tab. VIII). Cytology abnormalities always necessitate colposcopy and biopsy, however, only 0%–17% of relapses are diagnosed with this method [75, 76]. Cytology is less useful after radiotherapy [75].

An annual CXR is not recommended [65, 67, 69, 75] and, like other imaging methods (CT, MR and PET-CT), is indicated only in patients with symptoms or physical signs [77]. The value of transvaginal USG is questionable. Measurement of squamous cell carcinoma antigens is not recommended. Since almost 40% of patients come for unplanned follow-up visits due to worrying symptoms, they should be educated about recurrence symptoms [75]. In patients who have undergone a trachelectomy (a uterus-saving procedure) follow-up should be performed at the traeting institution.

Vulvar cancer

Recurrence usually occurs within the first two years after treatment, more often in patients with lymph node metastases. Beyond 24 months after treatment completion, the risk of re-

Table VIII. Recommended follow-up schedules in cervical and endometrial cancer (IV, 2B), vulvar cancer (V, 2B), vaginal cancer (V, 2B) and ovarian, fallopian tube and primary peritoneal cancer (IV, 2B)

Cancer	Examinations[a]	Frequency
endometrial cancer		
FIGO[b] stage IA G1/G2 (endometrioid type)	interview and physical examination with gynaecological and *per rectum* examination; optionally, transvaginal USG	every 6 months in the first year, every 6–12 months in the 2nd year, then annually
FIGO[b] stages IA G3, IB–II (endometrioid type)	as above	every 3 months in the first year, every 6 months until 5 years, then annually
FIGO[b] stages III–IV and all stages for non-endometrial cancers	as above	every 3 months for 2 years, every 6 months until 5 years, then annually
cervical cancer		
low recurrence risk: IA, patients treated with surgery alone	interview and physical examination, gynaecological and *per rectum* examination	every 6 months for 2 years, annually until 5 years, then standard care, as in the general population
	cytology	annually
	imaging	only if clinically indicated
increased risk of recurrence: patients treated with postoperative adjuvant treatment or undergoing radio(chemo)therapy	interview and physical examination with gynaecological and *per rectum* examination	every 3 months for 2 years, annually until 5 years, then standard care, as in the general population
	imaging	only if clinically indicated
vaginal and vulvar cancer		
FIGO[b] stages I–IV	interview and physical examination, gynaecological and *per rectum* examination; in patients with vulvar cancer, particularly careful macroscopic assessment of the vulva, perineum and groin (optionally vulvoscopy)	every 3 months for 2 years, every 6 months until 5 years, then annually
ovarian, fallopian tube and primary peritoneal cancer		
FiGO[b] stage I–IV	interview and physical examination with gynaecological and *per rectum* examination, transvaginal USG	every 3 months for 2 years, every 3–6 months in the 3rd year, every 6 months until 5 years, and then annually
	CA125	upon discussion with the patient, together with examination
	imaging	only if clinically indicated
	recommended genetic consultation	at the time of initiation of follow-up or onset of a new malignancy in the family
borderline malignancy ovarian tumours		
FiGO[b] stage I–IV	as in ovarian cancer	every 6 months until 5 years, then annually
FIGO[b] stage I with reproductive organ preservation (after adnexectomy or ovariectomy)	consider also hysterectomy and contralateral adnexectomy	after the end of reproduction
ovarian germ-cell tumours		
I. dysgerminoma	as in ovarian cancer	every 3 months for 2 years, then annually
II. non-dysgerminoma		
1. yolk sac tumour	physical examination, AFP[c], HCG[d], LDH[e]	every 3 months for 2 years
2. immature/malignant teratoma	imaging	only if clinically indicated and with increased marker levels, more often for the first 2 years in cases with normal marker levels during initial treatment
3. germ-cell carcinoma		
4. non-gestational choriocarcinoma		
III. mixed germ-cell tumours		

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Table VIII cont. Recommended follow-up schedules in cervical and endometrial cancer (IV, 2B), vulvar cancer (V, 2B), vaginal cancer (V, 2B) and ovarian, fallopian tube and primary peritoneal cancer (IV, 2B)

Cancer	Examinations[a]	Frequency
sex cord tumours		
I. granular and stromal tumours	as in ovarian cancer	every 3 months for 2 years, then every 6 months
1. folliculoma	imaging	only if clinically indicated
2. thecoma-fibroma		
II. Sertoli cell and stromal tumours		
1. Sertoli cell tumour		
2. Leydig cell tumour		
III. sex cord and stromal tumours with annular tubules		

[a] – imaging at all stages only when clinically indicated; [b] – FIGO (International Federation of Gynaecology and Obstetrics); [c] – AFP (alpha-fetoprotein); [d] – HCG (human chorionic gonadotropin, chorionic gonadotrophin); [e] – LDH (lactate dehydrogenase)

currence is not related to lymph node involvement but persists for many years (recurrence after five years occurs in 35% of patients) [78]. Late recurrence occurs locally in more than 90% of patients [79]. Due to the role of human papillomavirus in vulvar cancer, the diagnostics should also include cervical, vaginal and anal cancers, which have the same aetiology. Additional imaging has no proven value and is not recommended (tab. VIII). The value of transvaginal USG is questionable. Relapse or suspected symptoms necessitate imaging and treatment similar to that in cervical cancer [65].

