Article:

Smith, L orcid.org/0000-0002-4280-6323, Glaser, AW, Greenwood, DC orcid.org/0000-0001-7035-3096 et al. (1 more author) (2020) Cumulative burden of subsequent neoplasms, cardiovascular and respiratory morbidity in young people surviving cancer. Cancer Epidemiology, 66. 101711. ISSN 1877-7821

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eprints@whiterose.ac.uk
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Appendix A: Supplementary data

Table A.1: Summary of outcomes for cumulative burden analysis

Outcome	All N=3464 n (%)	Children N=1328 n (%)	AYA N=2136 n (%)
At least 1 respiratory admission	280 (8.1)	139 (10.5)	141 (6.6)
1 admission	*200 (5.8)*	*101 (7.6)*	*99 (4.6)*
2 admissions	*41 (1.2)*	*17 (1.3)*	*24 (1.1)*
3 admissions	*11 (0.3)*	*-*	*-*
4 admissions	*13 (0.4)*	*6 (0.5)*	*7 (0.3)*
5+ admissions	*15 (0.4)*	*8 (0.6)*	*7 (0.3)*
At least 1 cardiovascular admission	141 (4.1)	53 (4.0)	85 (4.0)
1 admission	*101 (2.9)*	*38 (2.9)*	*63 (2.9)*
2 admissions	*13 (0.4)*	*-*	*-*
3 admissions	*9 (0.3)*	*-*	*-*
4 admissions	*6 (0.2)*	*-*	*-*
5+ admissions	*9 (0.3)*	*-*	*-*
At least 1 SMN	74 (2.1)	27 (2.0)	47 (2.2)
Combined outcomes			
Respiratory and cardiovascular admission	37 (1.1)		
Respiratory and SMN	15 (0.4)		
Cardiovascular and SMN	7 (0.2)		
All 3 events	<5		

Cells with 5 or fewer cases have been suppressed due to potential identifiability of cases, other cells may be suppressed to avoid disclosure by difference.

Table A.2: Total number of HES episodes for respiratory and cardiovascular admissions

Group	ICD-10 code	Total number of episodes
Any respiratory disease	J00-J99	831
Acute upper respiratory infections	J00-J06	105
Influenza and pneumonia	J09-J18	218
Other acute lower respiratory infections	J20-J22	154
Other diseases of upper respiratory tract	J30-J39	98
Chronic lower respiratory diseases	J40-J47	106
Lung diseases due to external agents	J60-J70	50
Suppurative and necrotic conditions of lower respiratory tract	J85-J86	12
other diseases of the pleura	J90-J94	47
Other	J80-J84, J95-J99	39
Any cardiovascular disease	I00-I99, G45-G46	485
Hypertensive diseases	I10-I15	17
Ischaemic heart disease	I20-I25	55
Pulmonary heart disease and diseases of pulmonary circulation	I26-I28	68
Other form of heart disease	I30-I52	125
Cerebrovascular disease	I60-I69, G45, G46	49
Diseases of arteries, arterioles and capillaries	I70-I79	24
Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	I80-I89	141
Other	I00-I02 I05-I09 I95-I99	6

Table A.3: Association between treatment exposure and time to first event for each outcome, sub-distribution hazard ratios (sHR) and 95% CI

Treatment	Respiratory admission		Cardiovascular admission		SMN	
	Unadjusted sHR (95% CI)	Adjusted sHR † (95% CI)	Unadjusted sHR (95% CI)	Adjusted sHR † (95% CI)	Unadjusted sHR (95% CI)	Adjusted sHR † (95% CI)
Anthracycline						
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.44 (1.13, 1.83)	1.02 (0.70, 1.48)	1.09 (0.77, 1.55)	1.01 (0.62, 1.67)	0.51 (0.28, 0.90)	0.50 (0.24, 1.05)
Pulmonary toxic chemotherapy						
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.21 (0.94, 1.54)	1.30 (0.92, 1.85)	1.20 (0.85, 1.70)	1.47 (0.94, 2.30)	1.28 (0.79, 2.06)	1.80 (0.97, 3.32)
Chest Radiotherapy						
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.59 (1.00, 2.53)	1.40 (0.83, 2.37)	1.01 (0.48, 2.12)	1.01(0.46, 2.22)	0.83 (0.26, 2.65)	1.00 (0.31, 3.25)

