Appendix

Age, period and cohort effects in the prescription of benzodiazepine and statin in the Netherlands 1994 – 2008

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Appendix

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Appendix A. Measures in drug utilization studies

A number of pharmacoepidemiological measures can be used to study trends in drug prescription. In order to choose the optimal measure, the use of, and the strengths and weaknesses of four measures will be reviewed in this text. Four measures were chosen to be reviewed as they were found in drug utilization studies, or because they are discussed in pharmacoepidemiological literature on drug utilization studies (Lee & Bergman, 2005). The measures are the prescription rate (section 2), which has two different interpretations, one of which is referred to as 'user prevalence' (section 1), the defined daily dose (section 3) and user incidence (section 4). The choice for the measure that is used as the dependent variable in this study is elaborate upon at the end of this chapter (section 5).

A.1 User prevalence

The term 'prescription rate' has two definitions. The more common definition, to be reviewed in this section, is occasionally also referred to as 'apparent drug use' (Cosentino et al., 2000) or 'user prevalence' (Meijer et al., 2004) in some studies. In order to distinguish it from the second definition, which has no synonyms, it will be referred to as 'user prevalence' in this thesis. As it is based on the epidemiological measure 'prevalence', this is also considered the most appropriate way of referring to this measure by the author of this thesis (see also section 5.2). User prevalence is defined as 'the number of users in the population in a defined period'.

In order to determine for what purpose and in what manner this definition is used, a number of publications are examined. Publications using this measure (for example Uchida et al., 2009, Valiyeva et al., 2008) consider an individual a 'user' if he or she gets at least one unit of the drug prescribed in a time and age interval. Since it cannot be known whether an individual used the drug prescribed to him, Cosentino et al. (2000) emphasizes 'apparent' drug use. In the examined studies time intervals vary from a year (Ding et al., 2007, Donoghue et al., 1996) to a month (Uchida et al., 2009; Valiyeva et al., 2008) to a single day (Meijer et al., 2004). In all cases, the number of users is expressed as either a percentage of the total population or the number of users per 1000 population. Valiyeva et al. (2008) and Donoghue et al. (1996) use prescription datasets for the general population, and thus consider the total population, by age category where applicable, as their denominator. Uchida et al. (2009) and Ding et al. (2007) use information from a hospital setting, and therefore only consider part of the patient population of that hospital as the denominator.

Most of the above studies were trend studies, researching whether an educational intervention for doctors (Ding et al., 2007), a public warning (Valiyeva et al., 2008) or a guideline change (Donoghue et al., 1996) affected the levels of prescription rates of particular drugs. Uchida et al. (2009), on the other hand, compared user prevalence among age categories and looked at the association between user prevalence and concomitant prescription of a second drug.

None of the authors provided a motivation for choosing their construction of this measure, or their choice of this measure rather than another. Nevertheless, it is clear that the first definition should be used when the study requires information on the number of individuals in the population that use a drug. For example, this can provide information on the number of persons with a particular health problem (e.g. insulin use as a proxy for diabetes) or the uptake of prophylactic policies (e.g. use of contraceptive pill). A weakness of this measure is that it gives no information on whether users are incidental users, frequent-users, long-term users or first-time users.

A.2 Prescription rate

Authors using the second definition of prescription rate (DiMaggio et al. 2007; Gibbons et al. 2006) count either the total number of pills prescribed (Gibbons et al., 2006) or the total number of prescriptions (DiMaggio et al., 2007) in a time and age interval. Intervals are one week of length in DiMaggio et al. (2007) and two years in Gibbons et al. (2006). In both publications, the number of prescriptions or pills is expressed as a proportion of the total population. Both publications use information from registration data of the entire population, and therefore also consider the total population, by age category where applicable, in a defined area as the denominator.

Gibbons et al. (2006) looked at the relation between antidepressant prescriptions and suicide between various counties in the U.S. in a single period. DiMaggio et al. (2007) looked the effect of terrorist attacks on weekly prescription trends of antidepressants.

The second definition is of use for studies looking at prescription behaviours of doctors, and may have use for pharmacoeconomic research as the number of units prescribed may be a good indication of specific health-costs in a population. However, it gives only crude information on the health, or health trends, of a population, because a rise in prescriptions can be caused by an increase in the number of users or by more prescriptions for those that already use. Furthermore, while expressed as a proportion, this proportion is less clear in its interpretation than the prescription rate of the first definition. Taking the above into consideration, perhaps user prevalence, would have been a better measure for Gibbons et al. (2006) and DiMaggio et al. (2007).

A.3 Daily defined dose

Defined daily dose (DDD) is a unit of measurement designed by the WHO to make comparisons between countries and between time periods possible. It is a fixed unit of measurement and is independent of the cost of the drug or the dosage form (WHO, 2009). The DDD is the assumed global average maintenance dose per day for a drug. It is not necessarily the same as the recommended dose or the actual prescribed daily dose (PDD), for example because drug dose is dependent on characteristics of the individual to whom a drug is prescribed (WHO, 2009).

When used for population level research, DDD's are commonly expressed as the number of DDDs per 1000 population per day (DDD/1000/Day) (Truter et al., 1996). A number of studies have assessed the use of the DDD/1000/day measure. Olveira et al. 2009 conclude that it is a useful measure for cross-country comparison and trend analysis. It is also considered a good measure for the indirect estimation of user prevalence by Olveira et al. (2009). These findings are largely corroborated by the study of Cosentino et al. (2000), which also proposed a method for translating DDD/1000/day into an estimation of the number of users per 1000 population. Lee & Bergman (2005) on the other hand, write that DDD should not be used to estimate incidence and prevalence of drug use because of a number of important limitations.

While the measure should theoretically give a rough indication on the number of patients per 1000 populations are receiving a drug per day, it does not always do so. First, while it may give a good indication for drugs used continuously, such as antidiabetic drugs, it does not give a good indication for drugs use infrequently, such as benzodiazepine, or in short courses, such as antibiotics (Truter et al., 1996). Secondly, since the DDD is a standardized measure, it is not equivalent to the average doses actually prescribed (PDD). This is problematic for comparisons between countries with different ethnic compositions. For example, different ethnicities may, due to physiological differences, get lower actual prescribed daily dose (PDD) which would translate into lower DDDs and thereby into a lower number of apparent users (Truter et al., 1996). Truter et al.(1996) therefore suggest that the measure should be used in combination with other measures.

Taking into consideration the criticism of Truter et al. (1996), it is unfortunate that none of the above studies assessed the measure for comparisons between age groups. Age appears to be an important factor affecting defined daily dose. Lee and Bergman (2005) write that children have substantially lowers doses, resulting in lower DDD. Doctors are also advised to prescribe lower doses to elderly patients, due to physiological changes that come with ageing (Midlöv, 2009). When total DDD for younger or older age groups is then translated to total number of apparent users, it will appear as if there are fewer users, even if the number of users remains level with age. This is problematic for comparisons between age groups within one population, and comparisons between populations with different age structures.

A.4 User incidence

In drug utilization studies, user incidence measures the number of individuals that become a user in a defined period of time (Meijer et al., 2004). This requires a definition of 'first user'. As Truter et al. (1996) points out for the measure 'DDD/1000/day', the number of users of a drug cannot be estimated properly if the drug in question is used infrequently. The same applies to user incidence: a person cannot be considered a new user every time there is a short gap in-between use of the drug. Drug utilization studies using the incidence measure solve this by considering a person a 'new user' only if he or she has not used the studied drug at any point in a defined time period prior to current use. For example, Meijer et al. (2004) consider a user a 'new user' if he or she did not use an anti-depressant within one year prior to current use.

