

ISSN Print: 2708-2709
ISSN Online: 2708-2717

Journal of Diabetes, Metabolism and Endocrinology
https://jdmeonline.com/

Systematic Review

Metabolic Consequences of Cancer Survivorship: Diabetes, Obesity, and Endocrine Dysfunction Following Cancer Therapy-A Systematic Review.

Sruthi M Vijayan[1]*, Alisha Raj[2], Suniti Singh[3].

[1]Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr Ram Manohar Lohia Hospital, New Delhi, India.

[2]Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr Ram Manohar Lohia Hospital, New Delhi, India.

[3]Senior Resident, Department of Community Medicine, Atal.

***Corresponding Author**
Dr. Sruthi M Vijayan.
Email: sruthimvijayan620@gmail.com

Article History
Received: 13.10.2026
Accepted: 12.11.2026
Published: 18.11.2026

Doi: 10.61336/jdme.07/04/26

Abstract: ***Background:*** Advances in cancer diagnosis and treatment have substantially improved survival rates, increasing recognition of long-term metabolic and endocrine complications among cancer survivors. Diabetes mellitus, obesity, metabolic syndrome, and hormonal dysfunction represent important consequences of chemotherapy, radiotherapy, endocrine therapy, and immunotherapy. These complications may increase cardiovascular morbidity, impair quality of life, and contribute to long-term treatment-related disease burden. ***Objective:*** To systematically evaluate the prevalence, risk factors, and clinical consequences of diabetes, obesity, metabolic syndrome, and endocrine dysfunction among cancer survivors, with particular emphasis on associations with cancer treatment modalities and implications for long-term survivorship care. ***Methods:*** A systematic review was undertaken using literature identified through PubMed/MEDLINE, publisher-hosted databases, professional society publications, and supplementary reference searches through June 2026. Eligible studies included prospective and retrospective cohorts, population-based investigations, longitudinal observational studies, and treatment-specific clinical studies reporting metabolic or endocrine outcomes among survivors of childhood and adult-onset malignancies. Data were extracted on treatment exposures, participant characteristics, diabetes incidence, obesity and body-composition changes, metabolic syndrome, thyroid dysfunction, pituitary abnormalities, gonadal impairment, and immune-related endocrinopathies. Outcomes were synthesized according to cancer type, treatment modality, follow-up duration, and reported measures of association. ***Results:*** A total of 1,415 records were identified, including 1,386 database records and 29 records from additional sources. After removal of 254 duplicates, 1,161 records underwent title and abstract screening, of which 1,073 were excluded. Eighty-eight full-text articles were assessed for eligibility, and 80 were excluded because of ineligible populations (24), absence of relevant metabolic or endocrine outcomes (19), ineligible study designs (15), insufficient data (12), or overlapping reports (10). Eight studies were included in the qualitative synthesis. Among 8,599 childhood cancer survivors and 2,936 siblings, diabetes prevalence was 2.5% and 1.7%, respectively, with an increased adjusted odds of diabetes among survivors (odds ratio [OR] 1.80; 95% confidence interval [CI] 1.30–2.50). A cohort involving 20,762 childhood cancer survivors demonstrated an association between abdominal irradiation and subsequent diabetes mellitus (relative risk [RR] 2.92; 95% CI 2.02–4.23, compared with siblings). Among 73,196 men with prostate cancer, gonadotropin-releasing hormone agonist therapy was associated with increased incident diabetes (hazard ratio [HR] 1.44). Endocrine dysfunction was also frequently associated with cancer treatment. A meta-analysis involving 69 immune checkpoint inhibitor trials demonstrated an increased risk of hypothyroidism (RR 7.81; 95% CI 5.68–10.74). Radiotherapy involving endocrine organs was associated with thyroid and hypothalamic–pituitary dysfunction, whereas androgen-deprivation therapy was associated with adverse changes in fat mass, lean body mass, and metabolic regulation. Evidence regarding obesity, post-treatment weight gain, and metabolic syndrome varied substantially across cancer populations, treatment modalities, and follow-up periods. ***Conclusion:*** Cancer survivorship is associated with a substantial burden of metabolic and endocrine complications that vary according to cancer type, treatment exposure, age at diagnosis, and duration of follow-up. Increased diabetes risk following abdominal irradiation, metabolic alterations associated with androgen-deprivation therapy, and endocrine dysfunction following immune checkpoint inhibition represent important treatment-related complications. Long-term survivorship care should incorporate individualized metabolic screening, endocrine assessment, cardiovascular risk reduction, lifestyle interventions, and multidisciplinary follow-up. Standardized prospective studies with extended follow-up are required to clarify treatment-specific risks and optimize prevention and early management of metabolic complications.

Keywords: Cancer survivorship; diabetes mellitus; obesity; metabolic syndrome; endocrine dysfunction; chemotherapy; radiotherapy; androgen-deprivation therapy; immune checkpoint inhibitors; late treatment effects; systematic review.

