Appendix 2: Statistical analysis – negative binomial count model specification

As Age Period Cohort (APC) regression modelling was not appropriate in this study, we used a multivariable regression framework to model the count of deaths over time. We fitted separate models for deaths from CeVD and IHD (see main manuscript for definitions). As data were count data (i.e. a number of deaths) and the variance exceeded the mean (over-dispersion), we used negative binomial regression models. Variables included in both models were sex, single age at death and Carstairs deprivation (1 'most deprived 40%', 2 'central 20%' and 3 'least deprived 40%'). Carstairs' quintiles were collapsed into the variables in the model in order to maintain consistency with rates and SCP analysis (see main manuscript for detail). Population was accounted for as an offset variable. As counts increased exponentially with age we included an age squared explanatory variable in both disease models. The underlying trend over time in the count data was modelled in a different way for each disease. For CeVD, we used a year squared variable which allowed the underlying trend to be constant but non-linear. For IHD, the study period was split into two sections (pre and post 1990) using the command *mkspline* (Stata/SE 14 (Stata Corp, Texas, 2015). This command creates multiple cubic splines (where a spline is a curve joining two points). 1990 was chosen as the split point as a change of trend is evident at this point in the descriptive data. We also split the study period into 2-6 equal sections in turn and recorded the Bayes Information Criterion (BIC) for each. The selected model had a lower BIC (indicating a better fit) than any of the alternative specifications.

Interaction variables were added where they were significant (measured using the likelihood ratio test). Interaction variables allow effects of one variable to be different in sub-groups of another, such as age effect being different in males and females. Interaction variables included in the IHD and CeVD models are shown in Table 1. We assessed goodness of fit of the selected model by comparing predicted values with observed values using the R^2 statistic. R^2 is a statistical measure of how close the data are to the fitted model (it is the amount of variance in the outcome variable that is explained by the model) which takes values between zero and one with one being a perfect fit. Our models had R^2 in excess of 99%. Regression analyses were undertaken using STATA/SE 14 software (STATA Corp, Texas, USA).

Parkinson J, *et al. Heart* 2020; 106:584–589. doi: 10.1136/heartjnl-2019-315029

Table 1 Interaction variables in negative binomial models

	IHD – name of interaction variable	CeVD - name of interaction variable
Age and sex	Int1	Not statistically significant
Year and sex	Year replaced by pre and post 1990	Not statistically significant
Year and Carstairs	Year replaced by pre and post 1990	Int3
Pre-1990 and sex	Int2	Not applicable
Post-1990 and sex	Int3	Not applicable
Pre-1990 and Carstairs	Int4	Not applicable
Post-1990 and Carstairs	Int5	Not applicable
Year and age	-	Int7
Year and age squared	-	Int8
Pre-1990 and age	Int6	Not applicable
Post-1990 and age	Int7	Not applicable
Pre-1990 and age squared	Int8	Not applicable
Post-1990 and age squared	Int9	Not applicable
Carstairs and age	Int10	Int5
Carstairs and sex	Int11	Int4

Carstairs variable is 1- most deprived 40% of areas, 2 – central 20% areas, 3 – least deprived 40% of areas

Full model specifications and output are shown as Figures 1 (IHD) and 2 (CeVD) below.

Plots of predicted and observed data are included as Figures 3 (IHD) and 4 (CeVD).

Parkinson J, *et al. Heart* 2020; 106:584–589. doi: 10.1136/heartjnl-2019-315029

Figure 1 IHD model specification and regression output

xi: nbreg numer nsex age agesq spl* cars int*, exp(denom) iter(50) irr
estat ic

```
Negative binomial regression                    Number of obs     =     35,700
                                                LR chi2(17)       =  103551.03
Dispersion     = mean                           Prob > chi2       =     0.0000
Log likelihood = -58966.381                     Pseudo R2         =     0.4675

------------------------------------------------------------------------------
       numer |        IRR   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        nsex |   15.05245   .4346664    93.90   0.000     14.22418    15.92895
         age |   1.389669   .0057602    79.39   0.000     1.378424    1.401004
       agesq |   .9983702   .0000314   -51.89   0.000     .9983087    .9984317
        spl1 |    .942366   .0113597    -4.92   0.000     .9203623    .9648957
        spl2 |   1.236406   .0231675    11.33   0.000     1.191822    1.282657
        cars |   .4740241    .008127   -43.54   0.000     .4583601    .4902233
        int1 |   .9713315   .0003749   -75.36   0.000     .9705969    .9720666
        int2 |   .9985249   .0009732    -1.51   0.130     .9966192    1.000434
        int3 |   1.008344   .0015728     5.33   0.000     1.005266    1.011432
        int4 |   .9933911   .0005247   -12.55   0.000     .9923632    .9944201
        int5 |   1.001216   .0008446     1.44   0.150     .9995622    1.002873
        int6 |   1.000569   .0003738     1.52   0.128     .9998363    1.001302
        int7 |   .9926032   .0005757   -12.80   0.000     .9914754    .9937322
        int8 |   1.000006   2.90e-06     2.10   0.036            1    1.000012
        int9 |   1.000047   4.49e-06    10.46   0.000     1.000038    1.000056
       int10 |    1.00885   .0002004    44.36   0.000     1.008457    1.009243
       int11 |   1.053473   .0045182    12.15   0.000     1.044655    1.062366
       _cons |   1.73e-09   2.47e-10  -141.85   0.000     1.31e-09    2.29e-09
  ln(denom) |          1  (exposure)
-------------+----------------------------------------------------------------
    /lnalpha |  -4.223118   .0380815                     -4.297756   -4.148479
-------------+----------------------------------------------------------------
       alpha |   .0146529    .000558                       .013599    .0157884
------------------------------------------------------------------------------
LR test of alpha=0: chibar2(01) = 1360.49              Prob >= chibar2 = 0.000

. estat ic

Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |        Obs  ll(null)  ll(model)      df         AIC        BIC
-------------+---------------------------------------------------------------
           . |     35,700 -110741.9  -58966.38      19    117970.8   118131.9
-----------------------------------------------------------------------------
               Note: N=Obs used in calculating BIC; see [R] BIC note.

.
```


