

Supplementary Table 1. Adverse Health Outcomes Comprising the Cumulative Burden of Morbidity (CBM) Score^a.

Adverse Health Outcome	Platinum Study item(s) used to assign severity grade	Grade 1	Grade 2	Grade 3	Grade 4
Peripheral sensory neuropathy	Tingling fingers/hands or toes/feet ^b Numbness in fingers/hands or toes/feet ^b Shooting or burning pain in fingers/hands or toes/feet ^b Difficulty distinguishing between hot and cold water ^b Problems standing/walking because of difficulty feeling ground under feet ^b Pain and tingling in fingers/hands or toes/feet ^d Prescription medication use ^g	A little	Quite a bit	Very much	NA ^c
Autonomic neuropathy	Dizzy when standing up from a sitting or lying position ^b	A little	Quite a bit	Very much	NA
Hearing loss/damage	Difficulty hearing ^b Reduced hearing ^d Hearing loss requiring a hearing aid ^e Complete deafness ^e Persistent dizziness or vertigo ^e	A little (difficulty hearing or reduced hearing) OR Yes (persistent dizziness or vertigo)	Quite a bit or very much (difficulty hearing or reduced hearing)	Hearing loss requiring a hearing aid in one or both ears OR complete deafness in one ear	Complete deafness in both ears
Tinnitus	Ringing in ears ^d	A little	Quite a bit	Very much	NA
Raynaud phenomenon	White cold fingers/hands or toes/feet when it is cold ^d	A little	Quite a bit	Very much	NA
Pain	How much did pain interfere in normal work (including work outside the home and inside the house, yard) ^f Prescription medication use ^g	A little bit	Moderately OR quite a bit OR medication use	Extremely	NA
Kidney disease	Told by doctor of condition Prescription medication use ^g	Have condition	Have condition AND medication use	NA	NA
Hypercholesterolemia	Told by doctor of condition Prescription medication use for high total cholesterol or low HDL cholesterol ^g	NA	Have condition AND medication use	NA	NA
Hypertriglyceridemia	Prescription medication use ^g	NA	Medication use for condition	NA	NA
Adverse Health Outcome	Platinum Study item(s) used to assign severity grade	Grade 1	Grade 2	Grade 3	Grade 4
Hypertension	Told by doctor of condition Prescription medication use ^g	NA	Have condition AND medication use	NA	NA

Diabetes	Told by doctor of condition Prescription medication use ^g	NA	Have condition AND taking tablets or pills	Have condition AND taking insulin	NA
Coronary artery disease	Told by doctor of condition - angina Told by doctor of condition - coronary artery disease Heart attack or myocardial infarction Had relevant procedure	Have angina or coronary artery disease	Have angina or coronary artery disease AND either medication use, angioplasty, or stent placement	Had heart attack or myocardial infarction OR have had coronary bypass surgery	NA
Transient ischemic attack	Told by doctor of condition	Have condition	NA	NA	NA
Stroke	Told by doctor of condition Surgical procedure	NA	Have condition	NA	Have condition AND had carotid artery surgery
Peripheral artery disease	Pain in calf when walking (intermittent claudication) Had relevant procedure Prescription medication use ^g	Have condition	Have condition AND medication use	Have condition AND had peripheral artery surgery	NA
Thromboembolic event	Blood clot in leg (deep vein thrombosis) Blood clot in lung (pulmonary embolism) Prescription medication use ^g	NA	Have deep vein thrombosis	Have pulmonary embolism OR medication use	NA
Obesity	Body mass index ^h (measured at time of study assessment)	NA	BMI: 25-29 kg/m ²	BMI:30-39 kg/m ²	BMI ≥ 40 kg/m ²
Thyroid disease	Overactive thyroid Underactive thyroid Prescription medication use ^g	Have condition	Have condition AND medication use	NA	NA
Anxiety/depression	Prescription medication use ^g	NA	Medication use for condition	NA	NA

Comment [SK1]: MOVE FOOTNOTE

Adverse Health Outcome	Platinum Study item(s) used to assign severity grade	Grade 1	Grade 2	Grade 3	Grade 4
Erectile dysfunction	Difficulty getting or maintaining an erection ^b Prescription medication use ^g	A little	Quite a bit or very much OR medication use	NA	NA
Hypogonadism	Prescription medication use ^g	NA	Medication use for condition	NA	NA

^a All questions were asked in the context of considering symptoms in the past 4 weeks.

^b For conditions based on more than one question, the severity grade was assigned based on the response reporting the greatest or most severe symptom.