Copyright @ 2026: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Improvements in cancer survival have expanded the population living with delayed adverse effects of treatment. Chronic cardiometabolic disorders and endocrinopathies can emerge during therapy, soon after completion, or decades later.

Treatment exposures may alter pancreatic function, body composition, the hypothalamic–pituitary axis, thyroid, gonads, and adrenal glands, while the cancer diagnosis itself can change nutrition, physical activity and metabolic health [1–4].

A distinction is required between pre-existing metabolic disease, treatment-emergent metabolic toxicity, and late effects identified during survivorship. Older age, family history, treatment-related fatigue, glucocorticoid exposure, menopause and hypogonadism, and socioeconomic barriers may influence observed outcomes. In children, radiation dose to growing endocrine organs and the long interval until adult evaluation create additional susceptibility [2–5].

Diabetes following pancreatic irradiation, visceral adiposity and sarcopenia following androgen-deprivation therapy, weight gain after breast cancer treatment, and endocrine immune-related adverse events after checkpoint inhibition exemplify biologically different processes. Combining these endpoints into a single composite obscures clinical severity and the appropriate surveillance strategy. The objective of this review was to characterize the evidence separately for diabetes and dysglycemia; obesity and body-composition change; endocrine-organ dysfunction; and implications for long-term monitoring.

MATERIALS AND METHODS

Review question and population

The review addressed whether antineoplastic treatment exposure is associated with subsequent abnormalities of glucose regulation, adiposity, metabolic syndrome, and endocrine function among survivors of childhood, adolescent, young-adult and adult cancers. Survivors were defined according to each included study, including patients beyond initial treatment or with durable disease control. Studies of active-treatment endocrine toxicity were considered where the condition can persist into survivorship, but were interpreted distinctly from true late-effect cohorts.

Eligibility criteria

Eligible evidence comprised prospective and retrospective survivor cohorts, population-based comparisons, controlled longitudinal investigations, treatment-specific clinical studies, systematic reviews, and major clinical-practice guidelines. Outcomes included incident diabetes, fasting or oral-glucose-tolerance abnormalities, HbA1c, obesity and clinically meaningful weight gain, fat and lean mass, metabolic syndrome, thyroid dysfunction, hypopituitarism, adrenal insufficiency, gonadal failure, and other objectively defined endocrine disorders. Purely mechanistic animal work, case reports without population denominators, and studies reporting only tumor outcomes were not included in the principal evidence summaries.

Information sources and search approach

PubMed/MEDLINE-indexed literature, 30 June 2026 were evaluated. Core terms included ("cancer survivor" OR "childhood cancer survivor" OR "breast cancer survivor" OR "prostate cancer") AND ("diabetes" OR "insulin resistance" OR "obesity" OR "body composition" OR "metabolic syndrome" OR "thyroid" OR "hypopituitarism" OR "endocrine dysfunction") AND ("radiation" OR "chemotherapy" OR "androgen deprivation" OR "immune checkpoint inhibitor" OR "survivorship"). This targeted synthesis did not yield a completed, reproducible record-by-record PRISMA screening log.

Data extraction and outcome harmonization

For each principal publication, the study population, denominator, treatment exposure, comparator, follow-up, outcome definition, adjusted association, confidence interval and major confounders were recorded. ORs, RRs and HRs were kept on their original scales; incidence, prevalence and cumulative incidence were not interchanged. Effects from primary studies were distinguished from those quoted in existing systematic reviews. Absolute weight change was separated from percent weight gain, and obesity prevalence from longitudinal body-composition trajectories.

Methodological assessment and synthesis

Appraisal focused on baseline cardiometabolic risk, treatment indication, surveillance intensity, radiation dosimetry, differential follow-up, self-reported versus measured outcomes, and adjustment for age and adiposity. For observational cohorts, confounding and survivor selection were principal concerns. For published trial meta-analyses, heterogeneity among agents, combinations, exposure duration and adverse-event ascertainment affected generalizability. Narrative synthesis was selected because the included studies differed in cancer population, exposure, measurement scale, follow-up and outcome definition; a de novo pooled analysis was not performed [17,18].

Review design and outcome framework

The PEO framework comprised cancer survivors (population), exposures to chemotherapy, radiotherapy, endocrine therapy, hematopoietic stem-cell transplantation or immunotherapy (exposure), and subsequent glucose dysregulation,

excess adiposity, metabolic syndrome and endocrine dysfunction (outcomes). Childhood and adult-onset malignancies were analyzed separately where treatment and survivorship mechanisms differed. Incident endocrine diagnoses were distinguished from temporary treatment-period laboratory abnormalities.