Rockett (1999) writes that incidence is a useful measure for studying etiology because a change in risk factors should result in a similar change in incidence. This should also be the case for drug utilization studies. For example, the change in policy regarding first use of benzodiazepine described in should result in a lower number of new users in the affected period.

A.5 Choice of the dependent variable

Two considerations have to be made for each measure: would their use contribute towards answering the research questions posed in this thesis and can the measures be used in APC-analysis?

The primary research question refers to users. Coupled to the hypotheses, questions can be asked such as 'is there a rise in the number of statin-users aged 70+ after the guideline change in 2006?', 'Does the number of users of benzodiazepine remain level due to addiction?'. It is clear then that the prescription rate, measuring number of prescriptions rather than users, is of no use for this study. The daily defined dose could be of use to estimate the number of users in a population, but this is not required as direct information on the number of persons receiving a prescription is available. Therefore, user prevalence is the most useful measure for the study. However, this measure gives no information on whether an individual is a first user or long-time users. Therefore user incidence will also be calculated for the descriptive analysis in order to identify first users. Furthermore, all of the measures reviewed above can be expressed as age and sex standardized measures. By controlling for population composition, changes in the trends in drug prescription cannot be attributed to the size of cohorts and can therefore be attributed to another effect, such as guideline changes.

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Appendix B. Models

Benzodiazepine models

Statin models

B.1.1 Benzodiazepine - Male – Age

Goodness of Fit

	Value	df	Value/df
Deviance	2629	88	29.875
Scaled Deviance	2629	88	
Pearson Chi-Square	2658.845	88	30.214
Scaled Pearson Chi-Square	2658.845	88	
Log Likelihood	-1828.154		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	1001112.673	1	0
Age	49651.051	21	0

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.95	0.02	-3.99	-3.91	40135.60	1.00	0.00
Age 83-85	2.55	0.02	2.51	2.60	11728.97	1.00	0.00
Age 80-82	2.45	0.02	2.41	2.49	11556.09	1.00	0.00
Age 77-79	2.34	0.02	2.30	2.39	10977.59	1.00	0.00
Age 74-76	2.27	0.02	2.23	2.32	10529.78	1.00	0.00
Age 71-73	2.18	0.02	2.14	2.23	9758.52	1.00	0.00
Age 68-70	2.09	0.02	2.05	2.14	9036.40	1.00	0.00
Age 65-67	2.01	0.02	1.97	2.05	8344.71	1.00	0.00
Age 62-64	1.95	0.02	1.90	1.99	7957.06	1.00	0.00
Age 59-61	1.89	0.02	1.84	1.93	7611.86	1.00	0.00
Age 56-58	1.85	0.02	1.81	1.90	7452.73	1.00	0.00
Age 53-55	1.83	0.02	1.79	1.88	7365.70	1.00	0.00
Age 50-52	1.80	0.02	1.75	1.84	7092.23	1.00	0.00
Age 47-49	1.72	0.02	1.68	1.77	6494.90	1.00	0.00
Age 44-46	1.64	0.02	1.60	1.69	5871.89	1.00	0.00
Age 41-43	1.59	0.02	1.55	1.63	5459.94	1.00	0.00
Age 38-40	1.50	0.02	1.46	1.54	4813.75	1.00	0.00
Age 35-37	1.37	0.02	1.33	1.41	3961.63	1.00	0.00
Age 32-34	1.25	0.02	1.21	1.30	3228.50	1.00	0.00
Age 29-31	1.05	0.02	1.01	1.10	2184.89	1.00	0.00
Age 26-28	0.79	0.02	0.75	0.84	1157.11	1.00	0.00
Age 23-25	0.41	0.02	0.36	0.46	275.91	1.00	0.00
Age baseline	0.00	.	.	.	.	.	.
(Scale)	1.00						

B.1.2 Benzodiazepine - Male – Age Drift

Goodness of Fit

	Value	df	Value/df
Deviance	321.863	87	3.700
Scaled Deviance	321.863	87	
Pearson Chi-Square	320.562	87	3.685
Scaled Pearson Chi-Square	320.562	87	
Log Likelihood	-674.585		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	117259.223	1	.000
Age	50301.808	21	.000
pdrift	2320.665	1	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.687	.0204	-3.727	-3.647	32547.973	1	.000
Age 83-85	2.568	.0236	2.521	2.614	11848.996	1	.000
Age 80-82	2.458	.0228	2.414	2.503	11638.427	1	.000
Age 77-79	2.347	.0224	2.303	2.391	11005.148	1	.000
Age 74-76	2.273	.0221	2.230	2.316	10534.211	1	.000
Age 71-73	2.184	.0221	2.141	2.227	9778.669	1	.000
Age 68-70	2.098	.0220	2.054	2.141	9071.137	1	.000
Age 65-67	2.015	.0220	1.972	2.058	8401.767	1	.000
Age 62-64	1.960	.0218	1.917	2.002	8073.944	1	.000
Age 59-61	1.902	.0216	1.860	1.945	7746.957	1	.000
Age 56-58	1.867	.0215	1.825	1.909	7555.495	1	.000
Age 53-55	1.839	.0214	1.797	1.881	7416.432	1	.000
Age 50-52	1.798	.0213	1.756	1.840	7108.254	1	.000
Age 47-49	1.724	.0214	1.682	1.766	6499.594	1	.000
Age 44-46	1.645	.0214	1.603	1.687	5882.654	1	.000
Age 41-43	1.590	.0215	1.548	1.632	5467.142	1	.000
Age 38-40	1.500	.0216	1.457	1.542	4823.673	1	.000
Age 35-37	1.371	.0218	1.328	1.414	3961.817	1	.000
Age 32-34	1.247	.0220	1.203	1.290	3199.987	1	.000
Age 29-31	1.046	.0225	1.001	1.090	2154.921	1	.000
Age 26-28	.788	.0233	.743	.834	1146.049	1	.000
Age 23-25	.412	.0248	.364	.461	276.075	1	.000
Age baseline	0	.	.	.	.	.	.
pdrift	-.080	.0017	-.083	-.076	2320.665	1	.000
(Scale)	1						

B.1.3 Benzodiazepine - Male – Age Period Drift

Goodness of Fit

	Value	df	Value/df
Deviance	312.557	84	3.721
Scaled Deviance	312.557	84	
Pearson Chi-Square	312.293	84	3.718
Scaled Pearson Chi-Square	312.293	84	
Log Likelihood	-669.932		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	77540.072	1	.000
acode	50305.891	21	.000
pdrift	1371.185	1	.000
prdfactor	9.299	3	.026

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.698	.0216	-3.740	-3.655	29217.779	1	.000
Age 83-85	2.567	.0236	2.521	2.614	11846.854	1	.000
Age 80-82	2.458	.0228	2.413	2.503	11635.599	1	.000
Age 77-79	2.347	.0224	2.303	2.391	11004.165	1	.000
Age 74-76	2.273	.0221	2.230	2.317	10534.813	1	.000
Age 71-73	2.184	.0221	2.141	2.227	9778.472	1	.000
Age 68-70	2.098	.0220	2.054	2.141	9071.833	1	.000
Age 65-67	2.015	.0220	1.972	2.058	8402.316	1	.000
Age 62-64	1.960	.0218	1.917	2.003	8076.468	1	.000
Age 59-61	1.902	.0216	1.860	1.945	7747.544	1	.000
Age 56-58	1.866	.0215	1.824	1.908	7552.528	1	.000
Age 53-55	1.839	.0214	1.797	1.881	7414.507	1	.000
Age 50-52	1.798	.0213	1.756	1.840	7107.719	1	.000
Age 47-49	1.724	.0214	1.682	1.766	6499.396	1	.000
Age 44-46	1.645	.0214	1.603	1.687	5882.595	1	.000
Age 41-43	1.590	.0215	1.548	1.632	5466.474	1	.000
Age 38-40	1.500	.0216	1.457	1.542	4823.302	1	.000
Age 35-37	1.371	.0218	1.328	1.413	3959.955	1	.000
Age 32-34	1.246	.0220	1.203	1.289	3197.953	1	.000
Age 29-31	1.045	.0225	1.001	1.090	2154.185	1	.000
Age 26-28	.788	.0233	.743	.834	1145.951	1	.000
Age 23-25	.412	.0248	.364	.461	275.956	1	.000
Age baseline	0	.	.	.	.	.	.