Vaginal cancer

Vaginal cancer is relatively rare, and data on post-treatment follow-up are scarce. There is no proven benefit of routine cytology or imaging (including transvaginal USG) in asymptomatic women (tab. VIII) [65].

Ovarian, fallopian tube and primary peritoneal cancer

Approximately 75% of patients with ovarian cancer relapse after primary treatment. In stages IIB-IV, the median time to recurrence is approximately 22 months [65]. In around 37% of patients, the first sign of recurrence is an elevation of CA125, which precedes the clinical symptoms by, on average, five months. In 15% of patients, the recurrence is first manifested by clinical symptoms, while in 4%, it is accompanied by an increased CA125 [65, 80]. A large, randomised study demonstrated that the initiation of chemotherapy based only on an increased CA125 does not prolong survival [81]. Therefore, it is advisable to discuss the need for regular marker measurement with the patient. Similarly, routine post-treatment serum HE4 measurement is not recommended [82].

Imaging examinations (CT, MRI or PET-CT) are used for the verification of suspected recurrence and for selection for salvage surgery [83]. There are no indications for routine use of these examinations in asymptomatic patients.

In borderline malignant ovarian tumours, the risk of relapse is about 8%, and about 30% of relapses are malignant [84]. Relapses often occur many years after primary treatment: 70% after five years and 30% after ten years [65]. The risk of relapse is greater after organ-sparing treatment [84, 85]. In this group, periodic transvaginal USG may allow for the early diagnosis of relapse in the preserved ovary and for salvage surgery [86, 87]. Imaging examinations (CT, MRI or PET-CT) are used only to verify suspected relapse.

Non-epithelial ovarian malignancies and sex cord tumours

A large proportion of patients with non-epithelial ovarian malignancies are managed with the preservation of the uterus and contralateral ovary. Recommendations in this group are based only on expert opinions [65, 68]. Long-term observation is necessary because half of the relapses occur more than five years after treatment completion, of which about half are in the pelvis. In patients with sex cord tumours, relapse may occur even 20 years after primary treatment [88]. Some patients may benefit from second-line chemotherapy [89].

Genitourinary malignancies

Prostate cancer

Routine follow-up after curative prostate cancer treatment should include an interview, prostate-specific antigen (PSA) measurement and, if necessary, rectal examination (tab. IX). The interview should consider psychological aspects and symptoms suggestive of relapse or late treatment complications. Follow-up visits should be performed every three months for the first year, every six months for another two years and then annually. There is no reason to perform imaging

Table IX. Recommended follow-up in patients with genitourinary malignancies after curative treatment

Cancer	Examinations	Frequency
prostate cancer		
	interview, PSA measurement[a]	3 months after treatment completion, every 6 months for 3 years, then annually
	per rectum examination[b]	as above
renal cancer		
low risk of recurrence[c]	USG and X-ray	at the 6th month and 2 years
	CT (chest, abdomen)	at the first and 3rd year, then every 2 years; the patient should be informed about the approximately 10% recurrence risk
medium and high risk of recurrence[c]	CT (chest, abdomen)	every 6 months in the first year, annually for 2 years, then every 2 years[d]
bladder cancer		
I. non-invasive carcinoma		
1. low risk of recurrence	cystoscopy	at the 3rd and 9th month, then annually
2. high risk of recurrence	cystoscopy	every 3 months for 2 years, then every 6 months for 3 years
	urine cytology	every 3 months for 2 years, then every 6 months for 3 years
	CT of the abdomen and pelvis, CXR	annual assessment of the upper urinary tract
	random biopsies of the bladder wall	in cases of positive cytology and normal cystoscopy
II. invasive carcinoma		
1. radical cystectomy	urine cytology	every 3–6 months for 2 years[d], then every 6–12 months[d]
	CT of the abdomen and pelvis, CXR	every 3–6 months for 2 years, then every 6–12 months
2. bladder preservation therapy	cystoscopy	every 3–4 months for 3 years, then every 6–12 months
	urine cytology	every 3–4 months for 3 years, then every 6–12 months
	CT of the abdomen and pelvis, CXR	every 3–6 months for 2 years, then every 6–12 months
	random biopsies of the bladder wall	every 3–6 months for 2 years
urothelial carcinoma of the upper urinary tract		
I. after nephroureterectomy		
1. low risk	cystoscopy	after 3 and 9 months, then annually
	CT of the abdomen and pelvis, CXR	every 6 months for 2 years, then annually
2. high risk	cystoscopy	every 3 months for 2 years, every 6 months for 3 years, then annually
	urine cytology	every 3 months for 2 years, every 6 months for 3 years, then annually
	CT of the abdomen and pelvis, CXR	every 6 months for 2 years, then annually
II. after organ sparing surgery		
1. low risk	cystoscopy	at the 3rd and 6th month, then annually
	ureteroscopy	3 months after the procedure
	CT of the abdomen and pelvis, CXR	every 6 months for 2 years, then annually
2. high risk	cystoscopy	at the 3rd and 6th month, then annually for 5 years