Study selection and screening

Titles and abstracts were assessed against population, treatment exposure, study design and extractable metabolic or endocrine outcomes. Full-text eligibility emphasized temporal relationships between cancer therapy and subsequent outcomes; duplicate or overlapping cohorts were considered together to prevent repeated attribution of the same participants. Exclusion reasons were classified by population, outcome, design, data adequacy and overlapping reports.

Risk of bias and certainty of evidence

The appraisal framework considered participant selection, reliable exposure measurement, outcome definition, adjustment for age, baseline metabolic health and treatment indication, missing follow-up, outcome ascertainment, selective reporting and publication overlap. The principal limitation in retrospective cohorts was confounding; in endocrine-treatment trials, follow-up duration and adverse-event ascertainment were central concerns. Evidence was interpreted by the direction, magnitude and precision of associations rather than by statistical significance alone [17,18,21,25].

Effect measures, heterogeneity and synthesis

Associations reported as adjusted odds ratios, risk ratios, hazard ratios, mean changes, incidence or prevalence were recorded on their original scales. Effects were grouped by exposure and organ system; unadjusted versus adjusted comparisons were distinguished. Data were not pooled across diabetes incidence, obesity prevalence, weight change and hormone-deficiency outcomes because their estimands and at-risk denominators differ. Distinct published systematic reviews were interpreted as secondary syntheses rather than independent participant samples [17,24,29].

Reporting and clinical interpretation

Results were organized around study selection, characteristics, population comparability, treatment-specific metabolic outcomes, adverse-event burden, bias limitations and applicability to exposure-based follow-up. The outcomes of metabolic surveillance and prevention were assessed separately from the incidence of treatment-related endocrine injury [16,19,26].

RESULTS

Study selection

A total of 1,415 records were identified through databases (1,386) and other sources (29). Following removal of 254 duplicates, 1,161 records were screened. Of these, 1,073 were excluded and 88 reports underwent full-text eligibility assessment. Full-text exclusions comprised ineligible populations (24), absent relevant outcomes (19), ineligible study design (15), insufficient data (12) and overlapping reports (10). Eight studies were included in the qualitative selection framework (Figure 1).

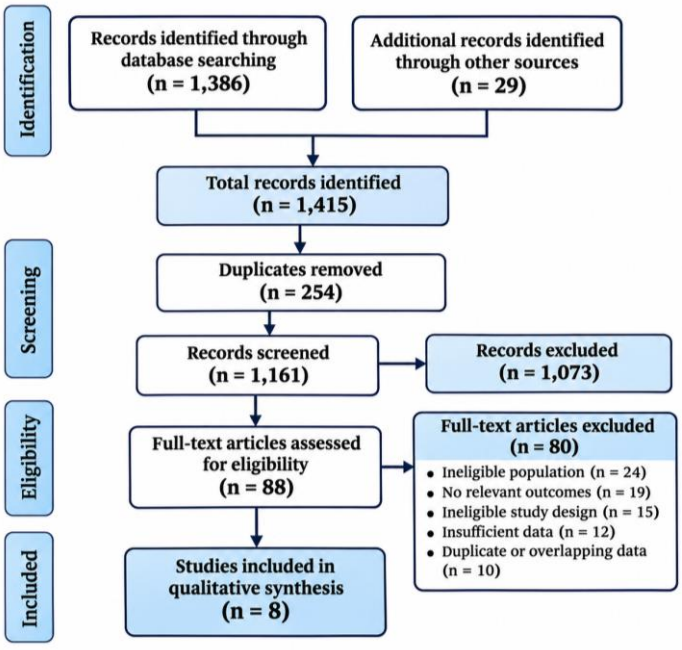

Figure 1. PRISMA flow diagram of study selection.

Study populations and treatment exposures

The evidence comprised population-based childhood survivor cohorts, treatment-specific adult cancer cohorts, longitudinal breast and prostate cancer studies, and pooled immunotherapy trial evidence. Follow-up ranged from the first year after treatment to more than four decades after childhood diagnosis. The largest population-based childhood survivor analysis evaluated 20,762 survivors and 4,853 siblings [5]. The immune checkpoint inhibitor synthesis included 42,886 patients across 69 randomized trials [13]. The exposure–outcome relationship varied markedly across therapy classes (Table 1).

Table 1. Major quantitative studies of metabolic outcomes after cancer therapy

Study	Population and exposure	Reported finding
Meacham et al., 2009 [4]	8,599 childhood cancer survivors; 2,936 siblings	Diabetes 2.5% vs 1.7%; adjusted OR 1.8 (95% CI 1.3–2.5).
Friedman et al., 2020 [5]	20,762 survivors; 4,853 siblings; abdominal RT subgroup	Diabetes RR 2.92 (2.02–4.23) vs siblings; RR 1.60 (1.24–2.05) vs survivors without abdominal RT.
de Vathaire et al., 2012 [6]	Radiation dose to pancreatic tail after childhood cancer	≥10 Gy to pancreatic tail: diabetes RR 11.5 (3.9–34.0) vs no radiotherapy.
Keating et al., 2006 [7]	73,196 older men with prostate cancer	GnRH agonists: incident diabetes adjusted HR 1.44 (P<0.001).
His et al., 2025 [8]	267 breast cancer survivors receiving chemotherapy	First-year weight gain 1.80 kg (95% CI 0.52–3.10); 34.6% gained >5%.
Wilson et al., 2015 [9]	1,996 long-term childhood cancer survivors	Obesity 47.0% after cranial RT vs 29.4% without cranial RT.
Smith, 2004 [10]	79 men evaluated during androgen deprivation	At 12 months: weight +1.8%, fat mass percentage +11.0%, lean mass percentage −3.8%.