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Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
pdrift	-.079	.0021	-.083	-.075	1371.185	1	.000
Period 2003 - 2005	.016	.0057	.005	.027	8.075	1	.004
Period 2000 - 2002	.013	.0060	.001	.025	4.679	1	.031
Period 1997 - 1999	.010	.0071	-.004	.024	1.857	1	.173
Period baseline	0	.	.	.	.	.	.
(Scale)	1						

B.1.4 Benzodiazepine - Male – Age Period Cohort (explicit drift)

Goodness of Fit

	Value	df	Value/df
Deviance	93.353	60	1.556
Scaled Deviance	93.353	60	
Pearson Chi-Square	92.703	60	1.545
Scaled Pearson Chi-Square	92.703	60	
Log Likelihood	-560.330		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	58637.414	1	.000
acode	9995.310	21	.000
pdrift	1114.183	1	.000
prdfactor	7.763	3	.051
cohfactor	218.438	24	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.624	.0287	-3.680	-3.568	15933.253	1	.000
Age 83-85	2.507	.0349	2.439	2.576	5164.902	1	.000
Age 80-82	2.404	.0331	2.339	2.468	5280.531	1	.000
Age 77-79	2.291	.0321	2.228	2.354	5078.942	1	.000
Age 74-76	2.210	.0318	2.147	2.272	4833.886	1	.000
Age 71-73	2.131	.0323	2.068	2.195	4342.562	1	.000
Age 68-70	2.057	.0328	1.993	2.121	3937.305	1	.000
Age 65-67	1.997	.0329	1.933	2.062	3681.283	1	.000
Age 62-64	1.963	.0329	1.899	2.028	3552.022	1	.000
Age 59-61	1.932	.0328	1.868	1.997	3467.819	1	.000
Age 56-58	1.905	.0326	1.841	1.968	3412.821	1	.000
Age 53-55	1.878	.0323	1.814	1.941	3379.704	1	.000
Age 50-52	1.824	.0320	1.761	1.887	3249.311	1	.000
Age 47-49	1.729	.0317	1.667	1.791	2971.958	1	.000
Age 44-46	1.622	.0314	1.561	1.684	2672.062	1	.000
Age 41-43	1.544	.0310	1.483	1.605	2482.791	1	.000
Age 38-40	1.438	.0305	1.378	1.498	2219.530	1	.000
Age 35-37	1.300	.0300	1.241	1.359	1875.101	1	.000
Age 32-34	1.174	.0295	1.116	1.232	1577.853	1	.000
Age 29-31	.985	.0286	.929	1.041	1184.196	1	.000
Age 26-28	.725	.0275	.671	.779	696.723	1	.000

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Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
Age 23-25	.373	.0270	.320	.426	191.510	1	.000
Age baseline	0	.	.	.	.	.	.
pdrift	-.079	.0024	-.084	-.075	1114.183	1	.000
Period 2003 - 2005	.014	.0058	.003	.026	6.238	1	.013
Period 2000 - 2002	.013	.0061	.001	.025	4.572	1	.032
Period 1997 - 1999	.011	.0072	-.003	.025	2.390	1	.122
Period baseline	0	.	.	.	.	.	.
Cohort 1986 - 1988	-.189	.0542	-.295	-.083	12.198	1	.000
Cohort 1983 - 1985	-.110	.0340	-.177	-.043	10.424	1	.001
Cohort 1980 - 1982	.020	.0245	-.028	.068	.680	1	.410
Cohort 1977 - 1979	-.067	.0204	-.107	-.027	10.853	1	.001
Cohort 1971 - 1973	.006	.0163	-.026	.038	.119	1	.730
Cohort 1968 - 1970	-.004	.0162	-.035	.028	.050	1	.823
Cohort 1965 - 1967	-.002	.0167	-.035	.031	.019	1	.891
Cohort 1962 - 1964	.003	.0171	-.030	.037	.038	1	.846
Cohort 1959 - 1961	-.028	.0175	-.062	.006	2.527	1	.112
Cohort 1956 - 1958	-.052	.0177	-.087	-.018	8.816	1	.003
Cohort 1953 - 1955	-.103	.0178	-.138	-.068	33.516	1	.000
Cohort 1950 - 1952	-.099	.0178	-.134	-.064	31.061	1	.000
Cohort 1947 - 1949	-.138	.0178	-.173	-.103	60.208	1	.000
Cohort 1944 - 1946	-.096	.0178	-.131	-.062	29.512	1	.000
Cohort 1941 - 1943	-.125	.0180	-.160	-.090	48.107	1	.000
Cohort 1938 - 1940	-.058	.0176	-.093	-.023	10.808	1	.001
Cohort 1935 - 1937	-.046	.0172	-.080	-.013	7.247	1	.007
Cohort 1932 - 1934	.010	.0162	-.022	.041	.359	1	.549
Cohort 1929 - 1931	-.043	.0156	-.074	-.013	7.761	1	.005
Cohort 1926 - 1928	-.008	.0150	-.037	.021	.286	1	.593
Cohort 1920 - 1922	.007	.0170	-.026	.040	.161	1	.689
Cohort 1917 - 1919	-.092	.0222	-.136	-.049	17.323	1	.000
Cohort 1914 - 1916	.003	.0292	-.054	.060	.009	1	.924
Cohort 1911 - 1913	.072	.0515	-.029	.173	1.962	1	.161
Cohort baseline	0	.	.	.	.	.	.
(Scale)	1						