^b Assessed with the EORTC/CIPN-20 questionnaire based on symptoms experienced over the past 4 weeks.⁶⁸ For each item, participants were asked whether the symptom started before, during or after chemotherapy. If participants responded that the symptoms started before chemotherapy, those responses were not considered when assigning severity grade.

^c NA, not applicable. Data needed to assign grade were not captured.

^d Assessed with the SCIN questionnaire based on symptoms experienced over the past 4 weeks.⁶⁹ For each item, participants were asked whether the symptom started before, during or after chemotherapy. If participants responded that the symptom started before chemotherapy, those responses were not considered when assigning severity grade.

^e Item is from the Hearing Handicap Inventory by Ventry and Weinstein and assessed symptoms at the time of clinical evaluation.⁷⁰ For each item, participants were asked to report the age (in years) at first occurrence. If onset of symptoms was prior to age of GCT diagnosis, those responses were not considered when assigning severity grade.

^f Item is from the SF36 questionnaire and assessed symptoms experienced over the past 4 weeks.⁷¹

^g Prescription medications taken for at least the past 4 weeks were only used to assign grade if the participant reported that the indication was for the given adverse health outcome and the medication was started during or after chemotherapy.

^h Body mass index is based on physical examination performed at time of clinical assessment.

Supplementary Table 2. Definition of the Cumulative Burden of Morbidity Score Based on Number and Severity of Individual Adverse Health Outcomes^a

	None	Very Low	Low	Medium	High	Very High	Severe
Grade 1	0	≥ 1	Any number	Any number	Any number	Any number	Any number
Grade 2	0	0	≥ 1	Any number	Any number	Any number	Any number
Grade 3	0	0	0	≥ 1	≥ 2	≤ 1	≥ 2
Grade 4	0	0	0	0	0	1	1

^a Methods adapted from Geenen et al.¹⁵ Modifications include division of the low category into very low and low, and division of the high category into high and very high to reflect the granularity of data collected in the present study.

No	14 (3.7)	20 (5.3)	123 (32.5)	116 (30.7)	76 (20.1)	29 (7.7)	
Yes	51 (6.1)	84 (10.1)	334 (40.0)	244 (29.2)	104 (12.5)	18 (2.2)	
Retroperitoneal lymph node dissection, number (%)^j							
No	39 (6.1)	50 (7.8)	227 (35.4)	199 (31.0)	95 (14.9)	32 (5.0)	0.11
Yes	26 (4.6)	53 (9.4)	228 (40.4)	159 (28.2)	83 (14.7)	15 (2.7)	
Bleomycin, number (%)							
No	25 (5.2)	42 (8.7)	195 (40.5)	134 (27.8)	71 (14.7)	15 (3.1)	0.58
Yes	40 (5.5)	62 (8.5)	263 (35.9)	226 (30.9)	109 (14.9)	32 (4.4)	
Type of chemotherapy, number (%)^k							
EP x 4 cycles	15 (4.3)	35 (9.9)	146 (41.4)	99 (28.1)	48 (13.6)	10 (2.8)	0.19
BEP x 3 cycles	31 (6.7)	40 (8.7)	169 (36.7)	138 (30.0)	59 (12.8)	23 (5.0)	
BEP x 4 cycles	9 (4.1)	16 (7.2)	88 (36.0)	66 (29.7)	43 (19.4)	8 (3.6)	
VIP x 4 cycles	2 (6.5)	0	9 (29.0)	13 (40.6)	7 (21.9)	1 (3.1)	

^a Categories were collapsed due to sparse data. Among the 47 individuals, 46 had a CBM score of 'very high' and 1 individual had a CBM score of 'severe'.

^b p-value derives from analysis of log-transformed values due to unequal variance between groups. Means and standard deviations are from untransformed values.

^c Data on race were not available for 35 participants.

^d Data on educational level were not available for 3 participants.

^e Data on marital status were not available for 15 participants.

^f Data on employment status were not available for 19 participants.

^g Data on smoking status were not available for 19 participants.

^h Data on alcohol consumption were not available for 9 participants.

ⁱ Data on physical activity were not available for 1 participant.

^j Data on RPLND were not available for 13 participants.

^k Other chemotherapy regimens not included in the comparisons are EP other than 4 cycles (n=28), BEP other than 3 or 4 cycles (n=28), VIP other than 4 cycles (n=12), or other platinum-based regimens (n=72).

Supplementary Table 4. Summary of U.S. Studies of Testicular Cancer Survivors (TCS).

