Projection of mesothelioma mortality in Great Britain

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Emma Tan & Nick Warren
Health and Safety Laboratory
Harpur Hill
Buxton
Derbyshire
SK17 9JN

There has been an increase in mesothelioma mortality in Great Britain, with 1705 deaths recorded in 2006. In 2005, a statistical model was developed based on a simple birth-cohort model, which assumes that the risk of mesothelioma depends on age and years of exposure and that an individual's asbestos exposure depends on the year of exposure. An optimisation technique was used to fit the model and a profile of the population exposure was estimated. Projections of the future burden of mesothelioma mortality were calculated, however statistical uncertainties in the formulation of the model could not be taken into account. In this report, the model has been refined and refitted using the MATLAB's fminsearch function and the Metropolis-Hastings algorithm, a Markov Chain Monte Carlo technique. Credible intervals for model parameters as well as prediction intervals for future cases of mortality amongst males are presented. Mortality amongst all males is expected to keep increasing, reaching a peak at around 2,040 deaths in the year 2016, with a rapid decline following the peak year. Around 91,000 deaths are predicted to occur by 2050 with around 61,000 of these occurring from 2007 onwards.

HSE Books

EXECUTIVE SUMMARY

Aims

This report presents a Bayesian statistical analysis of mesothelioma mortality in Great Britain between the years 1968 and 2006. This report updates previous work carried out by HSE Statistics Branch, using Bayesian Markov Chain Monte Carlo methods.

The aims of the statistical analysis were:

- Using suitable software, to construct a more efficient and statistically rigorous algorithm for model parameter estimation;

- To refit the collective population dose model to data up to and including 2006 and incorporate terms for background mesothelioma cases not caused by asbestos exposure;

- To test the adequacy of the models by running projections based on data up to earlier years and to assess the fit in later observed years; and

- To produce updated estimated annual mesothelioma deaths to 2050 with confidence and prediction intervals.

Main Findings

- The expected number of mesothelioma cases amongst males is projected to increase to a peak of 2038 (90% prediction interval [1929, 2156]) in the year 2016 (90% prediction interval [2015,2016]), decreasing thereafter and eventually reaching a point where the majority of deaths are 'background cases'. This is consistent with previous HSE work.

- The non-clearance model (with a clearance half-life of 1,000,000 years) provided a better fit to the data than a clearance model with a shorter half-life.

- Males aged 20 to 49 years were most likely to be exposed to asbestos.

- Estimated population exposure to asbestos increased rapidly from the 1930s to the late 1960s, reaching a global maximum year of exposure in 1963. There were also two periods around 1930 and 1950 where population exposure briefly reached local peaks. These peaks do not appear to be statistical artefacts. They may be related to events which occurred around the time of the peaks. The first coincides with the introduction of the Asbestos Industry Regulations in the UK in 1931 as well as the Great Depression. The second occurs just after World War II after which shipyard activity – especially in naval yards - will have reduced.

- The background rate was estimated at approximately 1.08 (90% C.I. [0.71, 1.51]) cases per million amongst males, suggesting that there are a small number of cases (about 23 per year) that are not caused by exposure to asbestos.

Limitations

- A comparison of predictions made by the model with selected early cutoffs for the input data (using data up to 1987, 1992 and 2002) with the observed data in later years suggested that the model does not systematically under- or over-predict the scale of mesothelioma mortality in later years. However care must be taken when making projections based on available data; any outlying data for the most recent years available may have high leverage and thus have a greater influence on the fit of the model.

- The updated model provides a reasonable basis for making relatively short-term projections of mesothelioma mortality in Britain, including the extent and timing of the peak number of deaths. However, longer-term predictions comprise two additional sources of uncertainty which are not captured within the prediction intervals for the annual number of deaths: 1) whether the form of the model is valid for more recent and future exposure contexts, and 2) if the model is valid in such contexts, the uncertainty arising from the particular choice of the population exposure profile beyond 1978.

Recommendations

- Comparisons of the projections with new data should be made in order to further assess the fit and the adequacy of the existing model. The model may also be refitted to obtain updated model parameters and model projections.

