**Supplementary data:**

**Burden of cardiovascular risk factors and cardiovascular disease in childhood cancer survivors: Data from the German CVSS-study**

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**Table S1:** Measurement and definition of cardiovascular risk factors in the CVSS-study cohort

|  |  |
| --- | --- |
| **CVRF** | **Definition/measurement** |
| Arterial hypertension | - Intake of antihypertensive medication within the past two weeks (CAPI, medical records and medication packages)  *and/ or*  - Mean systolic blood pressure of ≥ 140 mmHg and/ or mean diastolic blood pressure of ≥ 90 mmHg at rest in a three-time measurement in a sitting position after 5, 8 and 11 minutes (values reported corresponding to the average of the second and the third measurement) |
| Dyslipidaemia | - Physician´s diagnosis (CAPI, medical records)  *and/ or*  - LDL/HDL ratio > 3.5 and/ or a fasting blood triglyceride level ≥ 150 mg/dl |
| Obesity | - Body mass index (BMI) ≥ 30 kg/m² |
| Diabetes mellitus | - Physician`s diagnosis of any type of diabetes (CAPI, medical records)  *and/ or*  - Intake of antidiabetic medication within the past two weeks (CAPI, medical records, medication packages)  *and/ or*  - HBA1c ≥ 6.5% |
| Smoking | - Occasional and regular daily smokers (CAPI) |
| Positive family history for myocardial infarction and/ or stroke | - At least one reported first-degree relative with myocardial infarction or stroke at age ≤ 60 years (men) or ≤ 65 years (women) (CAPI) |
| Metabolic syndrome | At least 3 of the following 5 parameters:  - Waist circumference ≥ 94 cm (men), ≥ 80 cm (women)  - Fasting blood triglyceride level ≥ 150 mg/dl *and/ or* medication for elevated triglycerides  - Reduced HDL level ≤ 40 mg/dl (men), ≤ 50 mg/dl (women) *and/ or* medication for reduced HDL  - Elevated blood pressure (systolic ≥ 130 mmHG *and/ or* diastolic ≥ 85 mmHg *and/or* antihypertensive medication)  - HBA1c ≥ 6.5% *and/ or* physician´s diagnosis *and/ or* antidiabetic medication |

CAPI = Computer-assisted personal interview, CVRF = Cardiovascular risk factor,

HBA1c = Glycated haemoglobin A1c, HDL = High-density lipoprotein, LDL = Low-density lipoprotein

**Table S2:** Demographic characteristics of the CVSS-study sample and the comparison cohorts (GHS, DEGS, KORA)

a)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CVSS-study**  **N=**951 | **GHS**  **N=**8695 | **DEGS**  **N=**2915 | **KORA**  **N=**2034 |
|  | N (%) | N (%) | N (%) | N (%) |
| **Age at examination (years)** |  |  |  |  |
| 20-24 | 11 (1.2) |  | 158 (5.4) | 7 (0.3) |
| 25-29 | 216 (22.7) |  | 440 (15.1) | 319 (15.7) |
| 30-34 | 299 (31.4) |  | 469 (16.1) | 512 (25.2) |
| 35-39 | 256 (26.9) | 1468 (16.9) | 533 (18.3) | 456 (22.4) |
| 40-44 | 122 (12.8) | 1716 (19.7) | 686 (23.5) | 403 (19.8) |
| 45-49  50-54  55-59 | 47 (4.9) | 1874 (21.6)  1896 (21.8)  1741 (20.0) | 629 (21.6) | 337 (16.6) |
| **Sex** |  |  |  |  |
| Female | 425 (44.7) | 4279 (49.2) | 1,553 (53.3) | 1062 (52.2) |
| Male | 526 (55.3) | 4416 (50.8) | 1,362 (46.7) | 972 (47.8) |

b)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CVSS-study**  **N=**951 | **GHS**  **N=**8695 | **DEGS**  **N=**2915 | **KORA**  **N=**2034 |
| **Age at examination**  **(mean, SD)[years]** | 34.0 (5.6) | 47.4 (7.0) | 37.3 (7.5) | 36.7 (6.5) |
| **Period of data assessment** | 2013-2016 | 2007-2012 | 2008-2011 | 1999-2001 |

CVSS = Cardiac and vascular late sequelae in long-term survivors of childhood cancer, DEGS = German Health Interview and Examination Survey for Adults, GHS = Gutenberg Health Study, KORA = Cooperative Health Research in the region of Augsburg, SD = Standard deviation