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Table IX cont. Recommended follow-up in patients with genitourinary malignancies after curative treatment

Cancer	Examinations	Frequency
	ureteroscopy	3 and 6 months after the procedure
	urine cytology	at the 3rd and 6th month, then annually for 5 years
	urine sediment cytology (*in situ*)	after 3 and 6 months
testicular malignancies[e] [103]		
	physical examination, AFP[f], B-HCG[g] and LDH[h], CXR	every 3 months for the first 2 years, every 6 months for the next 3 years, then annually
	CT scan of the abdomen and pelvis	every 6 months for the first 2 years, then as indicated
	chest CT	as indicated
	head CT	as indicated
penile cancer [104]		
	physical examination	every 3 months for the first 2 years, then as indicated
	CT or MRI of the pelvis[i]	every 3 months for the first 2 years, then as indicated

[a] – PSA (prostate-specific antigen); [b] – particularly reasonable in patients with undifferentiated or non-glandular cancers (e.g. sarcomas) that do not secrete PSA; [c] – based on nomograms based on T, N and M stages, symptoms at diagnosis, tumour grade and diameter [98–101]; [d] – only if clinically indicated and upon an individual risk assessment; [e] – guidelines of the European Association of Urology (according to the ESMO guidelines, each patient with testicular cancer in the second and fifth year of follow-up should undergo biochemical serum measurements (urea, creatinine, triglycerides, glucose, luteinising hormone, follicle-stimulating hormone, testosterone and cholesterol fractions) to evaluate late adverse effects; [f] – alpha-fetoprotein; [g] – beta-gonadotrophin; [h] – lactate dehydrogenase; [i] – only in patients with initial inguinal lymph node metastases

in patients without symptoms or biochemical failure. A single increase in PSA level should be verified by other examinations before instituting further diagnostics. The definition of biochemical failure is still debatable. If the lowest PSA level after radical prostatectomy does not exceed 0.01 ng/ml, the risk of clinical relapse is about 4% [90]. Among those with a PSA level above 0.05 ng/ml, about 2/3 will survive five years without biochemical failure [91]. In 2006, the Radiation Therapy Oncology Group and the American Society for Radiation Oncology defined biochemical failure after radiotherapy as an increase in PSA level by 2 ng/ml above the nadir [92]. PSA level after successful surgery should become indeterminable within six weeks [93]. Persistent, detectable PSA indicates active disease (micrometastases or residual disease in the pelvis). A rapid increase in PSA level is more indicative of dissemination, whereas local relapse is characterised by a late and slowly increasing PSA [94]. Unlike radical prostatectomy, radiotherapy leads to a much slighter decrease in PSA, and the nadir can be reached even after three years. A PSA decrease below 0.05 ng/ml is associated with a good prognosis [95]. The PSA doubling time (PSADT) depends on the relapse location; a PSADT lasting years or many months suggests local relapse, whereas a short PSADT (a few weeks or months) may indicate disease dissemination [96].

Rectal examination is particularly reasonable in patients with undifferentiated cancers or non-epithelial prostate tumours (e.g. sarcomas) [97]. In such cases, there is no PSA increase during progression, and rectal examination may be the only method for asymptomatic recurrence detection.

Endoscopic diagnostics should be considered in irradiated patients who have symptoms within the lower gastrointestinal tract to identify their cause (post-radiation enteropathy, chronic inflammatory processes or bowel malignancy).

Renal cancer

There is no evidence that any follow-up strategy may improve renal cell carcinoma (RCC) outcomes in patients who have undergone radical surgery. The follow-up of RCC patients after curative treatment should consider recurrence risk determined by validated nomograms based on T, N and M stages, symptoms at diagnosis and tumour grade (tab. IX) [98–101]. Notably, the most common site of RCC metastases are the lungs, and the chest should be checked along with abdominal examinations.