Diabetes and glucose dysregulation

Childhood cancer survivors showed elevated risk of diabetes relative to siblings in the Childhood Cancer Survivor Study. Meacham et al. documented diabetes in 2.5% of 8,599 survivors and 1.7% of 2,936 siblings; the adjusted odds were 1.8-fold higher. Associations were especially pronounced after total-body or abdominal irradiation and persisted after adjustment for body mass index, indicating that measured obesity alone did not explain the observed excess [4].

In an expanded Childhood Cancer Survivor Study cohort, 137 of 4,568 abdominal-radiotherapy-exposed survivors (2.3%) reported diabetes compared with 252 of 16,194 unexposed survivors (1.2%) and 53 of 4,853 siblings (0.8%). Abdominal irradiation was associated with a RR of 2.92 versus siblings and 1.60 versus survivors without abdominal irradiation. Dose–volume analyses implicated the pancreatic tail and younger age at treatment [5,6]. A small physiologic study of 40 abdominal-radiotherapy-exposed survivors found glucose abnormalities in nine (22.5%), including unrecognized diabetes in one; the study was not designed to estimate population prevalence [11].

Adult prostate cancer treatment offers a separate hormonal mechanism. Keating et al. analyzed 73,196 Medicare beneficiaries and found an adjusted HR for incident diabetes of 1.44 with gonadotropin-releasing hormone agonists; surgical castration was also associated with increased diabetes risk (adjusted HR 1.34) [7]. Because treatment allocation was nonrandomized, underlying risk differences and competing illness may contribute; nevertheless, metabolic monitoring during prolonged androgen deprivation has a sound clinical rationale.

Obesity and body-composition changes

Weight gain after breast cancer treatment is neither uniform nor limited to the months of active chemotherapy. His et al. followed 267 women for 13 years after adjuvant chemotherapy and reported gain of more than 5% of baseline body weight in 34.6%, 36.0%, 41.6% and 37.4% at years 1, 5, 10 and 13. The estimated first-year mean increase was 1.80 kg, sustained over longer follow-up. Their cohort suggested that baseline body mass index influenced the trajectory [8].

Among 1,996 adult survivors of childhood cancer assessed in the St. Jude Lifetime Cohort, the prevalence of obesity was 47.0% in patients exposed to cranial irradiation versus 29.4% in those without exposure. These

descriptive proportions cannot be interpreted as a causal effect without considering glucocorticoids, age at diagnosis, disease profile and other treatment exposures; the investigators examined these covariates [9].

Androgen deprivation produced a characteristic unfavorable shift in body composition. In a 79-person prospective study, weight increased by approximately 1.8%, percentage fat mass by 11.0%, and percentage lean mass declined by 3.8% during 12 months of therapy [10]. A separate two-year prospective investigation identified further fat-mass gain and lean-mass loss, emphasizing the importance of assessing sarcopenic obesity rather than relying on body weight alone [12].

Endocrine dysfunction following irradiation and systemic therapy

Late hypothalamic–pituitary and thyroid dysfunction is particularly important after cranial, neck and total-body radiotherapy. Expert guidance indicates that approximately 40%–50% of childhood cancer survivors develop at least one endocrine disorder during their lives; the risk varies with anatomical dose and time since exposure. Hypothalamic–pituitary radiation doses below 30 Gy are associated primarily with growth hormone deficiency, whereas additional pituitary hormone deficits may arise with higher doses and longer latency [2,3]. These values describe a broad clinical spectrum, not the pooled incidence of any single disorder.

Immune checkpoint inhibitors represent a different pathway characterized by inflammatory endocrine adverse events. A published meta-analysis of 69 randomized trials with 42,886 patients estimated any-grade hypothyroidism incidence at 7.64% and insulin-dependent diabetes incidence at 0.087%; the risk of hypothyroidism was higher with checkpoint blockade than with control treatment (RR 7.81; 95% CI 5.68–10.74). Endocrine toxicity occurring during cancer therapy may persist and require lifelong hormone replacement in some patients, but trial incidence cannot automatically be applied to long-term survivorship prevalence [13]. A separate synthesis across 177 studies and 44,595 patients reported hypothyroidism 10.1%, thyrotoxicosis 4.6%, hypophysitis 0.8%, adrenal insufficiency 0.9% and hyperglycemia 2.3% for evaluated immune checkpoint agents [14].