- Alternative models where, for example, the risk of mesothelioma levels off with time since exposure, should be investigated.

- Further work should be carried out on female data. Different approaches to fitting models to female data should be considered, in particular, whether to assume a common value for certain parameters for both males and females.
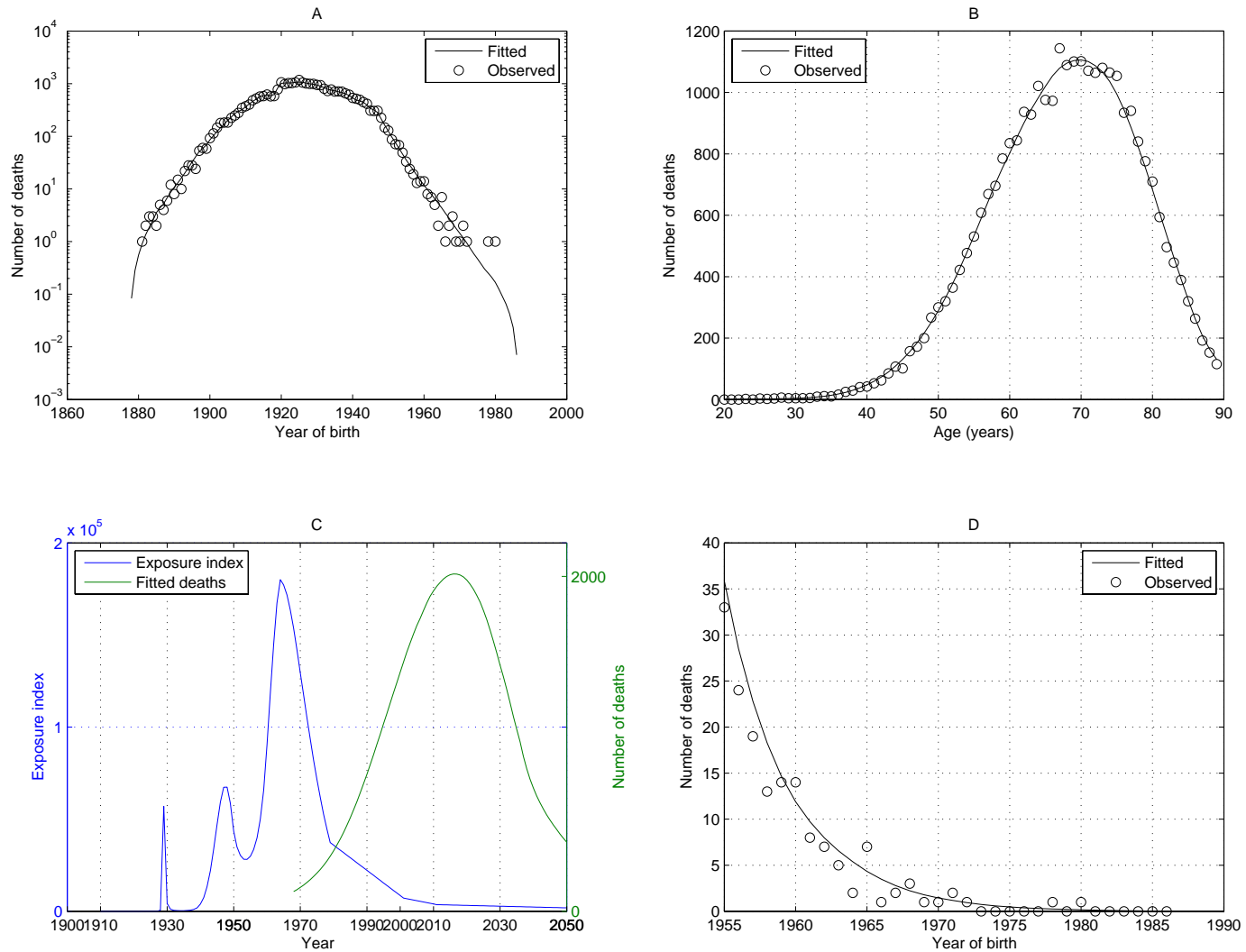
Figure 2 *fminsearch*: (A) Observed and fitted deaths by year of birth. (B) Observed and fitted deaths by age. (C) Observed and fitted deaths by year of death, with derived exposure index. (D) Observed and fitted deaths for 1955-1985 birth cohorts.