Bladder cancer

The risk of recurrence after radical cystectomy depends strictly on the pathological tumour stage, ranging from 5% in pT1 G3 to almost 100% in pN2. The risk of recurrence is greatest during the first two years, with a slight but continuous decrease thereafter. All patients undergoing transurethral electroresection of non-invasive bladder cancer (TURbt) and patients with invasive cancer managed with transurethral resection of the bladder tumour followed by concurrent chemotherapy and radiation should undergo cystoscopy after three months (tab. IX). In pT1 G2/G3 tumours, repeated electroresection of the involved sites should be performed after three months; more than one third of these patients will be diagnosed with

residual disease. For low-risk tumours (solitary tumour, pTa G1, diameter <3 cm), without recurrence within three months from the first TURbt, follow-up cystoscopy can be deferred until the ninth month and then performed annually. In high-risk patients, cystoscopy should be performed every three months during the first two years, every four months in the third year, every six months in fourth and fifth year and then annually. Determining the standard follow-up for intermediate-risk cancer is difficult due to the high variability of prognostic factors. At recurrence, periodic cystoscopy should be re-introduced. In patients with a single pTa G1 tumour who have not relapsed within five years, further cystoscopy may be waived. In other patients, an annual examination is advisable for ten years, and in patients with a high risk of relapse - throughout their lifetime. Follow-up, including USG of the kidney and bowel pouch and monitoring of creatinine and electrolytes, is carried out every three months during the first two years and then every six months up to a total of five years. Patients undergoing radiotherapy with bladder preservation require follow-up cystoscopy every three months for the first two years and then every six months [102].

Testicular malignancies

There is no generally accepted follow-up for testicular cancer. The primary aim of follow-up (lasting for 5–10 years, is the early detection of relapse and treatment complications. Routine examinations include periodic measurement of serum tumour markers (AFP, βHCG and LDH) and CT of the abdomen and pelvis. Recently, CT tends to be replaced with MRI, which allows lower exposure to radiography contrast and avoids ionising radiation [103].

Penile cancer

The five-year survival is approximately 85% in localised penile cancer, 60% in patients with lymph node metastases or regional invasion and 11% in metastatic disease. Some reports have demonstrated a better prognosis in HPV-associated penile cancers, but these findings warrant confirmation. Table IX presents the European Association of Urology guidelines for follow-up after curative treatment of penile cancer [104].

Skin melanomas

To date, no universal, evidence-based follow-up schedules for skin melanoma have been developed. The frequency, type and duration of follow-up should consider the individual risk of recurrence based on the initial tumour stage (II, 2A).

The risk of recurrence is highest in the first three years after treatment; therefore, follow-up should be more intensive during this period (tab. X). However, melanoma recurrence can occur even ten years after the primary treatment [105–112], and its early detection may allow for effective salvage surgery [113–117]. Approximately 20%–28% of first melanoma recurrences are local or in-transit, more than 25% involve regional lymph nodes (with decreasing frequency after the implementation of sentinel lymph node biopsy) and 15%–50% are distant metastases.

Follow-up is based on the assessment of scar after the primary lesion excision and lymphadenectomy. Particularly important is the observation of regional lymphatic drainage (potential seeding for in-transit relapse). In addition to physical examination, USG is recommended for the evaluation of regional lymph nodes. The specificity of CXR for lung metastasis detection is only about 50% and this examination is of little use in patients with stages I–II and no clinical symptoms [118]. Since patients themselves can detect about 60% of locoregional recurrences, they should be encouraged to practice lifelong self-control of primary lesions and regional lymph nodes (III, 2A) [111]. Beyond five years, the risk of recurrence is below 5% [111, 117]. In early melanoma suffices less intensive follow-up (II, 2A) [119, 120-122].

Follow-up imaging (e.g. CT) is not reasonable in asymptomatic stage IA–IIA patients; however, can be considered for the first 2–3 years after surgery or systemic adjuvant treatment in stage IIB–IIIC patients (IV, 2B) [109, 110, 118]. This recommendation, among others, results from increasing treatment efficacy of disseminated melanomas [123]. In stage IIIC/D patients, the risk of brain metastases in the first 13 months after local treatment is approximately 5%, which may justify a follow-up including brain MRI [124]. In turn, in patients with clinical symptoms suggesting distant metastases (liver enzyme abnormalities, bone pain, neurological symptoms, cough or weakness), there is a need for detailed imaging, including CT, MRI, PET-CT and bone scintigraphy [115, 124, 125]. Routine follow up does not include monitoring of serum tumour markers.

Regardless of the initial stage, examinations should include the entire skin (and not only the area of the primary disease). As the risk of developing a second independent melanoma or other skin malignancy exceeds 10%, dermoscopy should be performed every 6–12 months [126–130]. Patients with atypical nevus syndrome should be assessed with repeated photography of the entire skin or regular videodermatoscopy. Patients must follow the principles of skin photoprotection and should be informed that their relatives have a higher risk of developing melanoma. However, there are no indications for genetic testing. Further information for patients, among other sources, is available on the websites of scientific societies, (e.g. www.akademiaczerniaka.pl).

