

Appendix

Table 1: List of neurotoxic chemotherapy drugs used by chemotherapy group, and sources utilised for their neurotoxicity effects.

Type (names) of the chemotherapy	WHO ATC code*	Source (Author year)
Antimetabolite - Pyrimidine analogues (Fluorouracil)	L01BC02	(Verstappen, Heimans et al. 2003; Was, Borkowska et al. 2022)
Vinca Alkaloids (included Vinblastine, Vincristine and Vinorelbine)	L01CA01 L01CA02 L01CA04	(Verstappen, Heimans et al. 2003; Magge and DeAngelis 2015; Was, Borkowska et al. 2022)
Bortezomib	L01XX32	(Magge and DeAngelis 2015; Was, Borkowska et al. 2022)
Taxanes (Paclitaxel, Docetaxel and Cabazitaxel)	L01CD01 L01CD02 L01CD04	(Verstappen, Heimans et al. 2003; Was, Borkowska et al. 2022)
Platinum compounds (included Cisplatin, Carboplatin and Oxaliplatin)	L01XA01 L01XA02 L01XA03	(Verstappen, Heimans et al. 2003; Magge and DeAngelis 2015; Teng, Cohen et al. 2022)

*World Health Organisation (WHO) Anatomical Therapeutic Chemicals (ATC) classification codes

Magge, R. S. and L. M. DeAngelis (2015). "The double-edged sword: Neurotoxicity of chemotherapy." *Blood Reviews* **29**(2): 93-100.

Teng, C., J. Cohen, S. Egger, P. L. Blinman and J. L. Vardy (2022). "Systematic review of long-term chemotherapy-induced peripheral neuropathy (CIPN) following adjuvant oxaliplatin for colorectal cancer." *Supportive Care in Cancer* **30**(1): 33-47.

Verstappen, C. C. P., J. J. Heimans, K. Hoekman and T. J. Postma (2003). "Neurotoxic Complications of Chemotherapy in Patients with Cancer." *Drugs* **63**(15): 1549-1563.

Was, H., A. Borkowska, A. Bagues, L. Tu, J. Y. H. Liu, Z. Lu, J. A. Rudd, K. Nurgali and R. Abalo (2022). "Mechanisms of Chemotherapy-Induced Neurotoxicity." *Front Pharmacol* **13**: 750507.

Table 2: Podiatry service use among people with CRC, comparison between chemotherapy and non-chemotherapy groups across annual increments before and after diagnosis.

Any chemotherapy vs no chemotherapy					Unadjusted			Adjusted*		
Time period	Treatment group	No. receiving ≥1 podiatry service	Total number persons alive	Rate per 1000 persons	Incidence rate ratio	95% Confidence interval	p-value	Incidence rate ratio	95% Confidence interval	p-value [†]
3 - <4yrs pre-dx	Chemotherapy	59	1535	38.44	0.637	0.463 – 0.876	0.006 [†]	0.932	0.665 – 1.307	0.684
	No chemo	106	1757	60.33						
2 - <3yrs pre-dx	Chemotherapy	81	1535	52.77	0.576	0.441 – 0.752	<0.001 [†]	0.804	0.606 – 1.066	0.130
	No chemo	161	1757	91.63						
1 - <2yrs pre-dx-	Chemotherapy	120	1535	78.18	0.645	0.516 – 0.807	<0.001 [†]	0.925	0.729 – 1.173	0.518
	No chemo	213	1757	121.23						
<1yr pre-dx	Chemotherapy	142	1535	92.51	0.663	0.540 – 0.816	<0.001 [†]	0.944	0.758 – 1.176	0.608
	No chemo	245	1757	139.44						
0 -1yr post-dx	Chemotherapy	173	1535	112.70	0.736	0.608 – 0.891	0.002 [†]	1.039	0.848 – 1.274	0.711
	No chemo	269	1757	153.10						
1 - <2yrs post-dx	Chemotherapy	215	1334	161.17	0.844	0.706 – 1.009	0.063	1.221	1.010 – 1.476	0.039[†]
	No chemo	273	1430	190.91						
2 - <3yrs post-dx	Chemotherapy	197	1135	173.57	0.808	0.673 – 0.969	0.021 [†]	1.159	0.956 – 1.406	0.132
	No chemo	283	1317	214.88						
3 - <4yrs post-dx	Chemotherapy	196	1002	195.61	0.822	0.686 – 0.984	0.033 [†]	1.162	0.961 – 1.406	0.122
	No chemo	297	1248	237.98						
4-<5yrs post-dx	Chemotherapy	170	901	188.68	0.757	0.627 – 0.914	0.007 [†]	1.039	0.853 – 1.267	0.702
	No chemo	297	1191	249.37						

* Derived from Poisson regression models adjusted for diagnosis year, sex, age, pre-existing diabetes, remoteness, and socioeconomic status. [†]p-value< 0.05 = statistically significant.

