# Long-term and recent trends in serum cholesterol awareness, treatment, and control in 12 high-income countries: an analysis of 90 nationally representative surveys*

NCD Risk Factor Collaboration (NCD-RisC) †

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**Abstract**

Placeholder

**Keywords:** key1, key2, key3

*abc

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| | Non-HDL-C | Eligible | Treated |
|---|---|---|---|
| woman | −0.040 | −0.145*** | 0.043* |
| | (0.037) | (0.021) | (0.018) |
| age50-59 years | 0.255*** | 0.182*** | 0.071*** |
| | (0.021) | (0.020) | (0.008) |
| age60-69 years | 0.244*** | 0.405*** | 0.090*** |
| | (0.038) | (0.031) | (0.015) |
| age70-79 years | 0.131* | 0.634*** | 0.037 |
| | (0.051) | (0.028) | (0.029) |
| woman × post2010 | −0.418*** | 0.018 | 0.126*** |
| | (0.043) | (0.015) | (0.017) |
| age50-59 years × post2010 | −0.345*** | −0.019 | 0.034+ |
| | (0.029) | (0.013) | (0.016) |
| age60-69 years × post2010 | −0.620*** | −0.119*** | 0.125** |
| | (0.049) | (0.015) | (0.035) |
| age70-79 years × post2010 | −0.765*** | −0.171*** | 0.127* |
| | (0.068) | (0.018) | (0.042) |
| woman × age50-59 years × post2010 | 0.480*** | −0.002 | −0.017 |
| | (0.023) | (0.018) | (0.031) |
| woman × age60-69 years × post2010 | 0.692*** | 0.059+ | −0.094** |
| | (0.063) | (0.030) | (0.023) |
| woman × age70-79 years × post2010 | 0.779*** | 0.142*** | −0.190*** |
| | (0.049) | (0.027) | (0.019) |
| Observations | 314 368 | 255 369 | 107 879 |
| $R^2$ Adj. | 0.074 | 0.237 | 0.192 |
| FE: Country | Yes | Yes | Yes |
| FE: Year | Yes | Yes | Yes |