Figure 4 Metropolis-Hastings (males): (A) Observed and fitted deaths by year of birth. (B) Observed and fitted deaths by age. (C) Observed and fitted deaths by year of death, with derived exposure index. (D) Observed and fitted deaths for 1955-1985 birth cohorts.
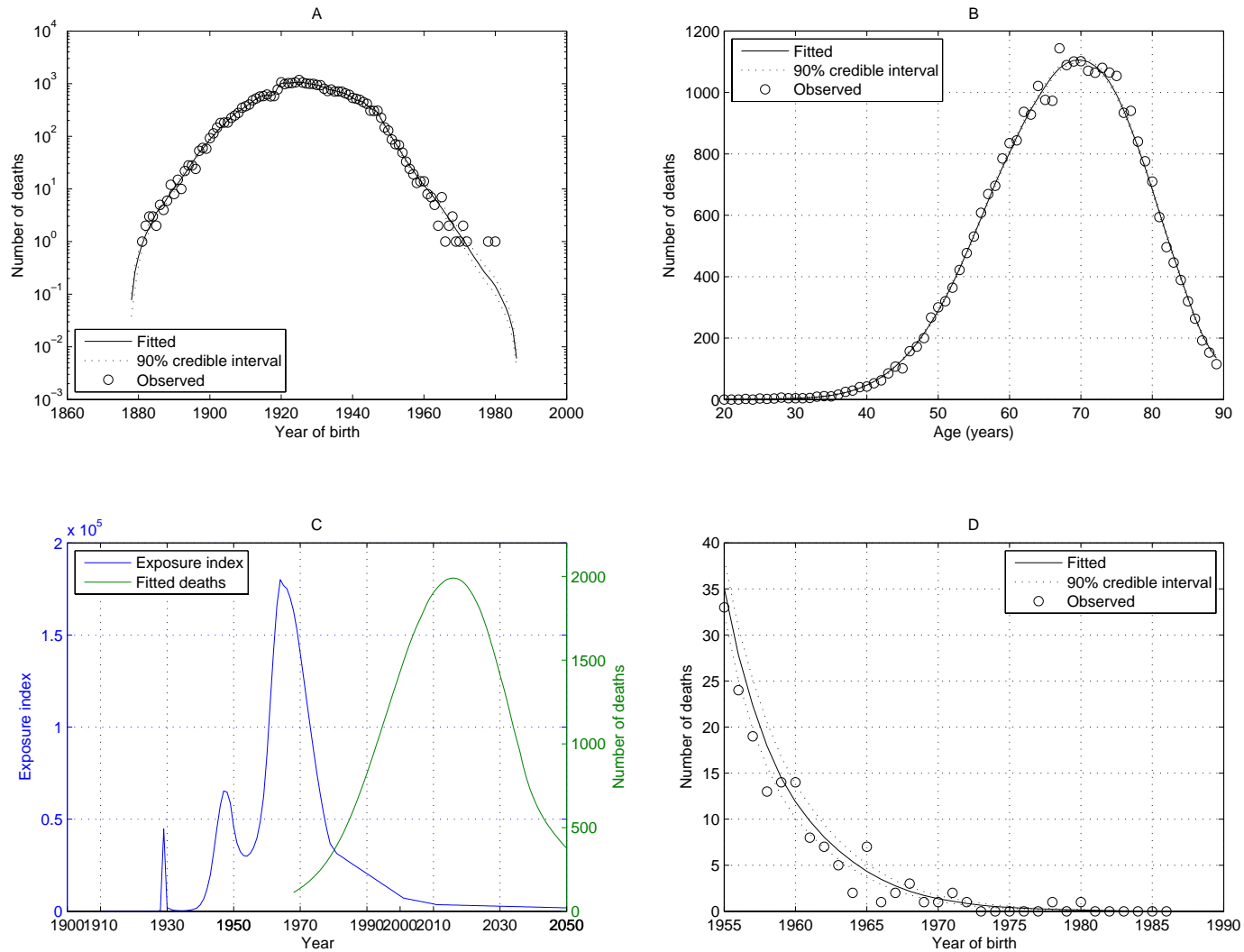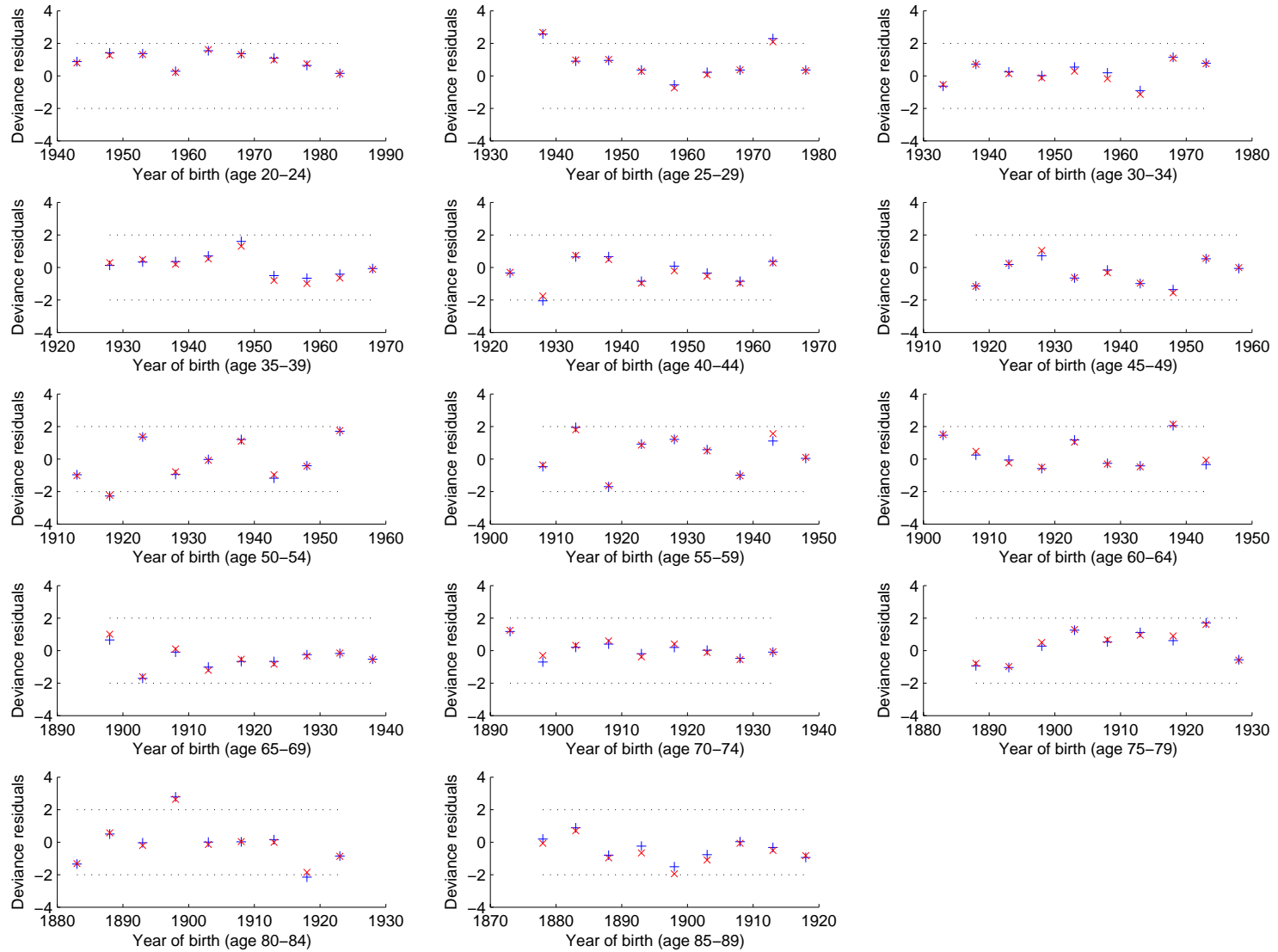
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Figure 5 Deviance residuals by age group and birth cohort from fitting Model A using *fminsearch* (+) and MCMC (x)