Reference (Author, year)	Fung 2017 ²	Reilley 2014 ^{a,23}	Kim 2011 ²¹		Oh 2007 ²²		Shinn 2007 ^{a,24}	Hashibe 2016 ^{b,20}	
Population	Testicular cancer	Testicular cancer	Testicular cancer	Cancer-free men	Testicular cancer; received platinum	Testicular cancer; no platinum	Testicular cancer	Testicular cancer	Cancer-free men ^c
Number of patients	952 ^d	189	246	236	118	25	162	785	3,323
Cohort source	8 cancer centers: U.S. and Canada	Pennsylvania Cancer Registry	STEED study ^e	STEED study	M.D. Anderson GU Cancer Clinic	M.D. Anderson GU Cancer Clinic	M.D. Anderson GU Cancer Clinic	Utah Population Database	Utah Population Database
Calendar years of TC diagnosis	1979-2015	1990-2005	1988-2002	---	NA	NA	NA	1991-2007	---
Age at TC diagnosis [mean ± SD or median (range)], years	31 (15-53)	NA	29.3 ^{f,g}	29.1 ^{h,g}	NA	NA	32.1 ± 8.6	31 (15-58)	--
Ethnicity, %									
White	86	95	90	94.1	NA	NA	87	99	94
Other	14	5	10	5.9	NA	NA	13	1	2.6
Unknown	0	0	0	0	NA	NA	0	0	3.5
Type of therapy, %									
Chemotherapy	100 ^j	33	18	---	NA ^k	NA ^k	61 ^l	21.4 ^l	---
Radiation	0	85	24	---	NA ^m	NA ^m	29 ⁿ	38.5 ⁿ	---
Surgery	100	69	58	---	NA ^o	NA ^o	1 ^p	37.1 ^p	---
Other treatment	0	0	0	----	NA	NA	8 ^q	3.1 ^r	----
Source of therapy data	Medical record	Self-report	Self-report	---	Medical record	Medical record	Medical record	Medical record	---
Duration of follow up [mean ± SD or median (range)], years	4.3 (1-29.9) ^s	6.78 ± 3.8 ^t	13.7 ^{f,g,t}	NA	8.6 ^{f,g,t}	7.3 ^{f,g,t}	4.5 ± 1.6 ^s	10 ^t (5-21)	11.8 (5-21)
Age at evaluation [mean ± SD or median (range)], years	37 (19-68)	43.6 ± 9.9	NA ^u	NA ^v	40.4 ^f (17-72)	44.6 ^f (20-74)	37.2 ± 9.0	NA (22-69) ^w	NA (22-69) ^x
BMI ≥ 25 kg/m ²	73.3 ^y	83.5	79.3 ^z	80.51 ^{aa}	NA	NA	NA	62.3 ^{bb}	63.8 ^{cc}
Waist circumference, cm (median, range)	94 (57-190)	NA	NA	NA	NA	NA	NA	NA	NA

Reference (Author, year)	Fung 2017 ²	Reilley 2014 ^{a,23}	Kim 2011 ²¹		Oh 2007 ²²		Shinn 2007 ^{a,24}	Hashibe 2016 ^{b,20}	
Population	Testicular cancer	Testicular cancer	Testicular cancer	Cancer-free men	Testicular cancer; received platinum	Testicular cancer; no platinum	Testicular cancer	Testicular cancer	Cancer-free men ^c
Prevalence of health behaviors, %^{dd}									

Current smoker	8.3	25	NA	NA	NA	NA	19	NA	NA
Physical activity									
Moderate level	95.8 ^{ee}	NA ^{ff}	NA	NA	NA	NA	NA	NA	NA
Vigorous level	69.0 ^{ee}	NA ^{ff}	NA	NA	NA	NA	15.9 ^{gg}	NA	NA
Heavy drinkingⁿⁿ	11.4	34.9	NA	NA	NA	NA	46	NA	NA
Prevalence of adverse health outcomes, %^{dd,ii,jj,kk}									
Cardiovascular and related disorders									
Hypertension	11.6	NA	NA	NA	33 ^{ll}	47.6 ^{ll}	NA	11.7 per 1000 PY	11.1 per 1000 PY
Hyperlipidemia	10.5	NA	NA	NA	14.6	28	NA	6.3 per 1000 PY ^{mm}	3.9 per 1000 PY ^{mm}
Coronary artery disease	0.7	NA	NA	NA	5.4	0	NA	1.2 per 1000 PY	1.3 per 1000 PY
Cerebrovascular disease	1.0	NA	NA	NA	0	0	NA	0.6 per 1000 PY	0.9 per 1000 PY
Peripheral vascular disease	3.0	NA	NA	NA	NA	NA	NA	NA	NA
Thromboembolic disease	0.5	NA	NA	NA	NA	NA	NA	1.2 per 1000 PY ⁿⁿ	1.0 per 1000 PY ⁿⁿ
Raynaud phenomenon	18.7	NA	NA	NA	NA ^{oo}	NA ^{oo}	NA	NA	NA
Neurotoxicity									
Hearing issues and/or tinnitus	47.9	NA	NA	NA	NA	NA	NA	0.6 per 1000 PY	0.2 per 1000 PY
CIPN	27.0	NA	NA	NA	NA	NA	NA	4.4 per 1000 PY	3.0 per 1000 PY
Others									
Renal disease	2.6	NA	NA	NA	5.8	0	NA	1.4 per 1000 PY	1.6 per 1000 PY
Diabetes on medication	3.1	NA	NA	NA	NA	NA	NA	3.3 per 1000 PY	4.0 per 1000 PY
Thyroid disease	2.4	NA	NA	NA	NA	NA	NA	NA	NA