**Table S3:** Continuous measures of cardiovascular risk factors among CVSS-study participants (N=951)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Mean / Standard deviation** | **Median (Q1/Q3)** | **Minimum** | **Maximum** |
|  |  |  |  |  |  |
| **Cardiovascular risk factor** |  |  |  |  |  |
| Body mass index (BMI) |  | 25.9 / ±5.3 | 24.9 (22.2/28.3) | 14.6 | 52.1 |
| Waist circumference | cm | 87.9 / ±13.8 | 86.6 (78.0/95.9) | 57.7 | 173.5 |
| High-density lipoprotein (HDL) | mg/dl | 55.2 / ±15.3 | 53.0 (44.0/64.0) | 19.0 | 123.0 |
| Low-density lipoprotein (LDL) | mg/dl | 131.2 / ±34.6 | 127.0 (107.0/152.0) | 22.0 | 284.0 |
| Lipids ratio (LDL/HDL) |  | 2.6 / ±1.0 | 2.4 (1.8/3.1) | 0.3 | 7.7 |
| Triglycerides | mg/dl | 119.1 / ±90.9 | 98.0 (72.0/137.0) | 26.0 | 1341.0 |
| Systolic blood pressure | mmHg | 123.0 / ±13.0 | 122.0 (113.5/131.0) | 87.5 | 185.0 |
| Diastolic blood pressure | mmHg | 79.9 / ±9.2 | 79.5 (73.5/85.5) | 51.5 | 119.5 |

CVSS = Cardiac and vascular late sequelae in long-term survivors of childhood cancer

**Table S4:** Age at examination and the prevalence of cardiovascular risk factors and cardiovascular disease among the CVSS-study participants according to ICCC 3 diagnoses and sex (without adjustment for age)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All** | **Age at examination** | **CVD** | **VTE** | **CHF** | **Arterial hypertension** | **Obesity** | **Dyslipidemia** | **Diabetes mellitus** | **Smoking** | **FH** |
|  | % (N) | Mean (SD)) | % (N) | % (N) | % (N) | % (N) | % (N) | % (N) | % (N) | % (N) | % (N) |
| All | 951 | 34.6 (5.5) | 4.5 (43)b | 2.0 (19)a | 1.2 (11)a | 23.0 (219)a | 17.4 (165)a | 28.3 (269)a | 2.0 (19)a | 21.5 (204)a | 19.7 (187)c |
| **ICCC3 diagnosis** |  |  |  |  |  |  |  |  |  |  |  |
| Leukaemia | 43.5 (414) | 34.3 (5.1) | 3.1 (13 )a | 1.5 (6)a | 0.5 (2)a | 20.1 (83)a | 19.3 (80) | 21.5 (89)a | 1.5 (6) | 23.2 (96)a | 21.7 (90)c |
| Lymphoma | 9.9 (94) | 37.5 (4.6) | 3.2 (3) | 1.1 (1) | 1.1 (1) | 31.9 (30) | 18.1 (17) | 42.6 (40)b | 2.1 (2) | 25.5 (24) | 22.3 (21)c |
| CNS tumours | 12.8 (122) | 35.5 (5.2) | 6.6 (8)b | 4.1 (5) | 0 (0) | 19.7 (24) | 20.5 (25) | 36.9 (45)a | 3.3 (4) | 19.7 (24)a | 18.0 (22)c |
| Sympathetic nervous system tumours | 7.6 (72) | 29.7 (4.1) | 2.8 (2)b | 1.4 (1) | 0 (0) | 20.8 (15) | 13.9 (10) | 25.0 (18)b | 2.8 (2) | 26.4 (19) | 11.1 (8)c |
| Retinoblastoma | 1.1 (10) | 29.2 (4.8) | 0 (0) | 0 (0) | 0 (0) | 20.0 (2) | 10.0 (1) | 30.0 (3 ) | 0 (0) | 50 (5) | 10.0 (1) |
| Renal tumours | 8.1 (77) | 32.8 (3.9) | 7.8 (6)b | 2.9 (3) | 2.6 (2) | 18.2 (14) | 14.3 (11) | 20.8 (16)b | 2.6 (2) | 16.9 (13) | 16.9 (13)b |
| Hepatic tumours | 0.7 (7 ) | 28.4 (2.0) | - (0) | 0 (0) | 0 (0) | - (0) | - (1) | - (1) | 0 (0) | - (1) | - (1) |
| Malignant bone tumours | 5.3 (50) | 40.6 (4.5) | 8.0 (4)b | 2.0 (1) | 4.0 (2) | 42 (21) | 10.0 (5) | 42 (21) | 4.0 (2) | 18.0 (9) | 32.0 (16)c |
| Soft tissue sarcomas | 7.5 (71) | 34.3 (6.2) | 8.5 (6)b | 2.8 (2) | 5.6 (4) | 36.6 (26) | 18.3 (13) | 33.8 (24) | 1.4 (1) | 11.3 (8) | 16.9 (12)c |
| Germ cell tumours | 2.7 (26) | 33.8 (7.4) | 3.9 (1)c | 0 (0) | 0 (0) | 11.5 (3) | 3.9 (1) | 34.6 (9) | 0 (0) | 15.4 (4) | 7.7 (2)b |
| Carcinoma | 0.7 (7) | 37.0 (8.5) | 0 (0) | 0 (0) | 0 (0) | - (1) | - (1) | - (3) | 0 (0) | - (0) | - (1)b |
| Other | 0.1 (1) | 33.7 (-) | 0 (0) | 0 | 0 | 0 (0) | 0 (0) | 0 | 0 | - (1) | 0 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Sex** |  |  |  |  |  |  |  |  |  |  |  |
| female | 44.7 (425) | 34.0 (5.6) | 6.6 (28)b | 3.3 (14)a | 1.7 (7)a | 17.9 (76)a | 19.5 (83) | 18.6 (79)b | 2.6 (11) | 19.8 (84)a | 18.4 (78)c |
| male | 55.3 (526) | 35.0 (5.5) | 2.9 (15)b | 1.0 (5) | 0.8 (4) | 27.2 (143) | 15.6 (82) | 36.1 (190)a | 1.5 (8) | 22.8 (120)a | 20.7 (109)b |

