PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Historical Cancer Incidence and Mortality Assessment in an Illinois Community Proximal to a Former Manufactured Gas Plant
AUTHORS	Fryzek, Jon; Alexander, Dominik; Jiang, Xiaohui; Bylsma, Lauren; Garabrant, David; Irvin, Sarah

VERSION 1 - REVIEW

REVIEWER	James J. Collins Saginaw Valley State University
REVIEW RETURNED	10-Oct-2014

GENERAL COMMENTS	Comments on Historical Cancer Incidence and Mortality Assessment in an Illinois Community Proximal to a Former Manufactured Gas Plant This ecological study compares cancer rates in a community near a former manufactured gas plant to similar counties demographically and to national rates to determine if cancer is higher in in the “exposed” county or zip code. The study finds that most cancer rates are lower in the exposed county/ZIP code than other counties or the US population. The study concludes that the exposed county did not have elevated cancer rates. The methods used in this study are consistent with well accepted methods for conducting ecological studies in epidemiology to assess increased cancer rates from past environmental exposures. The authors should consider the following: 1. The authors do a laudable job in assessing many cancers. However, they should consider providing an assessment of which cancers are most likely to appear in the community from exposures from the gas operations. The workers studies of coal gasification workers indicate an excess of lung and urinary tracts cancers (Bosetti et al. Annals of Oncology 18: 431–446, 2007; doi:10.1093/annonc/mdl172.). 2. The authors should provide a better description of the community studied and the comparison populations. A major university is located in this community. The matching criteria used to select the comparison populations do have an education variable. Although Champaign county has markedly lower percentage who did not graduate high school than the other counties. The low cancer rates observed in this community could be a result of confounding. 3. It is not clear why comparison populations were selected which also had coal gasification plants. I would think counties without these plant would be a better comparison. I am puzzled why the authors present the “coal gasification counties” in tables 1 and 2 and not the other counties without these facilities. 4. The authors focus on prostate and melanoma for the discussion since they are elevated in some of the analyses. Their discussion should also focus on what elements in the coal gasification process have previous ben related to these cancer in humans.

REVIEWER	Andrew Darnton Health and Safety Executive, UK
REVIEW RETURNED	17-Oct-2014

GENERAL COMMENTS	The basis of this ecological analysis is to assess whether there is higher incidence of cancer among a community living in a geographical area containing a former coal gas plant than among various comparison populations. Matching of the comparison populations on setting (urban or rural), population size, race, education status, age, unemployment, poverty, urban residence and smoking was carried out to try to eliminate any effects on cancer rates due to these variables. The analysis addresses the basic question about how cancer rates in the vicinity of the former plant compare to those in other similar areas. However, a more pertinent question is whether proximity of residence to this former plant has actually influenced cancer rates. While the results tend to rule out any large effect, the detection and attribution of more subtle effects to the plant – i.e. precisely the sort of effect that might be hypothesised – is unlikely based on this analysis because the assessment of "exposure" (i.e. the simple presence of the gas plant in the area of residence) is unlikely to be sufficiently specific, and control for factors that may influence cancer rates in the comparison groups is unlikely to be adequate. Thus, although this analysis appears to be been carried out carefully and thoroughly, I suspect it has little chance of detecting any effect that could be confidently attributed to the plant. On the one hand, any modest increases in cancer incidence (such as that seen for melanoma) could not be confidently attributed to the plant – but on the other hand the lack of increased cancer incidence does not allow one to rule out small effects with much confidence. Although proving a negative is impossible, greater confidence about no effect could be obtained from an analysis based on a more specific exposure assessment – for example, by looking at variation in cancer rates according to proximity of residence to the plant, or using an independent assessment of the extent to which specific agents of concern might be present in different geographical areas in the immediate vicinity of the plant. An analysis which looks at variation in cancer incidence according to degree of exposure would avoid problems of whether reference rates are appropriate. (In the current study comparisons populations also contained gas plants.) The timing of the exposure and the observation window also needs careful thought. The plant ceased operating in 1953, 37 years before the start of the current observation window. Presumably there was potential for exposure after 1953, but it is not clear to what extent (this is mentioned in the discussion). Any effect of exposure on cancer rates – again if it exists – may have reduced by the start of the observation window, particularly as it could be diluted by population movement over time. The matching to control out other influences was done at the county level. The extent to which the sub-population of most interest – namely the zip code areas in the immediate vicinity of the plant – was well matched to the comparison populations is not clear. In any case, I think this broad-level matching is unlikely to fully control for factors affecting cancer incidence among groupings of this kind,