Soft tissue sarcomas

The aim of post-treatment follow-up for soft tissue sarcomas (STS) is the early detection of local or distant relapse, assuming that earlier treatment initiation may increase its efficacy. Follow-up strategies are based on three principles: uncomplicated but effective methods, accuracy and cost--effectiveness [131, 132]. Several proposals for STS follow-up have been developed, but they are based on scarce evidence and vary widely [131, 133–138].

Table X. Recommended follow-up in skin melanomas

Cancer	Examinations	Frequency
early melanoma after excision of the primary lesion without lymph node metastases (stages IA–IIA)	interview and physical examination, including a thorough assessment of the entire skin, the primary tumour area and regional lymph nodes; USG of regional lymph nodes in stages ≥pt1b when a sentinel node biopsy was not performed; no indications for routine laboratory testing; CXR (optionally); contrast CT of the chest and abdomen, pelvis; neck CT or PET-CT, brain MRI and other imaging in all cases with clinical symptoms; patient education on risk factors and self-examination of the skin and lymph nodes	every 6–12 months for the first 5 years, examinations can be conducted if clinically indicated (follow-up can be performed outside of the specialist centre)
locally advanced melanoma after excision of the primary lesion without lymph node metastases (stages IIB–IIC)	CXR, optional abdominal USG; USG of regional lymph nodes if sentinel node biopsy was not performed in stages ≥pt1b; consider contrast-enhanced CT of the chest, abdomen, pelvis; neck CT or PET-CT, brain MRI and other imaging every 6–12 months for the first 2 years and every 6–12 months for the next 3 years (obligatory in all cases with clinical symptoms); no indications for routine imaging after 3–5 years; no indications for routine laboratory testing; patient education on risk factors and self-examination of the skin and lymph nodes	every 3–6 months for the first 2–3 years, then every 6–12 months up to 5 years and examination after 5 years if clinically indicated
after excision of regional lymph node metastases or local recurrence/ satellite focus/in-transit focus (stages IIIA–IIID) or positive sentinel lymph node biopsy without lymphadenectomy	interview and physical examination, including a thorough assessment of the entire skin, primary tumour area and regional lymph nodes; optional CXR; USG of lymphatic drainage every 4–6 months in cases of positive sentinel lymph node biopsy without lymphadenectomy; consider contrast-enhanced CT of the chest, abdomen, pelvis or neck along with PET-CT, brain MRI and other imaging every 3–12 months for the first 2 years, then every 6–12 months for the next 3 years, particularly in stage IIIC/IIID (obligatory in all cases with clinical symptoms); no indications for routine imaging after 3–5 years; no indications for routine laboratory testing; patient education on risk factors and self-examination of the skin and lymph nodes	every 3–4 months fo the first 2 years, every 3–6 months for the next 3 years and examination after 5 years if clinically indicated
after treatment of metastatic disease (stage IV)	assessment of metastatic lesions; serum LDH; contrast-enhanced CT of the chest, abdomen and pelvis; neck CT or PET-CT, brain MRI or other imaging, depending on the metastasis location	individual follow-up schedules

The estimated relapse rate in primary STS (depending on histological grade, primary tumour size, histology, location and local treatment accuracy) ranges between 40% and 60% [131, 135, 136, 139]. About 80% of relapses, particularly in high-grade STS, occur within three years after the primary treatment. The locations of relapses depend mainly on the primary tumour site. In patients with limb STS (the most common location), the first relapse most often develops in the lungs. With appropriate combined-modality treatment of the primary lesion, local recurrences are less common. In rare STS subtypes of the limbs and trunk (e.g. rhabdomyosarcoma, epithelioid sarcoma, clear cell sarcoma or synovial sarcoma), more common are lymph node metastases, and in myxoid liposarcoma, metastases to the abdominal cavity and soft tissues. In turn, in STS of the retroperitoneal space (most often liposarcoma) or viscera (mainly gastrointestinal stromal tumours, GIST), most common are local or intraperitoneal relapses, followed by liver metastases.

In high-grade STS, about half of patients will die due to dissemination. The combined-modality salvage treatment in some patients may allow for long-term survival. Complete excision of lung metastases allows for significantly better results than non-surgical methods [137, 139, 140]. This justifies earlier detection of resectable (often quantifiable) lung metastases (III, 2A). Regular CXR allow detection of asymptomatic lung metastases in more than half of cases [131, 139, 141]. It is estimated that complete resection of exclusive lung metastases allows for 30%–40% long-term survival [140, 142, 143], but this applies only to clinically asymptomatic, quantifiable lung metastases [144, 145]. CXR allow the detection of more than 60% of asymptomatic lung metastases. After five years, CXR should be performed annually. There is no need for routine chest CT. However, CT is indicated in detected or suspected changes in CXR to assess their number and location, and evaluation of the pleura, mediastinum, and hilar and mediastinal lymph nodes. American College of Radiology recommends periodic chest CT only in high risk STS and after metastasis excision (II, 2A). On the other hand, the only randomised trial evaluating follow-up schedules in STS showed no advantage of CT over CXR [146].