B.1.5 Benzodiazepine - Female – Age

Goodness of Fit

	Value	df	Value/df
Deviance	5376.314	88	61.094
Scaled Deviance	5376.314	88	
Pearson Chi-Square	5464.996	88	62.102
Scaled Pearson Chi-Square	5464.996	88	
Log Likelihood	-3235.911		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	1132458.029	1	.000
acode	125792.371	21	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.425	.0141	-3.453	-3.398	58827.533	1	.000
Age 83-85	2.513	.0159	2.482	2.544	25115.889	1	.000
Age 80-82	2.462	.0156	2.432	2.493	24814.915	1	.000
Age 77-79	2.407	.0155	2.377	2.437	24029.868	1	.000
Age 74-76	2.345	.0155	2.314	2.375	22795.126	1	.000
Age 71-73	2.273	.0156	2.242	2.303	21239.050	1	.000
Age 68-70	2.210	.0156	2.179	2.240	19973.949	1	.000
Age 65-67	2.126	.0157	2.096	2.157	18354.507	1	.000
Age 62-64	2.058	.0156	2.027	2.088	17328.208	1	.000
Age 59-61	1.975	.0156	1.944	2.005	16088.386	1	.000
Age 56-58	1.897	.0155	1.867	1.928	14928.233	1	.000
Age 53-55	1.810	.0155	1.780	1.840	13603.493	1	.000
Age 50-52	1.742	.0155	1.712	1.773	12600.759	1	.000
Age 47-49	1.657	.0156	1.626	1.687	11296.275	1	.000
Age 44-46	1.575	.0157	1.544	1.605	10112.049	1	.000
Age 41-43	1.481	.0158	1.450	1.512	8824.733	1	.000
Age 38-40	1.348	.0159	1.317	1.379	7154.885	1	.000
Age 35-37	1.229	.0161	1.198	1.261	5809.351	1	.000
Age 32-34	1.087	.0164	1.054	1.119	4379.586	1	.000
Age 29-31	.891	.0168	.858	.924	2808.127	1	.000
Age 26-28	.620	.0174	.586	.654	1275.356	1	.000
Age 23-25	.316	.0181	.280	.351	303.205	1	.000
Age baseline	0	.	.	.	.	.	.
(Scale)	1						

B.1.6 Benzodiazepine - Female – Age Drift

Goodness of Fit

	Value	df	Value/df
Deviance	357.649	87	4.111
Scaled Deviance	357.649	87	
Pearson Chi-Square	359.698	87	4.134
Scaled Pearson Chi-Square	359.698	87	
Log Likelihood	-726.578		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	120479.265	1	.000
acode	126327.027	21	.000
pdrift	5045.946	1	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.135	.0147	-3.164	-3.106	45614.306	1	.000
Age 83-85	2.519	.0159	2.488	2.550	25229.069	1	.000
Age 80-82	2.462	.0156	2.432	2.493	24819.063	1	.000
Age 77-79	2.400	.0155	2.370	2.430	23889.316	1	.000
Age 74-76	2.333	.0155	2.303	2.364	22565.698	1	.000
Age 71-73	2.265	.0156	2.234	2.295	21085.492	1	.000
Age 68-70	2.205	.0156	2.174	2.235	19881.370	1	.000
Age 65-67	2.126	.0157	2.095	2.157	18347.800	1	.000
Age 62-64	2.067	.0156	2.036	2.097	17482.743	1	.000
Age 59-61	1.988	.0156	1.957	2.018	16299.007	1	.000
Age 56-58	1.907	.0155	1.877	1.938	15083.321	1	.000
Age 53-55	1.814	.0155	1.783	1.844	13661.917	1	.000
Age 50-52	1.741	.0155	1.710	1.771	12581.310	1	.000
Age 47-49	1.655	.0156	1.625	1.686	11275.232	1	.000
Age 44-46	1.573	.0157	1.542	1.604	10090.844	1	.000
Age 41-43	1.478	.0158	1.447	1.509	8789.154	1	.000
Age 38-40	1.344	.0159	1.313	1.376	7117.823	1	.000
Age 35-37	1.223	.0161	1.192	1.255	5752.147	1	.000
Age 32-34	1.077	.0164	1.044	1.109	4299.586	1	.000
Age 29-31	.880	.0168	.847	.913	2738.746	1	.000
Age 26-28	.614	.0174	.580	.648	1247.843	1	.000
Age 23-25	.314	.0181	.279	.350	300.320	1	.000
Age baseline	0	.	.	.	.	.	.
pdrift	-.087	.0012	-.089	-.084	5045.946	1	.000
(Scale)	1						

B.1.7 Benzodiazepine - Female – Age Period Drift

Goodness of Fit

	Value	df	Value/df
Deviance	334.351	84	3.980
Scaled Deviance	334.351	84	
Pearson Chi-Square	335.769	84	3.997
Scaled Pearson Chi-Square	335.769	84	
Log Likelihood	-714.930		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	79967.923	1	.000
acode	126319.329	21	.000
pdrift	3442.782	1	.000
prdfactor	23.292	3	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.116	.0155	-3.147	-3.086	40310.743	1	.000
Age 83-85	2.519	.0159	2.488	2.550	25227.890	1	.000
Age 80-82	2.462	.0156	2.431	2.493	24811.799	1	.000
Age 77-79	2.400	.0155	2.370	2.431	23895.642	1	.000
Age 74-76	2.333	.0155	2.303	2.364	22564.798	1	.000
Age 71-73	2.264	.0156	2.234	2.295	21083.070	1	.000
Age 68-70	2.205	.0156	2.174	2.235	19880.462	1	.000
Age 65-67	2.126	.0157	2.095	2.157	18345.923	1	.000
Age 62-64	2.067	.0156	2.036	2.097	17482.004	1	.000
Age 59-61	1.988	.0156	1.957	2.018	16295.751	1	.000
Age 56-58	1.907	.0155	1.876	1.937	15076.783	1	.000
Age 53-55	1.814	.0155	1.784	1.844	13662.917	1	.000
Age 50-52	1.741	.0155	1.710	1.771	12581.012	1	.000
Age 47-49	1.655	.0156	1.625	1.686	11273.602	1	.000
Age 44-46	1.573	.0157	1.542	1.604	10089.812	1	.000
Age 41-43	1.478	.0158	1.447	1.509	8787.690	1	.000
Age 38-40	1.344	.0159	1.313	1.376	7117.616	1	.000
Age 35-37	1.223	.0161	1.192	1.255	5752.064	1	.000
Age 32-34	1.077	.0164	1.044	1.109	4298.951	1	.000
Age 29-31	.880	.0168	.847	.913	2740.211	1	.000
Age 26-28	.614	.0174	.580	.648	1247.835	1	.000
Age 23-25	.314	.0181	.279	.350	300.059	1	.000
Age baseline	0	.	.	.	.	.	.

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Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
pdrift	-.091	.0015	-.094	-.088	3442.782	1	.000
Period 2003 - 2005	.002	.0043	-.006	.011	.320	1	.571
Period 2000 - 2002	-.002	.0044	-.011	.006	.321	1	.571
Period 1997 - 1999	-.022	.0052	-.032	-.011	17.431	1	.000
Period baseline	0	.	.	.	.	.	.
(Scale)	1						

B.1.8 Benzodiazepine - Female – Age Period Cohort (explicit drift)

Goodness of Fit

	Value	df	Value/df
Deviance	64.558	60	1.076
Scaled Deviance	64.558	60	
Pearson Chi-Square	64.511	60	1.075
Scaled Pearson Chi-Square	64.511	60	
Log Likelihood	-580.033		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	60854.368	1	.000
acode	21804.337	21	.000
pdrift	2699.272	1	.000
prdfactor	21.032	3	.000
cohfactor	270.111	24	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-3.126	.0217	-3.169	-3.084	20731.747	1	.000
Age 83-85	2.545	.0250	2.497	2.594	10386.233	1	.000
Age 80-82	2.479	.0240	2.432	2.526	10635.300	1	.000
Age 77-79	2.405	.0235	2.359	2.451	10474.502	1	.000
Age 74-76	2.328	.0233	2.282	2.374	10013.000	1	.000
Age 71-73	2.250	.0236	2.204	2.296	9119.771	1	.000
Age 68-70	2.182	.0239	2.136	2.229	8370.671	1	.000
Age 65-67	2.121	.0240	2.074	2.168	7797.167	1	.000
Age 62-64	2.085	.0241	2.038	2.132	7480.169	1	.000
Age 59-61	2.028	.0241	1.980	2.075	7055.426	1	.000
Age 56-58	1.974	.0241	1.926	2.021	6702.219	1	.000
Age 53-55	1.892	.0240	1.845	1.939	6194.099	1	.000
Age 50-52	1.818	.0239	1.771	1.864	5769.057	1	.000
Age 47-49	1.725	.0238	1.679	1.772	5239.884	1	.000
Age 44-46	1.625	.0237	1.579	1.672	4707.616	1	.000
Age 41-43	1.520	.0235	1.473	1.566	4176.649	1	.000
Age 38-40	1.371	.0233	1.325	1.417	3471.670	1	.000
Age 35-37	1.238	.0229	1.193	1.283	2917.561	1	.000
Age 32-34	1.089	.0226	1.044	1.133	2319.074	1	.000
Age 29-31	.890	.0218	.848	.933	1667.450	1	.000
Age 26-28	.617	.0208	.576	.658	880.794	1	.000