Parkinson J, *et al. Heart* 2020; 106:584–589. doi: 10.1136/heartjnl-2019-315029

Figure 2 CeVD model specification and regression output

xi: nbreg numer agesq nsex age nyear cars int3 int4 int5 int6 int7 int8, exp(denom) iter(50) irr
estat ic

```
Negative binomial regression                    Number of obs     =     35,700
                                                LR chi2(12)       =   81815.84
Dispersion     = mean                           Prob > chi2       =     0.0000
Log likelihood = -48065.156                     Pseudo R2         =     0.4598
```

numer	IRR	Std. Err.	z	P>|z|	[95% Conf.	Interval]
agesq	.9996584	.0000383	-8.92	0.000	.9995833	.9997334
nsex	1.262057	.0152965	19.20	0.000	1.23243	1.292397
age	1.1648	.0057569	30.87	0.000	1.153571	1.176139
nyear	1.059597	.0051659	11.87	0.000	1.04952	1.069771
nyearsq	.9994498	.00002	-27.44	0.000	.9994105	.999489
cars	.9376628	.0598021	-1.01	0.313	.8274827	1.062513
int3	.9962351	.0002454	-15.31	0.000	.9957543	.9967161
int4	.9859688	.0055635	-2.50	0.012	.9751246	.9969335
int5	.9920457	.001943	-4.08	0.000	.9882449	.9958612
int6	1.000117	.0000151	7.75	0.000	1.000087	1.000147
int7	.9973626	.0001478	-17.82	0.000	.997073	.9976523
int8	1.000023	1.15e-06	20.33	0.000	1.000021	1.000026
_cons	6.16e-07	9.82e-08	-89.63	0.000	4.50e-07	8.42e-07
ln(denom)	1	(exposure)				
/lnalpha	-4.350457	.0718116			-4.491205	-4.209709
alpha	.0129009	.0009264			.0112071	.0148507

```
LR test of alpha=0: chibar2(01) = 292.74           Prob >= chibar2 = 0.000

. estat ic

Akaike's information criterion and Bayesian information criterion
```

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	35,700	-88973.08	-48065.16	14	96158.31	96277.07

Parkinson J, *et al. Heart* 2020; 106:584–589. doi: 10.1136/heartjnl-2019-315029

Figure 3 IHD Predicted and observed data

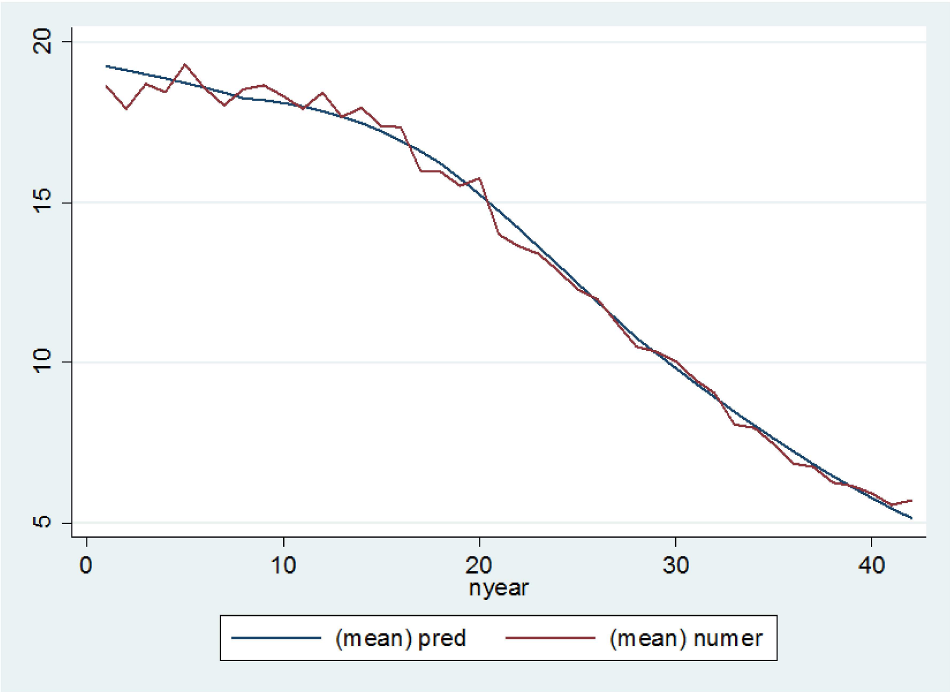

Figure 4 CeVD Predicted and observed data