+ p < 0.1, * p < 0.05, ** p < 0.01, *** p < 0.001

# Figures

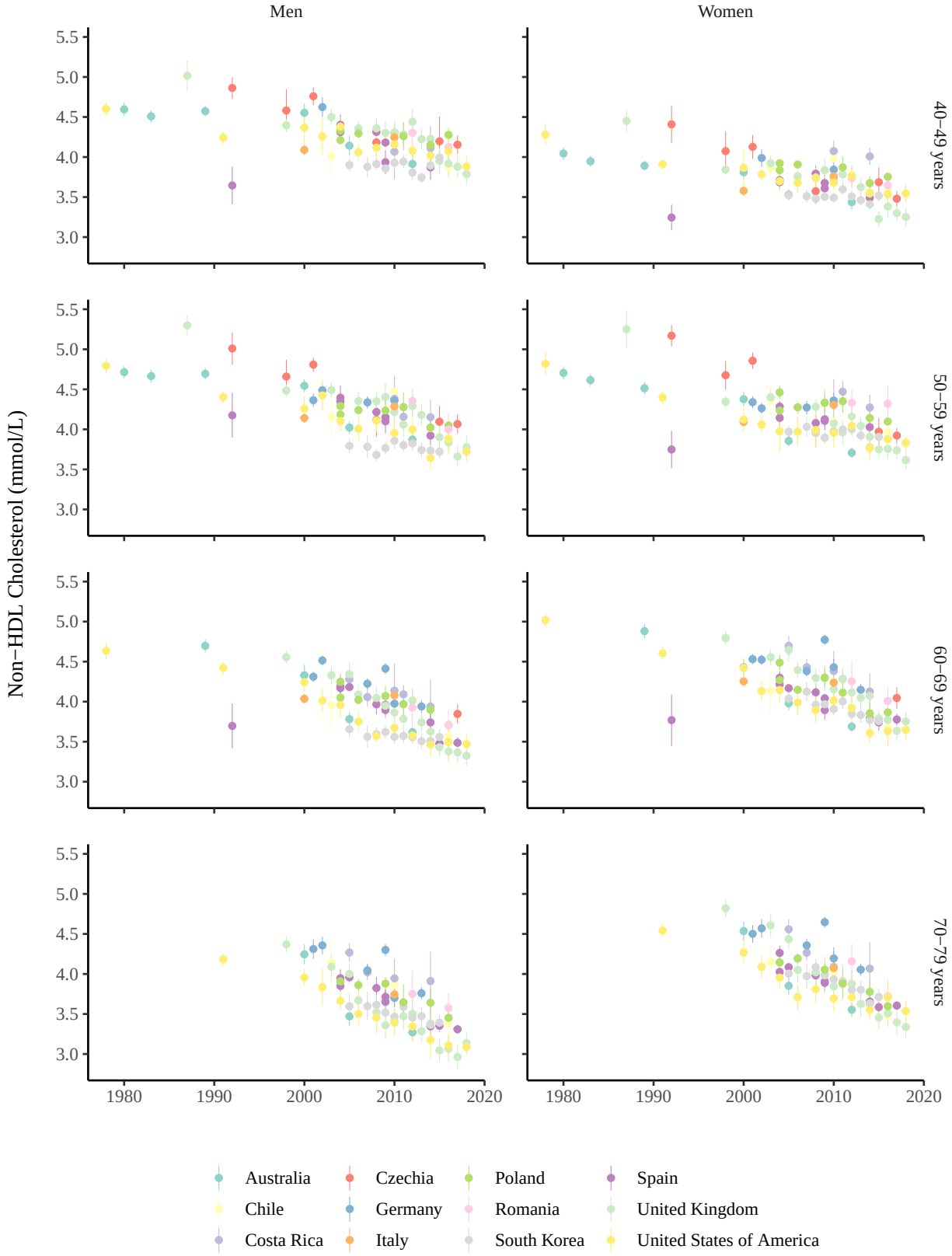


Figure 1: Trends in mean non-HDL serum cholesterol level, by country, sex, and age group.