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Table continued… Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
Age 23-25	.307	.0199	.268	.346	238.819	1	.000
Age baseline	0	.	.	.	.	.	.
pdrift	-.092	.0018	-.095	-.089	2699.272	1	.000
Period 2003 - 2005	.000	.0043	-.008	.009	.011	1	.916
Period 2000 - 2002	-.004	.0045	-.012	.005	.673	1	.412
Period 1997 - 1999	-.022	.0052	-.032	-.011	17.219	1	.000
Period baseline	0	.	.	.	.	.	.
Cohort 1986 - 1988	-.030	.0381	-.105	.044	.633	1	.426
Cohort 1983 - 1985	.071	.0250	.022	.120	8.139	1	.004
Cohort 1980 - 1982	.032	.0195	-.006	.070	2.703	1	.100
Cohort 1977 - 1979	-.016	.0165	-.048	.017	.898	1	.343
Cohort 1971 - 1973	.026	.0136	.000	.053	3.727	1	.054
Cohort 1968 - 1970	.012	.0135	-.014	.039	.817	1	.366
Cohort 1965 - 1967	-.033	.0139	-.060	-.005	5.536	1	.019
Cohort 1962 - 1964	.006	.0140	-.021	.034	.192	1	.661
Cohort 1959 - 1961	-.022	.0141	-.050	.006	2.468	1	.116
Cohort 1956 - 1958	-.046	.0141	-.074	-.019	10.845	1	.001
Cohort 1953 - 1955	-.071	.0139	-.098	-.044	25.951	1	.000
Cohort 1950 - 1952	-.087	.0137	-.114	-.061	40.516	1	.000
Cohort 1947 - 1949	-.048	.0133	-.074	-.022	12.759	1	.000
Cohort 1944 - 1946	-.052	.0131	-.077	-.026	15.749	1	.000
Cohort 1941 - 1943	-.053	.0130	-.079	-.028	16.934	1	.000
Cohort 1938 - 1940	.040	.0123	.016	.065	10.824	1	.001
Cohort 1935 - 1937	.041	.0116	.018	.064	12.436	1	.000
Cohort 1932 - 1934	.038	.0108	.017	.059	12.379	1	.000
Cohort 1929 - 1931	.036	.0099	.017	.056	13.334	1	.000
Cohort 1926 - 1928	.014	.0094	-.004	.032	2.194	1	.139
Cohort 1920 - 1922	.006	.0101	-.013	.026	.398	1	.528
Cohort 1917 - 1919	-.024	.0129	-.049	.001	3.422	1	.064
Cohort 1914 - 1916	-.031	.0166	-.064	.001	3.569	1	.059
Cohort 1911 - 1913	-.028	.0294	-.085	.030	.884	1	.347
Cohort baseline	0	.	.	.	.	.	.
(Scale)	1						

Appendix B

Benzodiazepine models

Statin models

B.2.1 Statin - Male – Age

Goodness of Fit

	Value	df	Value/df
Deviance	25266.895	88	287.124
Scaled Deviance	25266.895	88	
Pearson Chi-Square	23138.453	88	262.937
Scaled Pearson Chi-Square	23138.453	88	
Log Likelihood	-13078.926		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	177452.139	1	.000
acode	99400.348	21	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-7.384	.1098	-7.599	-7.169	4525.315	1	.000
Age 83-85	5.528	.1110	5.310	5.745	2481.476	1	.000
Age 80-82	5.734	.1105	5.517	5.950	2694.846	1	.000
Age 77-79	5.871	.1102	5.655	6.087	2836.853	1	.000
Age 74-76	5.957	.1101	5.741	6.173	2926.328	1	.000
Age 71-73	5.960	.1101	5.744	6.176	2931.440	1	.000
Age 68-70	5.910	.1101	5.695	6.126	2883.604	1	.000
Age 65-67	5.854	.1100	5.638	6.070	2829.737	1	.000
Age 62-64	5.759	.1100	5.544	5.975	2739.567	1	.000
Age 59-61	5.601	.1100	5.386	5.817	2591.373	1	.000
Age 56-58	5.384	.1101	5.169	5.600	2393.345	1	.000
Age 53-55	5.128	.1101	4.913	5.344	2169.004	1	.000
Age 50-52	4.847	.1102	4.631	5.063	1934.012	1	.000
Age 47-49	4.511	.1104	4.294	4.727	1670.636	1	.000
Age 44-46	4.116	.1106	3.899	4.332	1384.454	1	.000
Age 41-43	3.700	.1110	3.483	3.918	1110.946	1	.000
Age 38-40	3.232	.1117	3.013	3.451	837.439	1	.000
Age 35-37	2.703	.1129	2.481	2.924	572.921	1	.000
Age 32-34	2.211	.1149	1.986	2.436	370.339	1	.000
Age 29-31	1.634	.1188	1.401	1.867	189.379	1	.000
Age 26-28	1.075	.1250	.830	1.320	73.961	1	.000
Age 23-25	.424	.1378	.154	.694	9.483	1	.002
Age baseline	0	.	.	.	.	.	.
(Scale)	1						

B.2.2 Statin - Male – Age Drift

Goodness of Fit

	Value	df	Value/df
Deviance	3890.920	87	44.723
Scaled Deviance	3890.920	87	
Pearson Chi-Square	3468.202	87	39.864
Scaled Pearson Chi-Square	3468.202	87	
Log Likelihood	-2390.938		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	149382.103	1	.000
acode	97573.881	21	.000
pdrift	19875.188	1	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-8.455	.1101	-8.670	-8.239	5901.177	1	.000
Age 83-85	5.484	.1110	5.266	5.701	2442.202	1	.000
Age 80-82	5.707	.1105	5.491	5.924	2669.807	1	.000
Age 77-79	5.862	.1102	5.646	6.078	2827.889	1	.000
Age 74-76	5.954	.1101	5.738	6.170	2923.230	1	.000
Age 71-73	5.952	.1101	5.736	6.168	2923.538	1	.000
Age 68-70	5.895	.1101	5.679	6.111	2868.604	1	.000
Age 65-67	5.829	.1100	5.613	6.045	2805.408	1	.000
Age 62-64	5.707	.1100	5.491	5.922	2689.579	1	.000
Age 59-61	5.542	.1100	5.326	5.758	2536.755	1	.000
Age 56-58	5.344	.1101	5.128	5.560	2357.403	1	.000
Age 53-55	5.109	.1101	4.893	5.325	2152.900	1	.000
Age 50-52	4.840	.1102	4.624	5.056	1928.569	1	.000
Age 47-49	4.508	.1104	4.292	4.725	1668.905	1	.000
Age 44-46	4.110	.1106	3.893	4.327	1380.777	1	.000
Age 41-43	3.697	.1110	3.479	3.915	1109.017	1	.000
Age 38-40	3.227	.1117	3.008	3.446	834.968	1	.000
Age 35-37	2.706	.1129	2.484	2.927	574.228	1	.000
Age 32-34	2.235	.1149	2.010	2.460	378.497	1	.000
Age 29-31	1.662	.1188	1.429	1.895	195.925	1	.000
Age 26-28	1.089	.1250	.844	1.334	75.829	1	.000
Age 23-25	.425	.1378	.155	.695	9.506	1	.002
Age baseline	0	.	.	.	.	.	.
pdrift	.298	.0021	.293	.302	19875.188	1	.000
(Scale)	1						