Table 15 *fminsearch:* Parameter estimates for Model A (fitted to data to 1992)

Parameter estimates and 90% CI			
k	2.51	Background rate	1.53
Maximum exposure year	1965	Half-life (years)	1000000 (fixed)
Change in exposure index (% per year) in...		Relative exposure potential by age group	
1900 ($D(1)$)	0 (fixed)	0 to 4	0.000
1910 ($D(2)$)	1000 (fixed)	5 to 15	0.0007
1920 ($D(3)$)	100000 (fixed)	16 to 19	0.24
1930 ($D(4)$)	-67.5	20 to 29	1.00 (baseline)
1940 ($D(5)$)	60.4	30 to 39	1.71
1950 ($D(6)$)	-12.1	40 to 49	1.79
1960 ($D(7)$)	26.4	50 to 59	0.03
1965	0 (by definition)	60 to 64	0.06
1970 ($D(8)$)	-9.4	65+	0.00
1980 ($D(9)$)	-23.0		
Projections of future mesothelioma deaths in males aged 20-89			
Peak level	2080	Peak year	2016
Deviance	140	Diagnostic trend	-

Table 16 *fminsearch:* Parameter estimates for Model A (fitted to data to 1997)

Parameter estimates and 90% CI			
k	2.35	Background rate	1.11
Maximum exposure year	1965	Half-life (years)	1000000 (fixed)
Change in exposure index (% per year) in...		Relative exposure potential by age group	
1900 ($D(1)$)	0 (fixed)	0 to 4	0.000
1910 ($D(2)$)	1000 (fixed)	5 to 15	0.0044
1920 ($D(3)$)	100000 (fixed)	16 to 19	0.20
1930 ($D(4)$)	-70.1	20 to 29	1.00 (baseline)
1940 ($D(5)$)	63.1	30 to 39	1.82
1950 ($D(6)$)	-14.0	40 to 49	1.88
1960 ($D(7)$)	28.4	50 to 59	0.18
1965	0 (by definition)	60 to 64	0.33
1970 ($D(8)$)	-10.2	65+	0.00
1980 ($D(9)$)	-36.1		
Projections of future mesothelioma deaths in males aged 20-89			
Peak level	1765	Peak year	2013
Deviance	155	Diagnostic trend	-

Table 17 *fminsearch:* Parameter estimates for Model A (fitted to data to 2001)

Parameter estimates and 90% CI			
k	2.48	Background rate	1.52
Maximum exposure year	1965	Half-life (years)	1000000 (fixed)
Change in exposure index (% per year) in...		Relative exposure potential by age group	
1900 ($D(1)$)	0 (fixed)	0 to 4	0.000
1910 ($D(2)$)	1000 (fixed)	5 to 15	0.0006
1920 ($D(3)$)	100000 (fixed)	16 to 19	0.21
1930 ($D(4)$)	-66.0	20 to 29	1.00 (baseline)
1940 ($D(5)$)	58.9	30 to 39	1.58
1950 ($D(6)$)	-12.2	40 to 49	1.68
1960 ($D(7)$)	26.5	50 to 59	0.09
1965	0 (by definition)	60 to 64	0.05
1970 ($D(8)$)	-13.1	65+	0.00
1980 ($D(9)$)	-16.7		
Projections of future mesothelioma deaths in males aged 20-89			
Peak level	1969	Peak year	2015
Deviance	182	Diagnostic trend	-

Table 18 *fminsearch:* Parameter estimates for Model A (fitted to data to 2002)