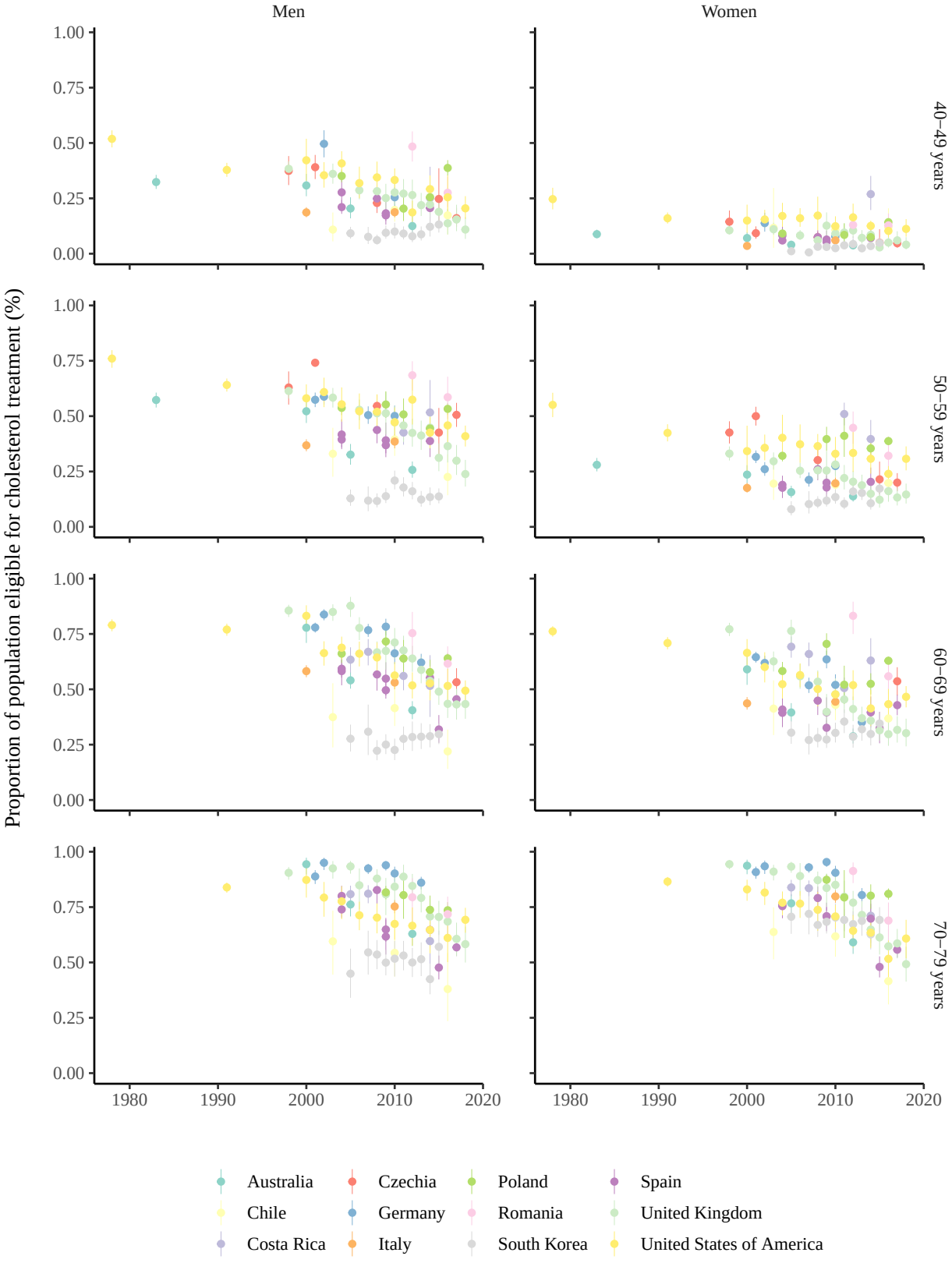


Figure 2: Trends in eligibility for cholesterol treatment, by country, sex, and age group.

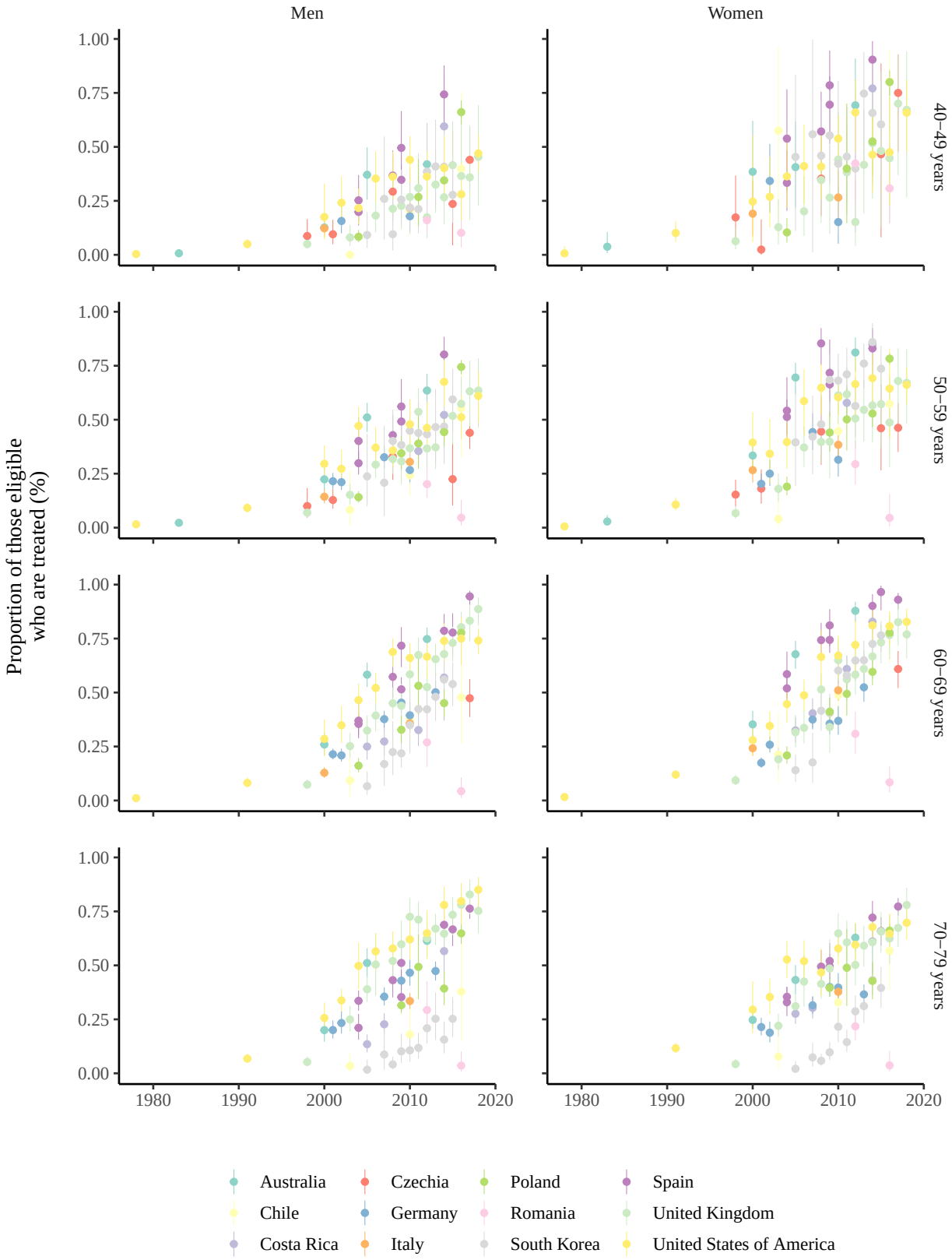


Figure 3: Trends in cholesterol treatment among people with elevated serum cholesterol, by country, sex, and age group.

