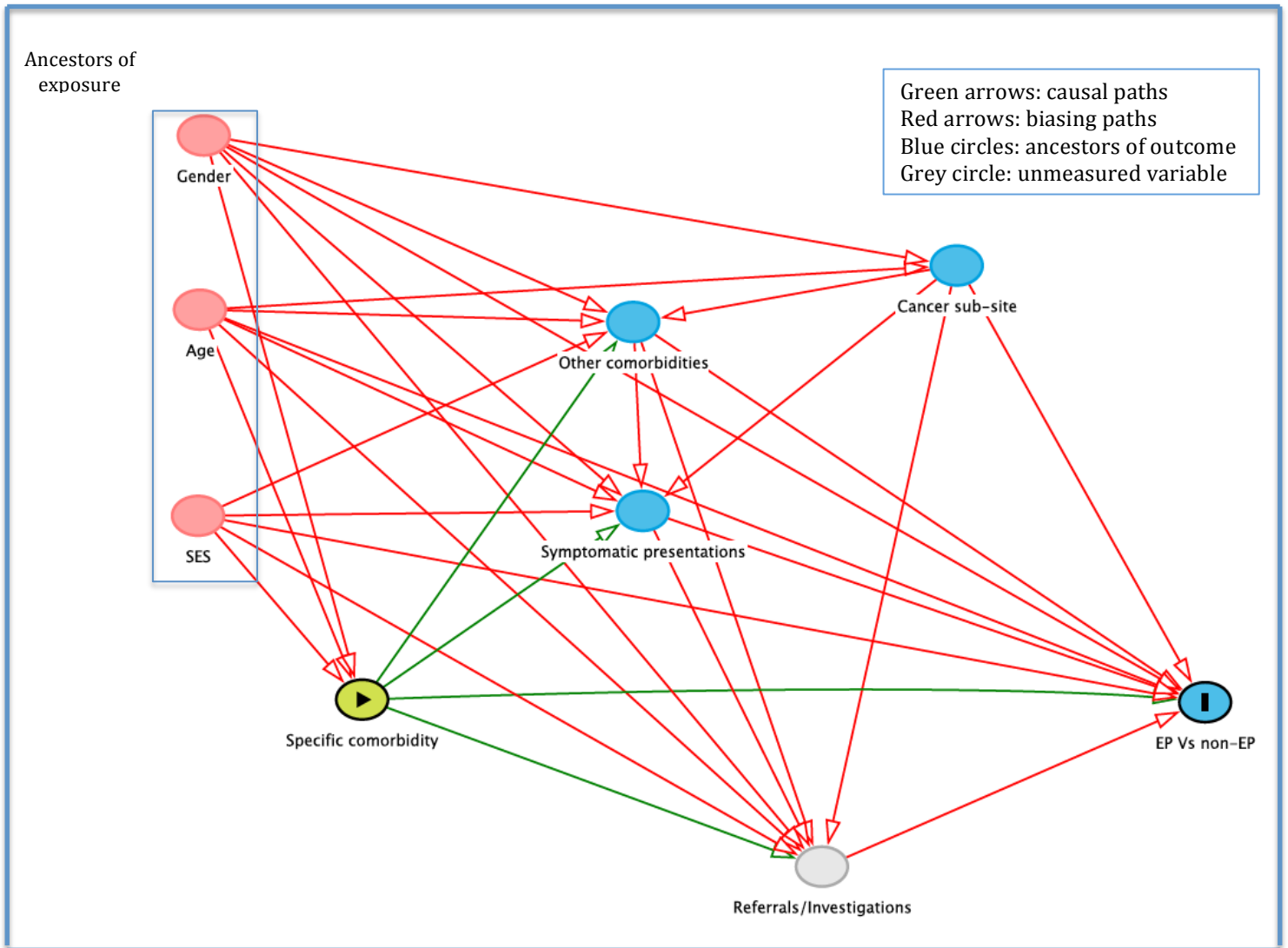


Figure: Pathways linking comorbidities to emergency presentations and relevant covariates



Causal paths (in green) linking comorbidities to emergency presentations can involve multiple mechanisms affecting:

- | Patients | Doctors | Healthcare system |
|--------------------------------------|--------------------------------------|--|
| ➤ Symptom interpretation/attribution | ➤ Symptom interpretation/attribution | ➤ Guidelines |
| ➤ Help-seeking/reporting of symptoms | ➤ Priorities | ➤ Availability of services/tests |
| ➤ Preferences for diagnostic tests | | ➤ Waiting list criteria for accessing services |
| ➤ Familiarity with healthcare system | | ➤ Duration of GP visits, booking systems, etc. |
| ➤ Opportunities to discuss symptoms | | |
| ➤ Overall health status | | |

Potential-outcomes methods: evaluating the effect of comorbidities on the risk of colon cancer being diagnosed through emergency versus non-emergency routes

We estimated the average effect of comorbidities on emergency presentations in the population of colon cancer patients, which corresponds to the difference between the mean of the potential-outcomes (i.e. emergency presentations) we would expect if all individuals in the population were exposed (i.e. had the comorbidity) and the mean of the potential-outcomes if all individuals in the population were not exposed. Unbiased potential outcome means can be obtained under specific assumptions, including consistency of exposure, conditional exchangeability of treatment and positivity¹². Similarly to recent cancer studies we used the doubly robust combinations of regression adjustment and inverse probability weighting (IPWRA)¹¹. We modelled emergency presentation, our outcome, with socio-demographic characteristics and alarm symptoms as explanatory variables in a logit model. This model was combined with a second model predicting the exposure (comorbidity), using the same covariates as explanatory variables. Each comorbidity type ('serious' non-GI comorbidity, IBS/diverticular disease, gynaecological condition, hypertension) was considered as the exposure in successive models and in turn combined with the outcome model. Using the `teffects` Stata command, we estimated the Potential Outcome mean (POmean), corresponding to the risk of emergency presentation among non-comorbid cancer patients, as well as the 'average treatment effect' (ATE) of comorbidities on emergency presentations¹⁰. The risk of emergency presentation in the population of cancer patients with each specific comorbidity was calculated by summing the comorbidity-specific ATE and the corresponding POmean.