Reference (Author, year)	Fung 2017 ²	Reilley 2014 ^{a,23}	Kim 2011 ²¹		Oh 2007 ²²		Shinn 2007 ^{a,24}	Hashibe 2016 ^{b,20}	
Population	Testicular cancer	Testicular cancer	Testicular cancer	Cancer-free men	Testicular cancer; received platinum	Testicular cancer; no platinum	Testicular cancer	Testicular cancer	Cancer-free men ^c
Hypogonadism on medication	9.9	NA	NA	NA	NA	NA	NA	NA	NA
Erectile dysfunction	12.1	NA	NA	NA	NA	NA	NA	NA	NA

BMI = body mass index; CI= confidence Interval; CIPN = chemotherapy-induced peripheral neuropathy; GU = genitourinary; HR = hazard ratio; MET = metabolic equivalent value; NA = not available; PY = person-years; SD = standard deviation; TC = testicular cancer; TCS = testicular cancer survivors; U.S. STEED = United States Servicemen's Testicular Tumor Environmental and Endocrine Determinants Study

- ^a No control group was included.
- ^b Statistically significant hazards ratios (HR) comparing results in testicular cancer patients vs. cancer free men were observed for hyperlipidemia (HR 1.70; 95% CI 1.19-2.41). Nonsignificant HR were observed for coronary artery disease (HR 0.93), cerebrovascular disease (HR 0.67), diabetes (HR 0.63), hypertension (HR 0.99), hypertriglyceridemia (HR 1.0), obesity (0.93), peripheral neuropathy (1.29), hearing loss (HR 1.79), thromboembolic disease (pulmonary embolism) (HR 1.3), renal failure (HR 0.79), and dyslipidemia (HR 1.14).
- ^c Cancer-free men were randomly selected from men in the Utah Population Database, for whom medical records were available at the University of Utah Health Sciences Center data warehouse or Intermountain system. Each testicular cancer case was matched to 4–5 cancer-free men on birth year, birth region, and date of last residence in Utah.
- ^d Of 952 patients, 842 (88.5%) had testicular germ cell tumors (GCT) whereas 109 (11.4%) had GCT at other sites. For 1 (0.1%) patient, GCT site was unknown. All patients in Fung et al² are also included in the present study.
- ^e The STEED study had a response rate of 47.6%. Men who never had a diagnosis of testicular germ cell tumor (TGCT) and had a blood serum sample in Department of Defense Serum Repository were eligible to be controls.
- ^f Mean value
- ^g Standard deviation is not available.
- ^h Mean age at reference date.
- ⁱ Since treatment groups in Reilly et al²³, Kim et al²¹, Oh et al²², Shinn et al²⁴, and Hashibe et al²⁰ did not consist of mutually exclusive categories, patients may have had more than one type of treatment. Patients with testicular germ cell tumors in Fung et al² received platinum-based chemotherapy after surgical management.
- ^j All TCS received cisplatin-based chemotherapy.
- ^k Among TCS given chemotherapy, 82.5% consisted of platinum-based regimens, although the number receiving cisplatin- vs. carboplatin-based chemotherapy was not provided. Remaining patients (17.5%) received non-platinum-based chemotherapy.
- ^l Surgery and chemotherapy.
- ^m Among all 143 survivors, 30 (21%) had received radiation.
- ⁿ Surgery and radiotherapy.
- ^o Among all 143 survivors, 138 (96.5%) had had orchiectomy.
- ^p Surgery only.
- ^q These patients received other treatments including surgery, radiation and chemotherapy.
- ^r Patients received other treatments including radiotherapy only; chemotherapy only; or radiation, chemotherapy and orchiectomy; or their treatments were unknown.
- ^s Duration of follow-up since completion of TC therapy.
- ^t Duration of follow-up since TC diagnosis.
- ^u Mean or median age at evaluation was not provided. However, the study reported the following percentage of TCS in the following age ranges: 18-29 years, 3%; 30-39 years, 36%; 40-49 years, 41%; and 50+ years, 20.5%.