Follow-up examinations to detect local STS recurrence should primarily include a careful physical examination, possibly with USG of the scar for easily accessible lesions, e.g. located in the limbs or trunk skin [147–149] (III, 2B). Patients should

also be informed about local recurrence symptoms because self-examination of the resection scar often allows the detection of interval recurrences. Some experts additionally recommend USG or MRI of the primary tumour area in high-grade limb STS, but the usefulness of MRI is controversial [150, 151] (III, 2B). Effective method in differentiating between tumour relapse and post-surgical changes is signal enhancement in T2-weighted contrast MRI. However, routine MRI is not reasonable considering its low cost-effectiveness.

Useful imaging in retroperitoneal or inguinal STS is spiral contrast-enhanced CT or MRI [134, 135] (III, 2A). Retroperitoneal or intraperitoneal STS recurrence is more common and more difficult to detect with physical examination than limb or skin recurrence. There is no evidence that earlier detection of retroperitoneal STS recurrence improves overall survival (III, 2B).

So far, no standard STS follow-up have been developed [134–137, 152–154]. Usually, it includes visits every 3–4 months for the first 2–3 years, every six months for the next two years and then annually. The recurrence risk depends on the tumour grade and size, completeness of the combined-modality treatment and time from treatment completion [134, 135, 137, 139] (III, 2A). For low-grade STS and those under 5 cm, the recurrence risk after curative treatment is very low. If the postsurgical scar can be assessed easily by a physical examination, there is no need for imaging other than a CXR every 6–12 months for the first three years and then annually (III, 2A). However, high-grade STS, which carries a significantly higher risk of pulmonary metastases and local recurrence, necessitates a regular CXR [139] (III, 2A). Assessment of regional lymph nodes is reasonable only for selected subtypes of STS (e.g. clear cell sarcoma and epithelioid sarcoma),

Table XI. Recommended follow-up in patients with soft-tissue sarcomas (excluding GIST)

Clinical situation	Examinations	Frequency
after curative treatment for stage IA-IB STS (G1)	interview and physical examination CXR every 6–12 months; chest CT only in cases of suspected changes in the X-ray; six months after the surgery, consider local assessment with MRI, CT or USG; for retroperitoneal and intraperitoneal sarcomas, regular follow-up every six months for the first 2–3 years, then annually, with contrast CT of the abdomen and pelvis (in other locations, imaging only with clinical suspicion of recurrence); patient education on self-examination	every 3–6 months for the first 2–3 years, then annually (over 10 years only in patients who underwent perioperative radiotherapy)
after curative treatment for stage II–III STS (G2/G3 or after resection of metastases to regional lymph nodes)	interview and physical examination, with particular attention to the area of the scar after the primary tumour resection and lymphadenectomy: check X-ray or CT; consider local post-resection MRI, CT or USG 3–6 months after the surgery, then not more frequently than annually; for retroperitoneal and intraperitoneal STS: contrast-enhanced CT of the abdomen and pelvis every 6 months for the first 2–3 years, then annually; patient education on self-examination	every 3–4 months for the first 2–3 years, then every 6 months up to 5 years, and then annually
after treatment for stage IV	imaging depends on the location of measurable metastatic foci	individual schedules

Table XII. Recommended follow-up in patients with gastrointestinal stromal tumours (GIST)

Clinical situation	Examinations	Frequency
after curative treatment for very low- and low-risk GIST (stage I)	no absolute indications for regular follow-up; consider USG or CT of the abdomen and pelvis; the patient should be informed about the small risk of late recurrence	annually
after curative treatment for intermediate-risk GIST (stage II)	contrast-enhanced CT of the abdomen and pelvis; other imaging depending on the primary tumour location (e.g. pelvic MRI for rectal GIST, chest CT for oesophageal GIST)	every 3–6 months for the first 2–3 years, then every 6–12 months until 5 years and annually after 5 years
after curative treatment for high-risk GIST (stage III)	interview and physical examination, contrast-enhanced CT of the abdomen and pelvis; other examinations depending on the primary tumour location (e.g. pelvic MRI for rectal GIST, chest CT for oesophageal GIST)	every 3–4 months for the first 2–3 years, every 6 months until 5 years, and annually beyond 5 years after surgery or adjuvant imatinib
after treatment for stage IV	imaging depending on the location of measurable metastatic foci, typically CT or MRI of the abdomen and pelvis	individualised schedules

and abdominal examination is only recommended for myxoid liposarcoma. Laboratory tests are useless for detecting STS recurrences [152] (III, 1). For tumours that are difficult to assess in a physical examination, e.g. those located retroperitoneally or intraperitoneally (such as GIST), regular double-contrast CT should be performed. The value of PET-CT is uncertain. Notably, patients should be informed that recurrence or radiotherapy-induced secondary malignancy may develop even after ten years [154, 155].

