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| **Supplementary Table 4. Risk of esophageal squamous cell carcinoma (ESCC) in metformin users with dosage level during the first year (expressed as defined daily dose, DDD) in Sweden in 2005-2015.**  |
| **Analysis** | **Number of participants** | **Number of****ESCC cases** | **Hazard ratio of ESCC with metformin therapy (95% CI)** |
| **Model 1** | **Model 2** | **Model 3** |
| <175 DDD | 122,744 | 22 | Reference | Reference | Reference |
| 175-300 DDD | 122,656 | 24 | 0.94 (0.53-1.68) | 0.90 (0.50-1.61) | 0.91 (0.51-1.63) |
| > 300 DDD | 128,188 | 27 | 0.83 (0.47-1.47) | 0.88 (0.49-1.59) | 0.89 (0.49-1.61) |
| *p* for trend |   |   | 0.518 | 0.692 | 0.716 |
| Model 1: crude analysis |  |  |  |  |
| Model 2: adjusted by sex, age, calendar year, residence, smoking, and alcohol overconsumption  |
| Model 3: model 2 further adjusted by non-steroidal anti-inflammatory drugs/aspirin and statin use |  |
| Note: All results met the proportionality assumption of the hazard |  |  |