B.2.3 Statin - Male – Age Period Drift

Goodness of Fit

	Value	df	Value/df
Deviance	3304.380	84	39.338
Scaled Deviance	3304.380	84	
Pearson Chi-Square	3065.683	84	36.496
Scaled Pearson Chi-Square	3065.683	84	
Log Likelihood	-2097.668		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	79436.439	1	.000
acode	97683.592	21	.000
pdrift	7422.727	1	.000
prdfactor	566.909	3	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-8.753	.1115	-8.971	-8.534	6164.064	1	.000
Age 83-85	5.482	.1110	5.264	5.699	2440.246	1	.000
Age 80-82	5.705	.1105	5.489	5.921	2667.845	1	.000
Age 77-79	5.861	.1102	5.645	6.077	2827.112	1	.000
Age 74-76	5.954	.1101	5.739	6.170	2923.601	1	.000
Age 71-73	5.952	.1101	5.736	6.168	2923.189	1	.000
Age 68-70	5.895	.1101	5.680	6.111	2869.087	1	.000
Age 65-67	5.829	.1100	5.613	6.045	2805.683	1	.000
Age 62-64	5.709	.1100	5.493	5.925	2691.813	1	.000
Age 59-61	5.542	.1100	5.326	5.758	2536.916	1	.000
Age 56-58	5.341	.1101	5.125	5.557	2354.762	1	.000
Age 53-55	5.107	.1101	4.892	5.323	2151.340	1	.000
Age 50-52	4.839	.1102	4.623	5.055	1927.979	1	.000
Age 47-49	4.508	.1104	4.292	4.724	1668.645	1	.000
Age 44-46	4.110	.1106	3.893	4.327	1380.641	1	.000
Age 41-43	3.696	.1110	3.478	3.913	1108.399	1	.000
Age 38-40	3.227	.1117	3.008	3.445	834.700	1	.000
Age 35-37	2.703	.1129	2.482	2.924	573.047	1	.000
Age 32-34	2.232	.1149	2.007	2.457	377.427	1	.000
Age 29-31	1.661	.1188	1.428	1.894	195.630	1	.000
Age 26-28	1.088	.1250	.843	1.333	75.779	1	.000
Age 23-25	.424	.1378	.154	.694	9.470	1	.002
Age baseline	0	.	.	.	.	.	.

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Table continued… Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
pdrift	.349	.0041	.341	.357	7422.727	1	.000
Period 2003 - 2005	.155	.0066	.142	.168	544.853	1	.000
Period 2000 - 2002	.166	.0098	.147	.185	287.599	1	.000
Period 1997 - 1999	.194	.0138	.167	.221	198.806	1	.000
Period baseline	0	.	.	.	.	.	.
(Scale)	1						

B.2.4 Statin - Male – Age Period Cohort (drift absorbed into period)

Goodness of Fit

	Value	df	Value/df
Deviance	79.618	60	1.327
Scaled Deviance	79.618	60	
Pearson Chi-Square	81.555	60	1.359
Scaled Pearson Chi-Square	81.555	60	
Log Likelihood	-485.287		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	35821.847	1	.000
acode	9325.345	21	.000
prdfactor	4331.681	4	.000
cohfactor	2726.187	24	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-7.953	.1594	-8.265	-7.640	2487.937	1	.000
Age 83-85	5.539	.1625	5.220	5.857	1161.855	1	.000
Age 80-82	5.450	.1615	5.133	5.766	1139.193	1	.000
Age 77-79	5.373	.1607	5.058	5.688	1117.323	1	.000
Age 74-76	5.319	.1602	5.005	5.633	1102.573	1	.000
Age 71-73	5.240	.1598	4.926	5.553	1075.130	1	.000
Age 68-70	5.147	.1595	4.834	5.459	1041.898	1	.000
Age 65-67	5.067	.1592	4.755	5.379	1013.315	1	.000
Age 62-64	4.944	.1590	4.632	5.255	966.750	1	.000
Age 59-61	4.817	.1589	4.505	5.128	919.049	1	.000
Age 56-58	4.651	.1589	4.339	4.962	857.012	1	.000
Age 53-55	4.470	.1589	4.158	4.781	790.934	1	.000
Age 50-52	4.277	.1591	3.965	4.588	722.384	1	.000
Age 47-49	4.037	.1594	3.724	4.349	641.447	1	.000
Age 44-46	3.733	.1597	3.420	4.046	546.143	1	.000
Age 41-43	3.364	.1601	3.050	3.678	441.357	1	.000
Age 38-40	2.933	.1605	2.619	3.248	334.109	1	.000
Age 35-37	2.459	.1608	2.144	2.774	233.893	1	.000
Age 32-34	1.966	.1611	1.650	2.281	148.904	1	.000
Age 29-31	1.429	.1590	1.118	1.741	80.852	1	.000
Age 26-28	.926	.1558	.621	1.231	35.342	1	.000
Age 23-25	.251	.1520	-.047	.549	2.717	1	.099
Age baseline	0	.	.	.	.	.	.

…

Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi- Square	df	Sig.
Period 2006 - 2008	1.258	.0220	1.215	1.301	3259.548	1	.000
Period 2003 - 2005	1.067	.0199	1.028	1.106	2880.978	1	.000
Period 2000 - 2002	.755	.0183	.719	.791	1693.902	1	.000
Period 1997 - 1999	.481	.0177	.446	.516	740.140	1	.000
Period baseline	0	.	.	.	.	.	.
[cohfactor=26,00]	-.712	.2758	-1.252	-.171	6.665	1	.010
[cohfactor=25,00]	-.108	.1589	-.419	.204	.461	1	.497
[cohfactor=24,00]	-.298	.1161	-.526	-.071	6.604	1	.010
[cohfactor=23,00]	-.179	.0835	-.343	-.015	4.601	1	.032
[cohfactor=21,00]	-.171	.0589	-.287	-.056	8.451	1	.004
[cohfactor=20,00]	-.069	.0559	-.179	.040	1.547	1	.214
[cohfactor=19,00]	-.015	.0542	-.121	.091	.075	1	.784
[cohfactor=18,00]	-.075	.0521	-.177	.028	2.046	1	.153
[cohfactor=17,00]	.002	.0491	-.094	.098	.002	1	.963
[cohfactor=16,00]	.122	.0456	.033	.212	7.168	1	.007
[cohfactor=15,00]	.225	.0422	.142	.307	28.373	1	.000
[cohfactor=14,00]	.310	.0387	.234	.386	63.856	1	.000
[cohfactor=13,00]	.336	.0353	.267	.405	90.536	1	.000
[cohfactor=12,00]	.440	.0320	.377	.502	189.233	1	.000
[cohfactor=11,00]	.437	.0289	.380	.494	228.935	1	.000
[cohfactor=10,00]	.431	.0258	.381	.482	279.329	1	.000
[cohfactor=9,00]	.427	.0229	.382	.472	348.784	1	.000
[cohfactor=8,00]	.429	.0200	.389	.468	458.817	1	.000
[cohfactor=7,00]	.375	.0176	.340	.410	451.466	1	.000
[cohfactor=6,00]	.204	.0163	.172	.236	156.193	1	.000
[cohfactor=4,00]	-.372	.0220	-.415	-.329	286.318	1	.000
[cohfactor=3,00]	-.940	.0392	-1.016	-.863	574.999	1	.000
[cohfactor=2,00]	-1.931	.0964	-2.120	-1.742	400.833	1	.000
[cohfactor=1,00]	-2.882	.3791	-3.625	-2.139	57.803	1	.000
[cohfactor=,00]	0	.	.	.	.	.	.
(Scale)	1						