In low-grade GIST, follow-up visits may be performed annually [154, 156]. Patients with high- and medium-grade GIST who received no adjuvant treatment should be subjected to strict observation, with contrast CT of the abdomen and pelvis performed every 3–4 months for the first 2–3 years (when the recurrence risk is highest), every six months up to five years and then annually [153, 154, 155, 156] (II, 2A). This regimen also applies to patients following adjuvant imatinib.

Bone sarcomas

The aim of post-treatment follow-up for bone sarcomas is the early detection of local or distant relapse, assuming that earlier treatment initiation may increase its efficacy [157–161]. In bone sarcomas, 70% of relapses occur in the lungs (in Ewing's sarcoma, relatively common are also bone metastases) [158–161]. Since most relapses occur within the first 2–3 years, during this time, follow-up visits every 3–4 months are reasonable, especially in higher-grade tumours. The follow-up should include an X-ray of the chest and the region of the operated bone (IV, 2A). Patients should also be informed about the need to observe the operated area, as they may detect some local recurrences themselves. Afterwards, follow-up visits may take place every 6–12 months (IV, 2A). A serious consequence of intensive combined-modality treatment (chemotherapy, radiotherapy and surgery) are secondary malignancies, which in small-cell sarcomas occur in 7%–10% of patients [162, 163]. Other important late sequelae of combined-modality treatment justifying long-term observation include heart failure, infertility and endoprosthesis complications [164–166] (V, 2A).

There is no standard follow-up based on randomised controlled clinical trials for bone sarcomas in adults. Routine follow-up visits are usually repeated every 3–4 months for the first 2–3 years, every six months for the next two years and then annually. The recurrence risk depends on the primary tumour grade and size, primary treatment radicalness and time from its completion. For low-grade sarcomas and those below 5 cm, the recurrence risk after curative treatment is very low. In such cases, X-ray imaging performed every 6–12 months for the first three years and then annually. In high-grade sarcomas, characterised by a significantly higher risk of pulmonary metastases and local recurrence, careful physical examination should be supplemented with CRX and imaging of the primary tumour area.

Primary bone malignancies in children and adolescents necessitate more intensive follow-up: every six weeks in the first and second years, every three months in the third year, every six months in the fourth year and then annually (IV, 2A).

The role of primary care physicians in cancer follow-up

Post-treatment follow-up of patients with solid malignancies carried out by primary care physicians is important for detecting cancer relapse or secondary malignancy and preventing post-treatment complications [167]. In a GP's office, the patient also expects psychological support and assistance in organising care and everyday life [167]. In turn, patients whose treatment failed or was abandoned expect assistance in ensuring the highest possible quality of life.

Table XIII. Recommended follow-up in patients with bone sarcomas

Clinical situation	Examinations	Frequency
after curative treatment of stage IA-IB sarcoma (G1/G2)	interview and physical examination every 6 months for the first 2–3 years, then annually; CXR every 6–12 months; chest CT only in cases of suspected changes in the X-ray	every 6 months for the first 2–3 years, then annually
	X-ray, MRI or CT of the primary tumour site	every 6 months for the first 2–3 years, then annually
	patient education on self-examination	
after curative treatment of stage II–III sarcoma (G3)	interview and physical examination, with a focus on the primary tumour site and regional lymph nodes; CXR or CT; radiographic, MRI or CT site evaluation after resection; in patients with Ewing's sarcoma, optional bone scintigraphy or PET-CT; patient education on self-examination	every 3–4 months for the first 2–3 years, then every 6 months until the 5th year, and then annually
after treatment of distant metastases (stage IV)	imaging depending on the location of measurable metastatic lesions	individualised schedules

A significant proportion of cancer patients receive inadequate post-treatment surveillance, including both insufficient and excessive supervision [168]. As high-quality, evidence-based data are missing, it is difficult to define generally the optimal moment for transferring patients from specialist care to a GP [169, 170]. Due to the small number of oncology specialists compared to the number of primary care physicians, it is increasingly important to define the latters' role in providing cancer care [171, 172]. The number of patients seeking post-treatment follow-up performed by GPs rather than oncologists gradually increases [173]. At the same time, during intensive cancer treatment, many patients lose contact with their GPs and do not know when or how to restore it [174].

It is difficult to standardise coordination rules for post-treatment cancer care, especially in the absence of data on cancer-related risks and the time elapsed from treatment. The authors of *Defining Survivorship Trajectories Across Patients with Solid Tumours. An Evidence-Based Approach*, published in 2018, attempted to estimate the high-risk period after treatment completion for each cancer based on the risk of death and the time since treatment completion [175]. During this period, care should be provided by an oncologist, or a multidisciplinary team including an oncologist, and may thereafter be continued by a GP.