Table 3: Podiatry service use among chemotherapy recipients, comparison between neurotoxic chemotherapy and non-neurotoxic chemotherapy groups across annual increments before and after diagnosis.

Neurotoxic vs non-neurotoxic chemotherapy					Unadjusted			Adjusted*		
Time period	Treatment group	No. receiving ≥1 podiatry service	Total number persons alive	Rate per 1000 persons	Incidence rate ratio	95% Confidence interval	p-value	Incidence rate ratio	95% Confidence interval	p-value ⁺
3 - <4yrs pre-dx	Neurotoxic	37	1293	28.62	0.315	0.186 – 0.534	<0.001 ⁺	0.572	0.323 – 1.012	0.055
	Non-neurotoxic	22	242	90.91						
2 - <3yrs pre-dx	Neurotoxic	58	1293	44.86	0.472	0.291 – 0.765	0.002 ⁺	0.811	0.486 – 1.355	0.424
	Non-neurotoxic	23	242	95.04						
1 - <2yrs pre-dx-	Neurotoxic	83	1293	64.19	0.420	0.285 – 0.619	<0.001 ⁺	0.741	0.490 – 1.119	0.154
	Non-neurotoxic	37	242	152.89						
<1yr pre-dx	Neurotoxic	101	1293	78.11	0.461	0.321 – 0.663	<0.001 ⁺	0.779	0.530 – 1.146	0.205
	Non-neurotoxic	41	242	169.42						
0 -1yr post-dx	Neurotoxic	125	1293	96.67	0.487	0.349 – 0.680	<0.001 ⁺	0.809	0.568 – 1.152	0.240
	Non-neurotoxic	48	242	198.35						
1 - <2yrs post-dx	Neurotoxic	155	1124	137.90	0.483	0.358 – 0.650	<0.001 ⁺	0.821	0.595 – 1.133	0.230
	Non-neurotoxic	60	210	285.71						
2 - <3yrs post-dx	Neurotoxic	141	954	147.80	0.478	0.351 – 0.651	<0.001 ⁺	0.827	0.591 – 1.157	0.267
	Non-neurotoxic	56	181	309.39						
3 - <4yrs post-dx	Neurotoxic	138	839	164.48	0.462	0.340 – 0.628	<0.001 ⁺	0.765	0.548 – 1.067	0.115
	Non-neurotoxic	58	163	355.83						
4-<5yrs post-dx	Neurotoxic	121	751	161.12	0.493	0.354 – 0.687	<0.001 ⁺	0.802	0.562 – 1.146	0.226
	Non-neurotoxic	49	150	326.67						

* Derived from Poisson regression models adjusted for diagnosis year, sex, age, pre-existing diabetes, remoteness, and socioeconomic status. ⁺p-value< 0.05 = statistically significant.

Table 4 – Factors associated with podiatry service use in the five years after CRC diagnosis.

Factors	Colorectal cancer cohort N=3,292			Chemotherapy recipients N= 1,535		
	IRR	95% CI	p-value	IRR	95% CI	p-value
Age at Diagnosis						
Under 60 years	0.46	0.35-0.60	<0.001 ⁺	0.43	0.31-0.61	0.000 ⁺
60-69 years	0.73	0.60-0.89	0.002 ⁺	0.62	0.46-0.83	0.001 ⁺
70-79 years (<i>Reference group</i>)	1.00	-	-	1.0	-	-
80+ years	1.28	1.07-1.53	0.006 ⁺	1.04	0.76-1.44	0.788
Sex (<i>Reference males</i>)	1.05	0.90-1.21	0.547	1.05	0.84-1.32	0.662
Charleson Comorbidity Index (CCI)						
CCI = 0 (<i>Reference</i>)	1.0	-	-			
CCI = 1	1.12	0.87-1.43	0.391	0.96	0.64-1.45	0.847
CCI = 2+	1.18	0.91-1.52	0.216	1.15	0.77-1.72	0.502
Pre-existing diabetes (<i>yes/no</i>)	1.26	1.01-1.57	0.037 ⁺	1.31	0.93-1.85	0.124
Prior use of podiatry services (<i>yes/no</i>)	4.08	3.48-4.79	<0.001 ⁺	4.34	3.34-5.64	0.000 ⁺
Received any chemotherapy (<i>yes/no</i>)	1.17	1.01-1.37	0.037 ⁺	-	-	-
Received neurotoxic chemotherapy (<i>Reference neurotoxic chemotherapy</i>)	-	-	-	1.06	0.81-1.39	0.677

⁺p-value<0.05 = statistically significant