B.2.5 Statin - Female – Age

Goodness of Fit

	Value	df	Value/df
Deviance	23547.943	88	267.590
Scaled Deviance	23547.943	88	
Pearson Chi-Square	22307.199	88	253.491
Scaled Pearson Chi-Square	22307.199	88	
Log Likelihood	-12209.037		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	265707.774	1	.000
acode	90750.531	21	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-6.962	.0828	-7.124	-6.799	7075.886	1	.000
Age 83-85	4.848	.0838	4.684	5.012	3346.687	1	.000
Age 80-82	5.089	.0834	4.926	5.253	3720.747	1	.000
Age 77-79	5.255	.0833	5.091	5.418	3982.893	1	.000
Age 74-76	5.308	.0832	5.145	5.471	4069.012	1	.000
Age 71-73	5.317	.0832	5.154	5.480	4084.254	1	.000
Age 68-70	5.267	.0832	5.104	5.431	4008.472	1	.000
Age 65-67	5.162	.0832	4.999	5.325	3847.432	1	.000
Age 62-64	5.040	.0832	4.877	5.203	3667.364	1	.000
Age 59-61	4.805	.0833	4.642	4.968	3328.564	1	.000
Age 56-58	4.525	.0834	4.362	4.689	2945.115	1	.000
Age 53-55	4.177	.0836	4.013	4.341	2498.961	1	.000
Age 50-52	3.799	.0839	3.634	3.963	2052.368	1	.000
Age 47-49	3.374	.0844	3.208	3.539	1599.026	1	.000
Age 44-46	2.950	.0851	2.783	3.117	1201.175	1	.000
Age 41-43	2.511	.0863	2.341	2.680	845.959	1	.000
Age 38-40	2.063	.0881	1.890	2.235	547.892	1	.000
Age 35-37	1.641	.0907	1.463	1.818	326.931	1	.000
Age 32-34	1.189	.0950	1.003	1.375	156.704	1	.000
Age 29-31	1.066	.0962	.878	1.255	122.977	1	.000
Age 26-28	.833	.0984	.640	1.026	71.569	1	.000
Age 23-25	.383	.1049	.177	.589	13.334	1	.000
Age baseline	0	.	.	.	.	.	.
(Scale)	1						

B.2.6 Statin - Female – Age Drift

Goodness of Fit

	Value	df	Value/df
Deviance	3038.687	87	34.927
Scaled Deviance	3038.687	87	
Pearson Chi-Square	2831.089	87	32.541
Scaled Pearson Chi-Square	2831.089	87	
Log Likelihood	-1954.409		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	172731.910	1	.000
acode	91539.882	21	.000
pdrift	18985.119	1	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-8.147	.0833	-8.310	-7.983	9572.968	1	.000
Age 83-85	4.829	.0838	4.665	4.993	3320.997	1	.000
Age 80-82	5.093	.0834	4.930	5.257	3726.771	1	.000
Age 77-79	5.282	.0833	5.119	5.445	4024.195	1	.000
Age 74-76	5.347	.0832	5.183	5.510	4128.752	1	.000
Age 71-73	5.342	.0832	5.179	5.505	4123.787	1	.000
Age 68-70	5.282	.0832	5.119	5.445	4031.075	1	.000
Age 65-67	5.162	.0832	4.999	5.325	3846.451	1	.000
Age 62-64	5.004	.0832	4.841	5.167	3614.643	1	.000
Age 59-61	4.759	.0833	4.596	4.923	3265.571	1	.000
Age 56-58	4.495	.0834	4.331	4.658	2905.712	1	.000
Age 53-55	4.167	.0836	4.003	4.330	2486.301	1	.000
Age 50-52	3.803	.0839	3.639	3.967	2056.879	1	.000
Age 47-49	3.378	.0844	3.213	3.543	1603.201	1	.000
Age 44-46	2.955	.0851	2.788	3.122	1205.144	1	.000
Age 41-43	2.521	.0863	2.352	2.691	853.254	1	.000
Age 38-40	2.075	.0881	1.902	2.247	554.359	1	.000
Age 35-37	1.664	.0907	1.486	1.842	336.329	1	.000
Age 32-34	1.228	.0950	1.042	1.414	167.085	1	.000
Age 29-31	1.106	.0962	.918	1.295	132.381	1	.000
Age 26-28	.855	.0984	.662	1.048	75.503	1	.000
Age 23-25	.390	.1049	.185	.596	13.833	1	.000
Age baseline	0	.	.	.	.	.	.
pdrift	.324	.0024	.319	.328	18985.119	1	.000
(Scale)	1						

B.2.7 Statin - Female – Age Period Drift

Goodness of Fit

	Value	df	Value/df
Deviance	2735.123	84	32.561
Scaled Deviance	2735.123	84	
Pearson Chi-Square	2604.704	84	31.008
Scaled Pearson Chi-Square	2604.704	84	
Log Likelihood	-1802.627		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	85495.343	1	.000
acode	91586.077	21	.000
pdrift	6789.437	1	.000
prdfactor	297.980	3	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-8.366	.0854	-8.533	-8.198	9589.799	1	.000
Age 83-85	4.826	.0838	4.662	4.991	3317.307	1	.000
Age 80-82	5.092	.0834	4.928	5.255	3724.399	1	.000
Age 77-79	5.280	.0833	5.117	5.443	4021.449	1	.000
Age 74-76	5.346	.0832	5.183	5.509	4128.059	1	.000
Age 71-73	5.343	.0832	5.180	5.506	4124.217	1	.000
Age 68-70	5.282	.0832	5.119	5.445	4030.741	1	.000
Age 65-67	5.161	.0832	4.998	5.324	3845.931	1	.000
Age 62-64	5.006	.0832	4.842	5.169	3616.949	1	.000
Age 59-61	4.758	.0833	4.595	4.922	3264.128	1	.000
Age 56-58	4.493	.0834	4.330	4.657	2903.532	1	.000
Age 53-55	4.165	.0836	4.001	4.329	2484.667	1	.000
Age 50-52	3.802	.0839	3.638	3.966	2055.928	1	.000
Age 47-49	3.378	.0844	3.212	3.543	1602.684	1	.000
Age 44-46	2.955	.0851	2.788	3.121	1204.624	1	.000
Age 41-43	2.520	.0863	2.351	2.689	852.453	1	.000
Age 38-40	2.074	.0881	1.901	2.247	553.985	1	.000
Age 35-37	1.662	.0907	1.484	1.840	335.406	1	.000
Age 32-34	1.226	.0950	1.040	1.412	166.575	1	.000
Age 29-31	1.105	.0962	.917	1.294	132.130	1	.000
Age 26-28	.854	.0984	.662	1.047	75.346	1	.000
Age 23-25	.389	.1049	.183	.594	13.738	1	.000
Age baseline	0	.	.	.	.	.	.