The time of increased death risk varies for particular malignancies: e.g. is short (around one year) for localised prostate cancer; may be long (6–7 years) for lung cancer and very long (more than ten years) for some gastrointestinal cancers. The leading causes of death in cancer patients are the failure of primary cancer treatment (on average, over half of patients) and secondary cancer, but common cause is also cardiovascular disease [176]. Patients with increased risk of cardiac death could benefit more from the care provided by a GP than from an oncologist. The selection of the optimal model for post-treatment care should also consider the patients' quality of life, their quality of care and the incidence of other diseases [169].

Monitoring of patients' compliance with periodic follow-up recommendations should include the following steps [177]:

- supervision of oncology follow-up attendance,
- supervision of performing periodic follow-up examinations (e.g. MRI, CT or USG),
- referring patients to palliative medicine clinics, palliative home care teams or pain treatment clinics,
- risk assessment and monitoring for tumour recurrence,
- risk assessment and monitoring for secondary cancer,
- educating patients about above risks,
- assessment of treatment complications and their prevention, diagnosis and treatment.

Specific indications concerning the GP's roles in selected solid malignancies are presented in table XIV.

There are differences between the recommendations of oncology and family medicine specialists [178]. The former pay more attention to cancer control and its consequences, and the latter to the prevention of lifestyle-related diseases. Of particular importance is building the professional experience and competencies of primary care physicians. Considering nearly 200,000 new malignancies per year diagnosed in Poland and the total number of primary care physicians (including those performing this role as an additional job), a primary care physician may diagnose, on average, only 3–4 cancer patients a year [179]. At the same time, a primary care physician manages more patients after cancer treatment. Monitoring of these patients for post-treatment complications and secondary cancers remains insufficient [180].

GPs' involvement in the care of patients after treatment for solid malignancies should additionally include the following:

- monitoring compliance with specialist recommendations, including medication use, especially steroids or antiepileptic agents,
- monitoring indications for rehabilitation after cancer treatment, particularly anti-oedema therapy and general rehabilitation,
- monitoring and supervision of the patient's family, regarding an increased cancer risk (determined by genetic and environmental factors, e.g. passive smoking),
- providing medical devices to patients as needed,
- referring patients to support groups and patient organisations,
- encouraging preventive vaccination against pneumococcus, meningococcus, seasonal flu and SARS-CoV-2.

This particularly applies to high-risk groups, e.g. patients who underwent chemotherapy and radiotherapy.

There is a need for coordination of post-treatment patient care, given the specific characteristics of particular patient groups and the potential of the primary care and specialist care systems. Such a mixed-care model (so-called coordinated or combined-modality care) is most effective in terms of survival and quality of life [178, 181].

Particular attention should be paid to systemic limitations restricting GPs from making referrals for certain examinations, such as CT or cancer markers. Primary care physicians can effectively perform such monitoring, provided that patient groups are properly selected and systemic support is provided [169, 182]. Without diagnostic capacity, primary care physicians cannot effectively supplement specialist oncological care, including post-treatment follow-up.

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Table XIV. Specific indications for GPs' roles in the post-treatment follow-up of selected solid malignancies

Cancer	GPs' roles	Evidence quality	Recommendation strength
head and neck cancer	evaluation of compliance with the specialist's follow-up recommendations, with special consideration of other respiratory or gastrointestinal malignancies	II	2A
	encouraging the patient to quit smoking		
CNS malignancies	evaluation of compliance with MRI follow-up scheme (as indicated by the specialist)	II	2A
non-small cell lung cancer	evaluation of compliance with chest CT follow-up scheme (as indicated by the specialist)	II	2A
	encouraging the patient to quit smoking	III	2B
oesophageal and gastric cancer	risk assessment for treatment complications, including alimentation disorders and deficiencies, e.g. B_{12}	IV	2B
pancreatic or ampullary cancer	diagnosis and management of treatment sequalae (including diabetes and pancreatic enzyme disorders)	II	2A
colorectal cancer	interview and physical examination every 3–6 months for 3 years and every 6–12 months for the next 2 years	II	2A
breast cancer	observation for local recurrence; assessment of risk and monitoring for early menopause and bone mineral density disorders	II	2A
	in patients with preserved uterus treated with tamoxifen, annual gynaecological examination	II	2A
	encouraging patients to maintain a BMI in the range of 20–25, physical activity and a proper diet	II	2A
prostate cancer	interview and physical examination, PSA monitoring, initially every 3 months, then every 6 months until 3 years and then annually	II	2A
melanoma	educating patients in self-examination of the skin and lymph nodes of the treated area	II	2A

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