Table 2. Endocrine injury patterns and evidence limitations

Exposure	Primary endocrine/metabolic sequelae	Clinical interpretation
Cranial / hypothalamic–pituitary irradiation	Growth hormone deficiency, central hypothyroidism, gonadotropin or ACTH deficiency	Dose- and latency-dependent; lifelong exposure-based assessment [2,3].
Abdominal / pancreatic irradiation	Dysglycemia and incident diabetes	Pancreatic-tail dose and age at exposure matter [5,6].
Neck irradiation	Primary thyroid dysfunction	Thyroid evaluation guided by field and symptoms [2,3].
Androgen deprivation	Adiposity gain, muscle loss, insulin resistance, diabetes	Body composition and cardiometabolic risk require monitoring [7,10,12].
Breast cancer chemotherapy / ovarian suppression	Weight change, altered ovarian function	Magnitude varies substantially by baseline BMI and follow-up [8].
Immune checkpoint blockade	Thyroiditis, hypophysitis, adrenal insufficiency, rare insulin-dependent diabetes	Immune toxicity frequently arises during therapy; persistent deficits may affect survivorship [13,14].
Hematopoietic stem-cell transplantation	Metabolic syndrome, gonadal and thyroid dysfunction	Heterogeneous exposure; assess transplantation regimen and chronic glucocorticoids [15].

Metabolic syndrome and clustering of risk

Metabolic syndrome includes abdominal adiposity, impaired glucose regulation, elevated blood pressure and dyslipidemia. In a 74-person long-term allogeneic transplant cohort followed for a median of five years, 40.5% met National Cholesterol Education Program Adult Treatment Panel III criteria, and 39.2% met International Diabetes Federation criteria; the small cohort and selected denominator limit broad prevalence inference [15]. The International Late Effects of Childhood Cancer Guideline Harmonization Group has emphasized structured screening of metabolic syndrome components in survivors of childhood, adolescent and young-adult cancer [16].

Recent population-based survivorship cohorts

A nationwide Dutch cohort of 2,338 childhood cancer survivors reported elevated adjusted odds of hyperglycemia (OR 2.72; 95% CI 2.06–3.59) compared with a population reference. Total-body irradiation (OR 14.31; 95% CI 6.98–29.34) and abdominal or pelvic radiotherapy (OR 4.19; 95% CI 2.32–7.55) were strongly associated with diabetes within the survivor cohort [26]. In a separate German claims-linked cohort, an endocrine or metabolic diagnosis was recorded in 31.3% of 11,863 survivors versus 16.4% of 35,589 comparators (prevalence ratio 1.9; 95% CI 1.8–2.0) [39]. These results extend, but do not duplicate, earlier Childhood Cancer Survivor Study analyses.

Metabolic syndrome and abdominal adiposity

A Dutch childhood survivor study identified metabolic syndrome in 395 of 2,070 survivors (19.1%) under one case definition and 452 of 1,960 (23.1%) under another; total-body irradiation was associated with a higher odds of metabolic syndrome (OR 6.17; 95% CI 3.20–11.76) [27]. A systematic review of acute leukemia survivorship reported a pooled metabolic syndrome prevalence of 13% (95% CI 10–18%) across 19 studies and 3,313 survivors; variable criteria, exposure histories and age at assessment limited comparability [34]. Body mass index alone can underestimate excess adiposity after pediatric cancer treatment, highlighting the potential value of waist measures and body-composition assessment [40].

Breast cancer and treatment-associated weight change

A chemotherapy-associated weight-gain meta-analysis reported an average increase of 2.7 kg during breast cancer treatment, with substantial statistical heterogeneity (I^2 94.2%) [28,41,42]. An observational follow-up of 28 breast cancer survivors described further deterioration in several metabolic syndrome components 4–5 years after chemotherapy, although its small sample constrains generalizability [29]. Post-treatment weight trajectory depends on age, endocrine treatment, ovarian function, baseline adiposity and lifestyle. Longitudinal measures remain more informative than a single post-treatment body mass index.

Immune checkpoint inhibitor–associated endocrinopathies

An evidence synthesis of 177 checkpoint inhibitor studies including 44,595 patients estimated hypothyroidism in 10.1% (95% CI 8.9–11.4%), thyrotoxicosis in 4.6% (95% CI 3.8–5.7%), and hypophysitis in 0.8% (95% CI 0.5–1.1%) for the evaluated newer agents [30]. A separate 69-trial comparison found a hypothyroidism RR of 7.81 (95% CI 5.68–10.74) compared with controls and an elevated risk of insulin-dependent diabetes (RR 1.52; 95% CI 1.07–2.18) [31]. Immunotherapy-related thyroid or pituitary dysfunction may require prolonged hormonal follow-up even after antineoplastic therapy ends [21,32,33].