…

Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
pdrift	.362	.0044	.354	.371	6789.437	1	.000
Period 2003 - 2005	.122	.0073	.107	.136	275.872	1	.000
Period 2000 - 2002	.089	.0108	.067	.110	67.299	1	.000
Period 1997 - 1999	.172	.0150	.142	.201	131.921	1	.000
Period baseline	0	.	.	.	.	.	.
(Scale)	1						

B.2.8 Statin - Female – Age Period Cohort (drift absorbed into period)

Goodness of Fit

	Value	df	Value/df
Deviance	95.552	60	1.593
Scaled Deviance	95.552	60	
Pearson Chi-Square	97.415	60	1.624
Scaled Pearson Chi-Square	97.415	60	
Log Likelihood	-482.842		

Tests of Model Effects

Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	95366.282	1	.000
acode	8445.126	21	.000
prdfactor	2748.583	4	.000
cohfactor	2339.767	24	.000

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	-7.470	.1278	-7.720	-7.220	3417.216	1	.000
Age 83-85	4.793	.1332	4.532	5.054	1295.635	1	.000
Age 80-82	4.794	.1314	4.537	5.052	1331.998	1	.000
Age 77-79	4.783	.1299	4.529	5.038	1355.537	1	.000
Age 74-76	4.731	.1287	4.479	4.984	1350.484	1	.000
Age 71-73	4.670	.1279	4.420	4.921	1334.090	1	.000
Age 68-70	4.593	.1272	4.344	4.843	1304.969	1	.000
Age 65-67	4.512	.1266	4.264	4.760	1269.482	1	.000
Age 62-64	4.405	.1263	4.157	4.652	1215.666	1	.000
Age 59-61	4.228	.1262	3.980	4.475	1122.065	1	.000
Age 56-58	3.998	.1263	3.750	4.245	1001.664	1	.000
Age 53-55	3.692	.1266	3.444	3.940	850.234	1	.000
Age 50-52	3.306	.1272	3.056	3.555	675.889	1	.000
Age 47-49	2.894	.1279	2.643	3.145	511.925	1	.000
Age 44-46	2.429	.1288	2.176	2.681	355.758	1	.000
Age 41-43	1.987	.1297	1.733	2.241	234.508	1	.000
Age 38-40	1.560	.1305	1.305	1.816	143.066	1	.000
Age 35-37	1.166	.1307	.910	1.422	79.587	1	.000
Age 32-34	.782	.1321	.524	1.041	35.088	1	.000
Age 29-31	.648	.1257	.402	.894	26.601	1	.000
Age 26-28	.523	.1210	.285	.760	18.638	1	.000
Age 23-25	.226	.1186	-.006	.458	3.630	1	.057
Age baseline	0	.	.	.	.	.	.

…

Table continued…. Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.
Period 2006 - 2008	1.220	.0265	1.168	1.271	2118.098	1	.000
Period 2003 - 2005	.996	.0233	.951	1.042	1832.591	1	.000
Period 2000 - 2002	.645	.0208	.604	.686	962.214	1	.000
Period 1997 - 1999	.442	.0194	.404	.480	518.471	1	.000
Period baseline	0	.	.	.	.	.	.
Cohort 1986 - 1988	-.580	.2018	-.976	-.185	8.262	1	.004
Cohort 1983 - 1985	-.476	.1389	-.749	-.204	11.766	1	.001
Cohort 1980 - 1982	-.292	.1056	-.499	-.085	7.662	1	.006
Cohort 1977 - 1979	.173	.0819	.012	.334	4.456	1	.035
Cohort 1971 - 1973	.102	.0719	-.038	.243	2.029	1	.154
Cohort 1968 - 1970	.133	.0710	-.006	.272	3.497	1	.061
Cohort 1965 - 1967	.178	.0701	.040	.315	6.423	1	.011
Cohort 1962 - 1964	.251	.0671	.120	.383	14.027	1	.000
Cohort 1959 - 1961	.106	.0638	-.019	.231	2.767	1	.096
Cohort 1956 - 1958	.207	.0591	.091	.323	12.304	1	.000
Cohort 1953 - 1955	.107	.0546	.000	.214	3.821	1	.051
Cohort 1950 - 1952	.130	.0498	.032	.227	6.789	1	.009
Cohort 1947 - 1949	.105	.0450	.017	.193	5.451	1	.020
Cohort 1944 - 1946	.215	.0401	.137	.294	28.867	1	.000
Cohort 1941 - 1943	.233	.0355	.163	.302	42.907	1	.000
Cohort 1938 - 1940	.332	.0308	.272	.392	116.431	1	.000
Cohort 1935 - 1937	.348	.0262	.296	.399	175.767	1	.000
Cohort 1932 - 1934	.370	.0218	.327	.412	288.110	1	.000
Cohort 1929 - 1931	.354	.0178	.319	.389	398.336	1	.000
Cohort 1926 - 1928	.207	.0150	.177	.236	189.165	1	.000
Cohort 1920 - 1922	-.242	.0186	-.278	-.205	168.835	1	.000
Cohort 1917 - 1919	-.647	.0308	-.707	-.587	442.412	1	.000
Cohort 1914 - 1916	-1.463	.0626	-1.586	-1.341	546.611	1	.000
Cohort 1911 - 1913	-2.076	.2024	-2.472	-1.679	105.146	1	.000
Cohort baseline	0	.	.	.	.	.	.
(Scale)	1						

B.3 χ^2 table

df	one-tailed *p*-value	0.050	0.010	0.005
1		3.84	6.63	7.88
2		5.99	9.21	7.88
3		7.81	11.34	12.84
4		9.49	13.28	14.86
5		11.07	15.09	16.75
6		12.59	16.81	18.55
7		14.07	18.48	20.28
8		15.51	20.09	21.96
9		16.92	21.67	23.59
10		18.31	23.21	25.19
11		19.68	24.73	26.76
12		21.03	26.22	28.30
13		22.36	27.69	29.82
14		23.68	29.14	31.32
15		25.00	30.58	32.80
16		26.30	32.00	34.27
17		27.59	33.41	35.72
18		28.87	34.81	37.16
19		30.14	36.19	38.58
20		31.41	37.57	40.00
21		32.67	38.93	41.40
22		33.92	40.29	42.80
23		35.17	41.64	44.18
24		36.42	42.98	45.56
25		37.65	44.31	46.93
26		38.89	45.64	48.29
27		40.11	46.96	49.65
28		41.34	48.28	50.99
29		42.56	49.59	52.34
30		43.77	50.89	53.67
40		55.76	63.69	66.77
50		67.50	76.15	79.49
60		79.08	88.38	91.95
70		90.53	100.43	104.22
80		101.88	112.33	116.32
90		113.15	124.12	128.30
100		124.34	135.81	140.17

Appendix C. Three-year age-specific user prevalence of statin by one-year cohorts and sex in the Netherlands. Figure *a* shows cohorts 1911, 1914, …., 1986. Figure *b* shows cohorts 1912, 1915, …., 1987. Figure *c* shows cohorts 1913, 1915, …., 1988.