**Ascertainment adjustment**

We propose to use the following working definition, which is developed by reviewing the “final papers” used in Ask2me, to screen in papers that are meta-analyses or have appropriate adjustment of ascertainment. All included papers will be discussed on the Bayes Mendal meetings.

We will include the paper if it is:

* **A meta-analysis**

OR

* **A general population-based study**

OR

* **A proband-based/family-based study with appropriate ascertainment adjustment: such as GRL, modified segregation analysis, like**

1. *“To adjust for ascertainment, we used an ascertainment assumption–free approach in which we evaluated each family separately.”*
2. *“This was achieved by using the genotype restricted likelihood (GRL) method, a maximum likelihood parametric method providing unbiased penetrance estimates irrespective of the criteria used for family selection.”*
3. *“We used a modified segregation analysis (as described in detail in the Appendix in the work by Dowty et al). This analytical method is not subject to population stratification, can be rigorously adjusted for ascertainment and uses data on all study participants, whether genotyped or not, thereby maximizing statistical power.”*
4. *“CRC and EC risks were estimated using modified segregation analysis implemented in the pedigree analysis software MENDEL (University of California, Los Angeles, Los Angeles, CA), as previously described.”*
5. *“We estimated the relative risk of pancreatic cancer as a standardized incidence ratio (SIR), defined as the number of pancreatic cancer cases observed divided by the number expected on the basis of incidence rates for the general population. The expected number of cases was calculated by multiplying person-years at risk with population incidence rates of pancreatic cancer……..Once we verified that the SIR estimates were not influenced by such cohort-effects, our final analyses were based on population rates specific for each country, sex, and 5-year age group averaged from 1950 to 2009 which were applied to all follow-up, regardless of calendar year.”*

OR

* **A hospital/lab-based case-control study with population-based or matched controls, like:**

1. *“We tested for association between deleterious mutations and ovarian cancer risk using unconditional logistic regression adjusted for geographical region of origin (Australia, continental Europe, the United Kingdom, and the United States), calculated the odds ratios, and performed segregation analysis to estimate risks associated with BRIP1 as previously described.”*
2. *“For age-adjusted analysis, the projected U.S. population (year 2000) was used; 84% of the 3,399 individuals were white, justifying the use of the U.S. SEER population.”*
3. *“Two publically available, overlapping, online exome sequencing data sets were used to estimate population mutation mutation frequencies: the European American (EA) data set from the National, Heart, Lung, and Blood Institute Exome Sequencing Project (ESP) and the Exome Aggregation Consortium (ExAC).”*
4. *“A control population was defined from the National Danish Civil Registration System, with five population controls, matched on sex and year of birth, for mutation carriers as well as first-degree relatives. “*
5. *“Cases and controls were matched 1:1 according to age (63 years), ancestry (exact match), and family cancer history (breast, ovarian, colon, uterine)…… Cumulative risks were calculated according to the product-limitmethod, with age specific incidences estimated as the product of age specific ORs and general population incidences.”*