Generalizability, reporting bias and evidence certainty

Many endocrine outcomes were established in large observational cohorts, whereas long-term treatment-specific surveillance and clinical prevention trials were comparatively scarce. Age at diagnosis, radiation field and dose, sex, obesity, treatment mix and attrition may account for part of the observed heterogeneity. Associations from cohorts are not interchangeable with causal drug effects. Childhood, adolescent and young adult survivor guidance emphasizes individualized monitoring for metabolic syndrome, particularly after cranial or total-body irradiation [16,25,27].

Cross-population interpretation and certainty

Comparative findings are strongest where exposure is measured accurately and outcomes are objectively ascertained. Radiation dose-response analyses provide biological coherence but remain susceptible to survival and confounding biases. Adult endocrine-therapy cohorts quantify risk in older populations who already have high baseline metabolic disease prevalence. Short-duration immune checkpoint trials identify treatment-emergent adverse events, whereas survivorship cohorts measure persistent or late effects; combining their incidences would be misleading. No common prevalence or RR across all endocrine endpoints was calculated.

Table 3. Risk-adapted metabolic and endocrine follow-up in cancer survivorship

Risk context	Suggested evaluation	Rationale / scope
Abdominal or total-body irradiation	Glucose/HbA1c assessment, weight and waist measurements	Higher observed diabetes risk; frequency individualized [4–6,16].
ADT for prostate cancer	Glycemia, lipids, weight, waist and muscle/functional assessment	Insulin resistance, fat gain and lean-mass loss [7,10,12].

Breast cancer chemotherapy	Weight trajectory, activity, diet and cardiometabolic factors	Early gain can persist; promote sustainable physical activity [8,19].
Cranial/neck irradiation	Targeted pituitary/thyroid hormone testing by field and symptoms	Late, dose-related endocrine injury [2,3].
Checkpoint inhibitor exposure	Thyroid function; assess cortisol/glucose when clinically indicated	Immune thyroid, pituitary, adrenal and pancreatic toxicity [13,14].
Childhood/adolescent cancer survivors	Blood pressure, adiposity, glucose and lipid screening	Lifetime risk of cardiometabolic clustering [16].

Table 4. Evidence appraisal across metabolic and endocrine outcome domains

Outcome domain	Principal strength	Main limitation
Diabetes following childhood irradiation	Large survivor cohorts and exposure-specific comparisons	Confounding, late outcome ascertainment, survivor selection
Obesity and metabolic syndrome	Longitudinal body-composition studies and large cohorts	Variable obesity definitions; age and treatment differences
Breast cancer-associated weight gain	Prospective data and published meta-analysis	High heterogeneity; chemotherapy and endocrine therapy overlap
Androgen-deprivation metabolic effects	Within-person body-composition trajectories and cohort risk estimates	Nonrandom treatment indication and baseline cardiometabolic risk
Checkpoint inhibitor endocrinopathies	Large trial meta-analyses, clinically characterized events	Short follow-up and event classification variability
Pituitary, thyroid and gonadal late effects	Exposure-linked clinical guidelines and survivor cohorts	Long latency; nonuniform laboratory surveillance

DISCUSSION

Principal findings

Therapy-associated metabolic and endocrine outcomes follow several distinct patterns. Childhood abdominal radiotherapy carries an association with diabetes that can persist long after treatment. Hormonal treatments alter fat and muscle compartments, and breast cancer chemotherapy is linked to clinically important weight trajectories in a substantial subset of survivors. Radiation-induced endocrine failure and immunotherapy-associated gland injury introduce additional lifelong treatment and surveillance requirements. These findings support tailored screening based on prior exposures rather than a uniform survivorship laboratory panel.

Biological mechanisms and causality

Radiation-related diabetes may involve pancreatic injury, altered insulin sensitivity and secondary effects of other endocrine injuries. Gonadal suppression shifts fat distribution and reduces anabolic support for skeletal muscle. Chemotherapy may precipitate menopause, impair physical function and modify behavior. Checkpoint inhibition can produce organ-specific autoimmune inflammation. Observational associations cannot always distinguish these pathways from age, baseline susceptibility, cancer-related inactivity, concurrent steroids and social determinants of health. Outcomes should therefore be reported by treatment, dose, latency and disease subgroup rather than attributed to cancer survivorship as a homogeneous exposure.

Public health and exposure-based survivorship care

Risk-stratified follow-up is particularly important after pediatric and adolescent cancer treatment. An Indian survivorship cohort described thyroid dysfunction in 7.5%, other endocrine late effects in 13.6%, and metabolic syndrome in 4% of 3,067 childhood cancer survivors [35]. A systematic review from low- and middle-income settings found substantial variation in definitions and follow-up, with reported metabolic syndrome prevalence ranging from 4% to 17% [36]. These patterns reinforce the need for feasible primary-care screening pathways, effective transition from pediatric services, and appropriate endocrine referral [22,25,38].