†Adjusted for diagnostic group, age at cancer diagnosis, year of diagnosis and deprivation, ethnicity and the other treatment exposures

Figure A.1: Diagrams of five hypothetical individuals with multiple and recurrent events
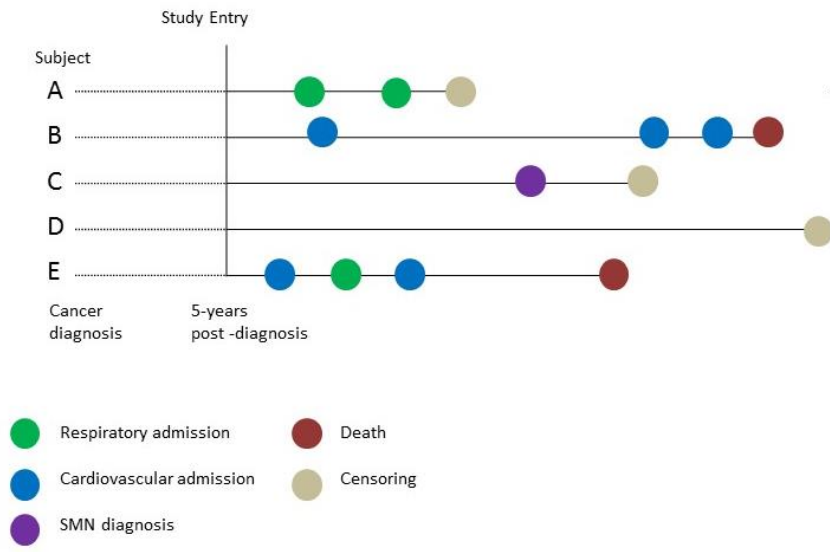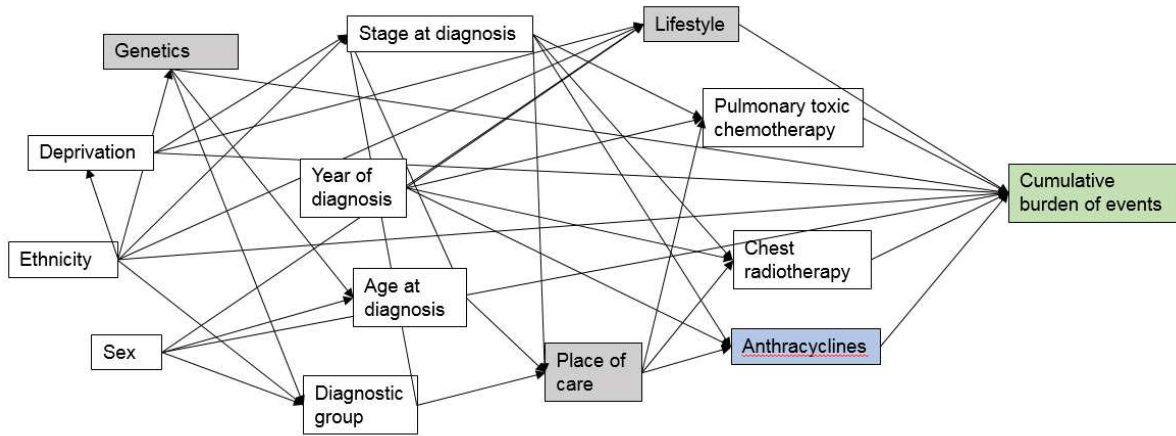
Figure A.2: Directed acyclic graph showing relationship between anthracyclines (exposure) and cumulative burden (outcome) and other patient and tumour related factors

Shaded blue box represents the exposure, the shaded green box the outcome of interest, white boxes potential (measured) confounders and the shaded grey boxes represent unmeasured latent variables

