

**Table SIV. Dose-response analysis when the case group only included those patients with an invasive cutaneous squamous cell carcinoma (cSCC) and their respective controls**

	Cases (n = 309)	Controls (n = 3,090)	OR (95% CI)	p-value
MTX exposure, n (%)				
Never	224 (72)	2,418 (78)	1 [Reference]	
Ever	85 (28)	672 (22)	1.37 (1.05–1.79)	0.020
MTX dose intervals (g), n (%)				
None	224 (72)	2,418 (78)	1 [Reference]	
(0, 2.5)	48 (16)	424 (14)	1.23 (0.88–1.71)	0.22
(2.5, 5)	25 (8)	149 (5)	1.81 (1.16–2.83)	0.008
(5, 7.5)	7 (2)	70 (2)	1.09 (0.50–2.41)	0.82
>7.5	5 (2)	29 (1)	1.91 (0.73–5.00)	0.19
Per oral MTX dose (g) <sup>a</sup> , median (range)*	2.25 (0.08,8.73) n=81	1.50 (0.08,11.10) n=654	1.08 (1.01–1.17) <sup>d</sup>	0.029
Subcutaneous MTX dose (g) <sup>b</sup> , median (range)*	1.03 (0.04,4.97) n=13	0.95 (0.03,11.40) n=98	0.99 (0.77–1.28) <sup>d</sup>	0.96
Total MTX dose (g) <sup>c</sup> , median (range)*	2.25 (0.04,8.73) n=85	1.65 (0.03,11.40) n=672	1.07 (1.00–1.15) <sup>d</sup>	0.040

Data on filled prescriptions of methotrexate (MTX) were available for the period July 2005 to 2016. The accumulated MTX doses were calculated up to the index date, which was in the period 2010 to 2016.

<sup>a</sup>The oral MTX doses are the accumulated doses of oral MTX among cases and controls. For this specific OR, conditional logistic regression controlling for the subcutaneous dose was used. <sup>b</sup>The subcutaneous MTX doses are the accumulated doses of subcutaneous MTX among cases and controls. For this specific OR, conditional logistic regression controlling for the oral dose was used. <sup>c</sup>Conditional logistic regression was used with only the total dose as the independent variable. <sup>d</sup>ORs indicating the increase in risk of cSCC per 1 g increment in MTX dose.

\*Dose among exposed.

95% CI: 95% confidence interval; OR: odds ratio.