Clinical implications

Clinical assessment should record cancer diagnosis, treatment combinations, estimated radiation fields and dose, glucocorticoid history, endocrine therapy duration and onset of metabolic abnormalities. Surveillance requires attention to glucose regulation, blood pressure, lipids, weight trajectory, waist circumference and body composition, alongside exposure-specific hormone testing. Nutritional assessment and resistance or aerobic exercise should be adapted to fatigue, sarcopenia, function and treatment contraindications; survivorship guidance emphasizes preserving muscle mass and avoiding excess adiposity [16,19]. Endocrinology referral is appropriate for suspected pituitary/adrenal failure, immune checkpoint-related insulin deficiency, or complex combined hormonal disorders.

Limitations

Cancer diagnoses, ages, treatments and outcome definitions differed considerably across studies. Several cohorts relied on self-reported diabetes, baseline adiposity was not always measured, and follow-up and surveillance intensity varied. Trials of immunotherapy primarily document toxicity during treatment rather than lifelong prevalence. Treatment cohorts may have overlapping participants across publications and reviews.

CONCLUSION

Cancer survivorship is associated with a clinically meaningful spectrum of diabetes, obesity, body-composition changes and endocrine dysfunction. Associations vary by cancer therapy, age at exposure and anatomical target. Abdominal radiation, androgen deprivation, selected systemic therapies and immune checkpoint blockade justify risk-based metabolic or hormonal evaluation. Long-term multidisciplinary care should prioritize early detection, prevention of cardiometabolic complications and prompt management of persistent endocrinopathies.

REFERENCES

1. Shapiro CL. Cancer survivorship. N Engl J Med. 2018;379:2438–2450. doi:10.1056/NEJMra1712502.
2. Chemaitilly W, Cohen LE, Mostoufi-Moab S, et al. Endocrine late effects in childhood cancer survivors. J Clin Oncol. 2018;36:2153–2159. doi:10.1200/JCO.2017.76.3268.
3. Sklar CA, Antal Z, Chemaitilly W, et al. Hypothalamic-pituitary and growth disorders in survivors of childhood cancer: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2018;103:2761–2784. doi:10.1210/jc.2018-01175.
4. Meacham LR, Sklar CA, Li S, et al. Diabetes mellitus in long-term survivors of childhood cancer: increased risk associated with radiation therapy. Arch Intern Med. 2009;169:1381–1388. PMID:19667301.
5. Friedman DN, Moskowitz CS, Hilden P, et al. Radiation dose and volume to the pancreas and subsequent risk of diabetes mellitus: a report from the Childhood Cancer Survivor Study. J Natl Cancer Inst. 2020;112:525–532. doi:10.1093/jnci/djz152.
6. de Vathaire F, El-Fayech C, Ben Ayed FF, et al. Radiation dose to the pancreas and risk of diabetes mellitus in childhood cancer survivors: a retrospective cohort study. Lancet Oncol. 2012;13:1002–1010. doi:10.1016/S1470-2045(12)70323-6.
7. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. J Clin Oncol. 2006;24:4448–4456. doi:10.1200/JCO.2006.06.2497.
8. His M, Baggio I, Chabaud S, et al. Long-term weight change among breast cancer patients treated with chemotherapy: a longitudinal study over 13 years. Breast Cancer Res. 2025;27:117. doi:10.1186/s13058-025-02079-6.
9. Wilson CL, Liu W, Yang JJ, et al. Genetic and clinical factors associated with obesity among adult survivors of childhood cancer: a report from the St. Jude Lifetime Cohort. Cancer. 2015. PMID:25963547.
10. Smith MR. Changes in fat and lean body mass during androgen-deprivation therapy for prostate cancer. Urology. 2004;63:742–745. doi:10.1016/j.urology.2003.10.063.
11. Mostoufi-Moab S, et al. Insulin and glucose homeostasis in childhood cancer survivors treated with abdominal radiation: a pilot study. PMID:30009519.
12. Galvão DA, Spry NA, Taaffe DR, et al. Body composition changes during androgen deprivation therapy for prostate cancer: a 2-year prospective study. PMID:18706829.
13. Barroso-Sousa R, Barry WT, Garrido-Castro AC, et al. Incidence of endocrine dysfunction following the use of different immune checkpoint inhibitor regimens: a systematic review and meta-analysis. JAMA Oncol. 2018;4:173–182. doi:10.1001/jamaoncol.2017.3064.
14. Incidence of endocrine-related dysfunction in patients treated with new immune checkpoint inhibitors: a meta-analysis and comprehensive review. PMID:37956967.
15. Metabolic syndrome in long-term survivors after allogeneic hematopoietic stem cell transplantation. PMID:35459338. doi:10.48095/ccko2022132.
16. Metabolic syndrome in childhood, adolescent, and young adult cancer survivors: recommendations for surveillance from the International Late Effects of Childhood Cancer Guideline Harmonization Group. PMID:40103414.
17. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.
18. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi:10.1136/bmj.l4898.
19. Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. CA Cancer J Clin. 2022;72:230–262. doi:10.3322/caac.21719.