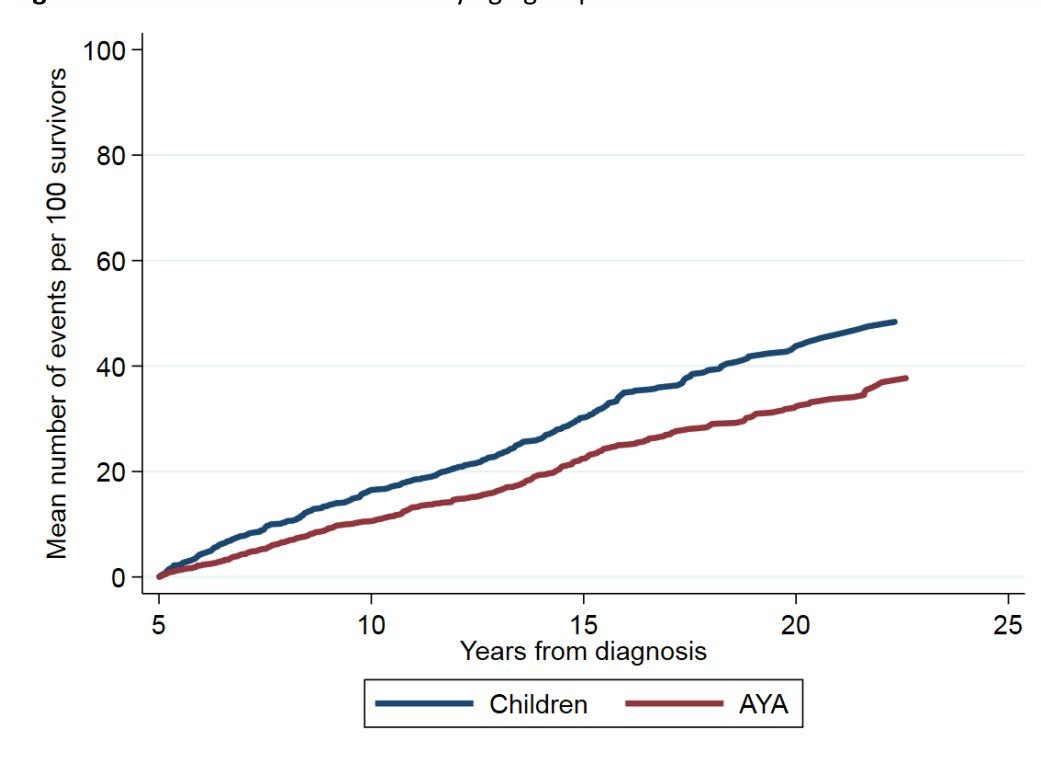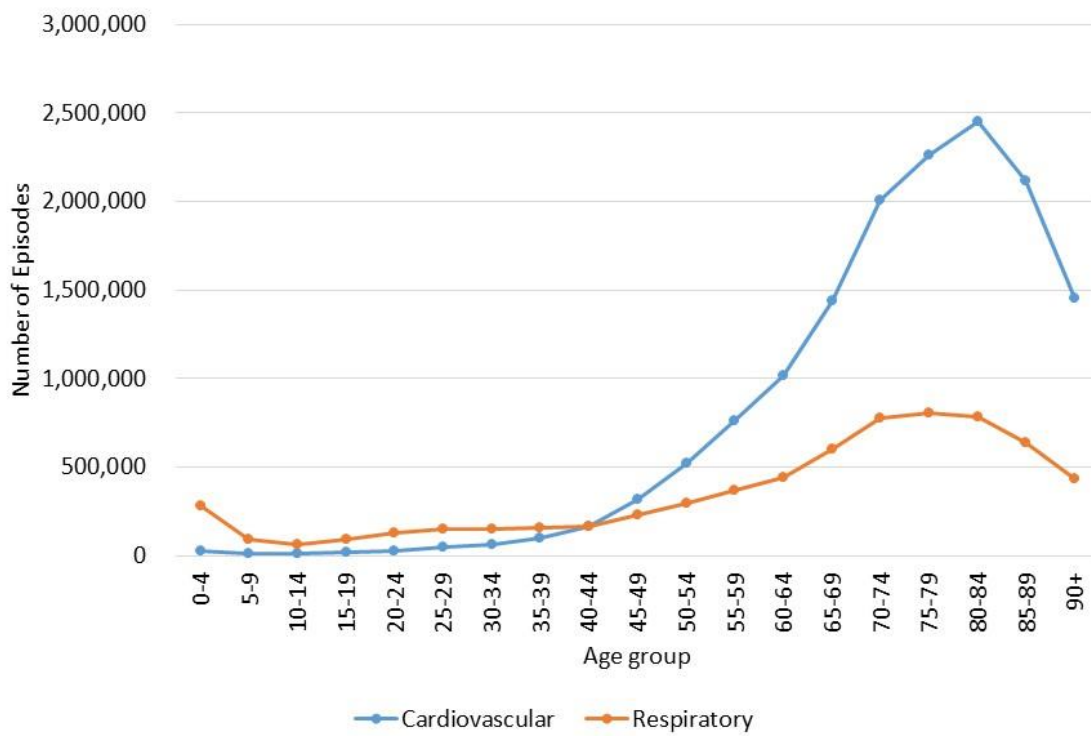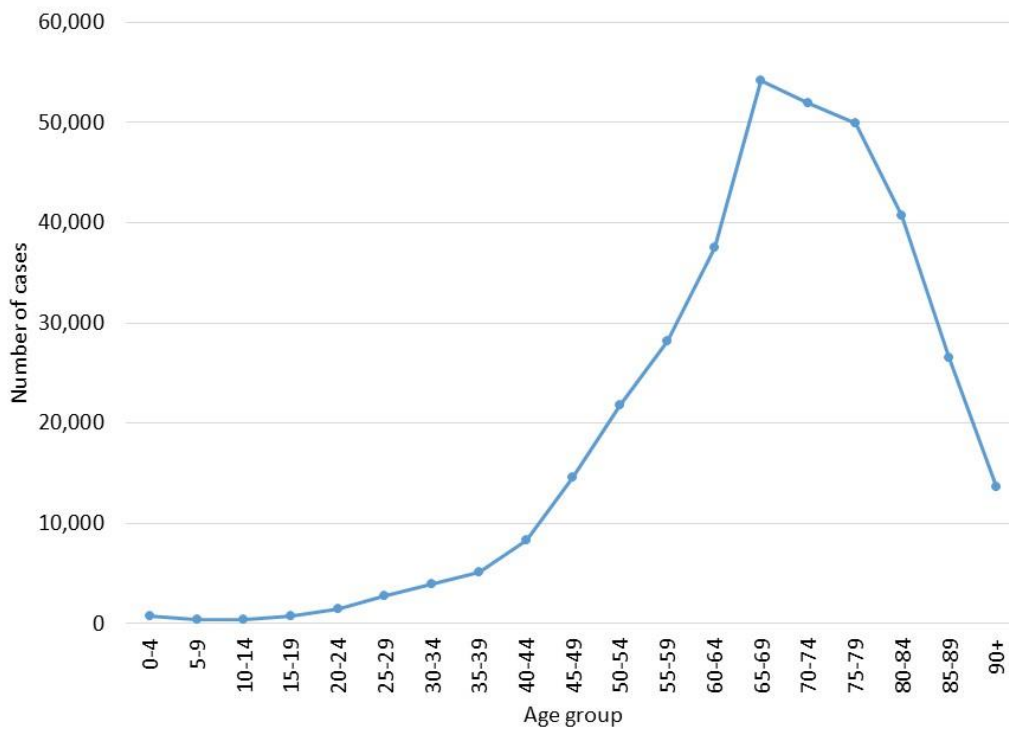**Figure A.3:** Mean cumulative count by age group

Figure A.4: HES episodes by age group, England, 2017-2018

Source: NHS Digital https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18

Figure A.5: Number of new cancer cases by age group, UK, 2014-2016

Source: CRUK https://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Zero