- ^v Mean or median age at evaluation was not provided. However, the study reported the following percentages of controls in the following age ranges: 18-29 years, 3.4%; 30-39 years, 32.5%; 40-49 years, 44.1%; and 50+ years, 19.9%.
- ^w Mean or median age at the end of follow-up was not provided. However, the study reported the following percentage of patients in the following age ranges: 22-35 years (18.2%); 35-44 years (33.8%), 45-54 years (31.7%), 55-69 years (16.3%).
- ^x Mean or median age was not provided. However, the study reported the following percentage of controls in the following age ranges: 22-35 years (16%); 35-44 years (35.1%), 45-54 years (31.7%), 55-69 years (17.2%).
- ^y Among 952 TCS, 42.4% were overweight (BMI: 25 to <30 kg/m²) and 30.9% were obese (BMI ≥ 30 kg/m²).
- ^z Among 246 TCS, 47.2% were overweight (BMI 25-29.9 kg/m²) and 32.1% were obese (BMI >30 kg/m²).
- ^{aa} Among 236 controls, 42.8% were overweight (BMI 25-29.9 kg/m²) and 37.71% were obese (BMI >30 kg/m²).
- ^{bb} BMI at baseline. Among 785 TCS, 44.3% were overweight (BMI 25-29.9 kg/m²) and 18% were obese (BMI >30 kg/m²).
- ^{cc} BMI at baseline. Among 3,323 cancer-free men, 43.5% were overweight (BMI 25-29.9 kg/m²) and 20.3% were obese (BMI >30 kg/m²).
- ^{dd} For four studies ^{21,23,24} that included TCS from multiple treatment groups, health behaviors and outcomes were not stratified by type of therapy.
- ^{ee} Vigorous activity defined as MET ≥ 6 and moderate activity defined as MET 3 to <6.
- ^{ff} Reported that 50.3% of survivors had adequate aerobic exercise and 28% had adequate strength/flexibility. The authors used the Rapid Assessment of Physical Activity, which assesses aerobic activity and strength and flexibility in adults.
- ^{gg} Definition of vigorous activity not provided.
- ^{hh} Heavy drinking was defined as ≥ 2 alcoholic drinks daily. Reilly et al.²³ and Shinn et al.²⁴ defined heavy drinking as 5 or more drinks at one time in past month
- ⁱⁱ Refer to methods section in Fung et al² and Appendix Table 1 therein for definitions of adverse health outcomes (AHO), which were also stratified by type of chemotherapy. AHO are based on patient report. Diagnoses of hypertension, hypercholesterolemia and diabetes required that patients have been (1) told by a physician that they had the condition, and (2) were currently on prescription medications for the condition.

ⁱⁱ Definitions provided by Oh et al.²² are as follows: 1) hypertension: prior diagnosis or use of antihypertensive medication; 2) hyperlipidemia: prior diagnosis or use of cholesterol-lowering agents; 3) coronary artery disease: prior diagnosis of angina or myocardial infarction, and 4) renal insufficiency: prior diagnosis or creatinine level higher than 1.5 mg/dL; diagnostic criteria were not provided for Raynaud phenomenon.

^{kk} To determine adverse health outcomes, Hashibe et al²⁰ used ICD-9 and CPT (current procedural terminology) codes.

^{ll} Hypertension diagnosis was based on history plus measured blood pressure.

^{mmm} Percentages are shown for hypercholesterolemia. Hypertriglyceridemia was also assessed (incidence rate: 0.7 and 0.6 per 1,000 PY for cases and controls, respectively (HR, 1.0, 95% CI, 0.37-2.70)). The incidence rate of dyslipidemia (defined as high TG, high cholesterol, and low HDL) was 9.7 and 8.7 per 1,000 PY for cases and controls, respectively (HR, 1.14, 95% CI, 0.86-1.49). Definitions were not provided for hypercholesterolemia, hypertriglyceridemia, or dyslipidemia.

ⁿⁿ Pulmonary embolism.

^{oo} Among all 143 survivors, 16 (11.2%) reported Raynaud phenomenon.