Parameter estimates and 90% CI			
k	2.51	Background rate	1.52
Maximum exposure year	1965	Half-life (years)	1000000 (fixed)
Change in exposure index (% per year) in...		Relative exposure potential by age group	
1900 ($D(1)$)	0 (fixed)	0 to 4	0.000
1910 ($D(2)$)	1000 (fixed)	5 to 15	0.0007
1920 ($D(3)$)	100000 (fixed)	16 to 19	0.21
1930 ($D(4)$)	-67.2	20 to 29	1.00 (baseline)
1940 ($D(5)$)	59.7	30 to 39	1.58
1950 ($D(6)$)	-12.5	40 to 49	1.56
1960 ($D(7)$)	26.4	50 to 59	0.04
1965	0 (by definition)	60 to 64	0.06
1970 ($D(8)$)	-11.2	65+	0.00
1980 ($D(9)$)	-24.6		
Projections of future mesothelioma deaths in males aged 20-89			
Peak level	1976	Peak year	2015
Deviance	181	Diagnostic trend	-

APPENDIX 3 CORRELATION PLOTS

Correlation plots for pairs of parameter values from the MCMC chain for Model A (fitted to data on males aged 20 to 89) can be found in Figures 11 to 15. There appears to be little correlation between parameters apart from the correlations between k and $W(3)$, $W(4)$, $W(5)$ and $W(6)$. As the value of k increases, $W(3)$ is seen to increase whereas $W(4)$, $W(5)$ and $W(6)$ are seen to decrease. These correlations, although interesting to note, would not have affected the posterior distribution statistics presented in this report.
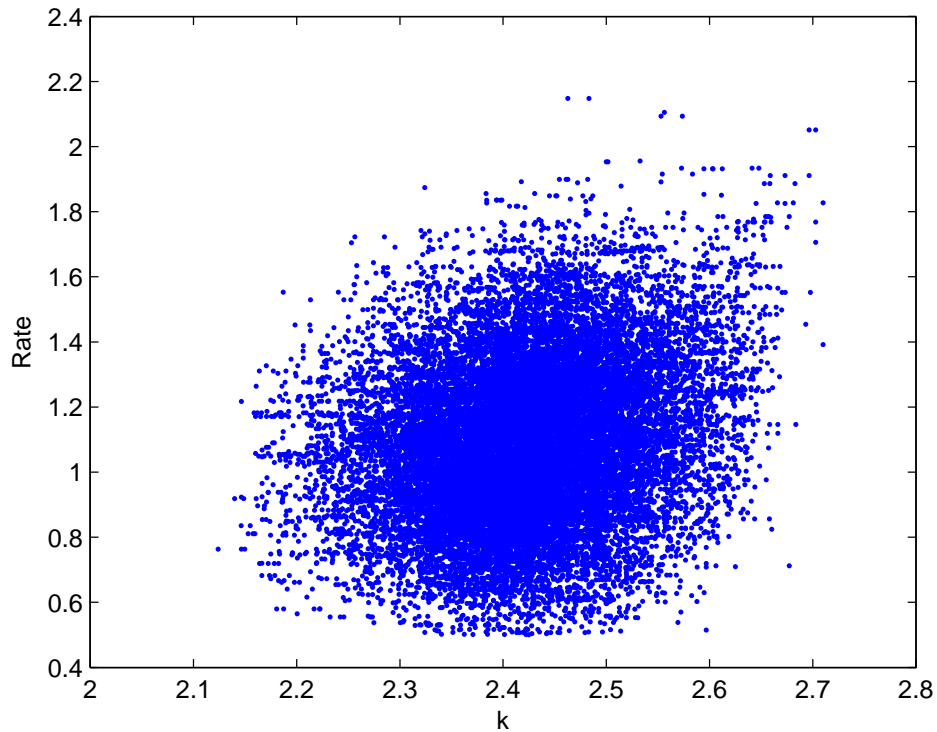

Figure 11 Correlation plot between k and $Rate$ using Metropolis-Hastings