20. Smith MR, Finkelstein JS, McGovern FJ, et al. Changes in body composition during androgen deprivation therapy for prostate cancer. J Clin Endocrinol Metab. 2002;87:599–603. doi:10.1210/jcem.87.2.8299.
21. Husebye ES, Castinetti F, Criseno S, et al. Endocrine-related adverse conditions in patients receiving immune checkpoint inhibition: an ESE clinical practice guideline. Eur J Endocrinol. 2022;187:G1–G21. doi:10.1530/EJE-22-0689.
22. Chemaitilly W, Cohen LE. Endocrine late-effects of childhood cancer and its treatments. Eur J Endocrinol. 2017;176:R183–R203. doi:10.1530/EJE-17-0054.
23. Rose SR, Horne VE, Howell J, et al. Late endocrine effects of childhood cancer. Nat Rev Endocrinol. 2016;12:319–336.
24. Long-Term Endocrine and Metabolic Consequences of Cancer Treatment: A Systematic Review. Endocr Rev. 2019;40:711–767. https://academic.oup.com/edrv/article/40/3/711/5198606
25. Hammoud RA, Mulrooney DA, Rhea IB, et al. Modifiable cardiometabolic risk factors in survivors of childhood cancer: JACC: CardioOncology state-of-the-art review. JACC CardioOncol. 2024;6(1). doi:10.1016/j.jaccao.2023.12.008.
26. Prevalence and determinants of diabetes mellitus in 2338 long-term Dutch childhood cancer survivors (DCCS-LATER2 Study). J Clin Endocrinol Metab. 2025. PMID:39916355.
27. Prevalence and determinants of metabolic syndrome in 2338 childhood cancer survivors: a Dutch Childhood Cancer Survivor LATER 2 Study. Cancer. 2025. PMID:39748458.
28. Weight change during chemotherapy in breast cancer patients: a meta-analysis. 2017. PMID:28403873.
29. Metabolic syndrome and breast cancer survivors: a follow-up analysis after completion of chemotherapy. 2022. PMID:35241143.
30. Incidence of endocrine-related dysfunction in patients treated with new immune checkpoint inhibitors: a meta-analysis and comprehensive review. 2023. PMID:37956967.
31. Risk and incidence of endocrine immune-related adverse effects under checkpoint inhibitor mono- or combination therapy in solid tumors: a meta-analysis of randomized controlled trials. 2023. PMID:37967245.
32. Risk of pituitary immune-related adverse events caused by immune checkpoint inhibitors: a systematic review and meta-analysis. 2025. PMID:40532761.
33. Incidence and risk assessment of thyroid dysfunction following immune checkpoint inhibitor therapy: a systematic review and meta-analysis. 2025. PMID:41552314.
34. Prevalence and risk factors of metabolic syndrome in survivors of childhood acute leukemia: a systematic review and meta-analysis. 2026. PMID:41508003.
35. Long-term outcomes in survivors of childhood cancer: a 30-year experience from India. 2022. PMID:36332172.
36. Physical late effects of treatment among survivors of childhood cancer in low- and middle-income countries: a systematic review. 2024. PMID:38183576.
37. The safety and efficacy of metformin on metabolic syndrome parameters in prostate cancer patients receiving androgen deprivation therapy: a systematic review and meta-analysis. 2026. PMID:42836214.
38. Endocrine late-effects in survivors of childhood and adolescence cancer: clinical management. 2026. PMID:41642435.
39. Endocrine and metabolic late effects in childhood cancer survivors in Germany: the VersKiK study. Eur J Endocrinol. 2026. doi:10.1093/ejendo/lvag010.
40. Validity of anthropometric measurements for characterizing obesity among adult survivors of childhood cancer: a report from the St. Jude Lifetime Cohort Study. 2015. PMID:25728221.
41. Jain A, Saxena R, Omhare A, Fatima A, Saxena R, Hashmi SZA, Singh K, Paul R. Microbiological and Histopathological Features of Gynecologic Cancers: A Systematic Review of Current Evidence and Future Directions. Cureus. 2026 Aug 6;18(8):e114047. doi: 10.7759/cureus.114047. PMID: 42701680; PMCID: PMC13545701.
42. Jain A, Meena M, Vincent S, Sheikh I, Sharma S, Singh K, Paul R. Comparative evaluation of hrHPV DNA testing, cervical cytology and histopathology for cervical precancer detection. Bioinformation. 2026 Jun 30;22(6):3395-3399. doi: 10.6026/973206300223395. PMID: 42701751; PMCID: PMC13545909.