CHF = Congestive heart failure, CVD = Cardiovascular disease, CVSS = Cardiac and vascular late sequelae in long-term survivors of childhood cancer, FH = Positive family history for myocardial infarction/ stroke, ICCC 3 = International classification of childhood cancer, CNS = Central nervous system, SD = Standard deviation, VTE = Venous thromboembolism, a = <1% missings, b = <5% missings, c = < 10% missings

**Table S5:** Intake of drugs among the CVSS-study sample and comparison with DEGS and KORA samples after weighting for the age and sex distribution of the CVSS-study sample

a)

|  |  |
| --- | --- |
|  | **CVSS-study** |
|  | % (N) |
|  |  |
| **Intake of Drugs** |  |
| Any drug intake (ATC) | 69.3 (659) a |
| Genitourinary system and reproductive hormones (ATC-G) | 20.4 (194) a |
| Musculoskeletal system (ATC-M) | 18.7 (178) a |
| Systemic hormonal preparations, excluding reproductive hormones and insulins (ATC-H) | 18.1 (172) a |
| Nervous system (ATC-N) | 18.0 (171) a |
| Respiratory system (ATC-R) | 17.9 (170) a |
| Alimentary tract and metabolism (ATC-A) | 16.6 (158) a |
| Various ATC structures (ATC-V) | 13.8 (131) a |
| Cardiovascular system (ATC-C) | 11.0 (105) a |
| Dermatological drugs (ATC-D) | 10.2 (97) a |
| Sensory organs (ATC-S) | 5.1 (48) a |
| Antiinfectives for systemic use (ATC-J) | 3.7 (35) a |
| Drugs used in diabetes (ATC-a10) | 1.0 (9) a |
| Antineoplastic and immunomodulating agents (ATC-L) | 0.6 (6) a |
| Antiparasitic products, insecticides and repellents (ATC-P) | 0.2 (2) a |

b)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CVSS-study** | **DEGS** | **KORA** |
|  | % (N) | % (N) | % (N) |
| Any drug intake (ATC) | 69.3 (659)a | 56.5 (1536)a | 46.5 (996)a |
| Cardiovascular system (ATC-C) | 11.0 (105)a | 5.9 (221)a | 4.2 (123)a |
| Drugs used in diabetes (ATC a10) | 1.0 (9)a | 0.8 (28)a | 0.7 (19)a |
| Cardiovascular system and/ or drugs used in diabetes (ATC C and/or ATC a10) | 11.8 (112)a | 6.4 (237)a | 4.7 (135)a |

ATC = Anatomical Therapeutic Chemical classification system of the World Health Organization Collaborating Centre for Drug Statistics Methodology, CVSS = Cardiac and vascular late sequelae in long-term survivors of childhood cancer, DEGS = German Health Interview and Examination Survey for Adults, KORA = Cooperative Health Research in the region of Augsburg, a = <1% missings