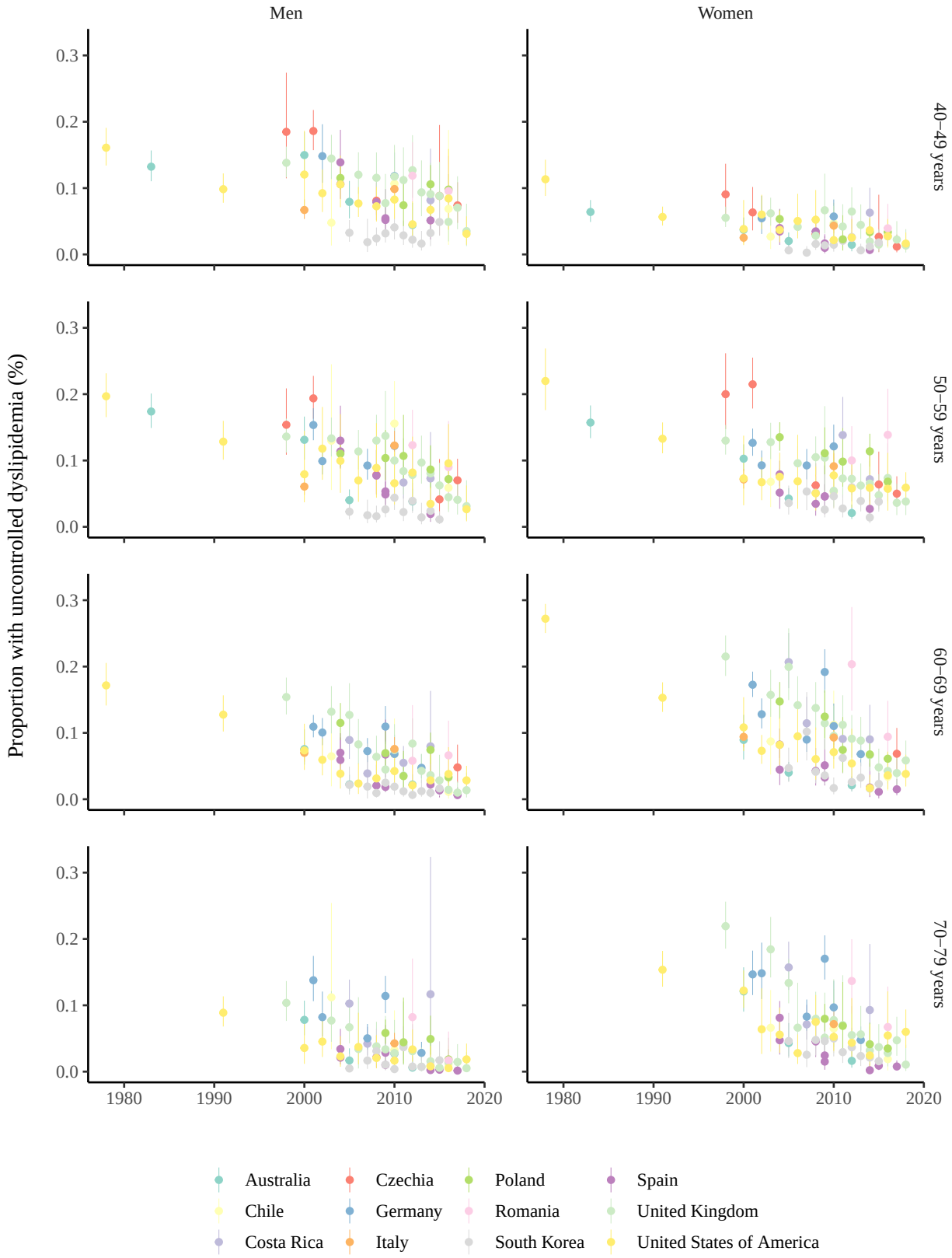


Figure 4: Trends in uncontrolled dyslipidemia by country, sex, and age group.

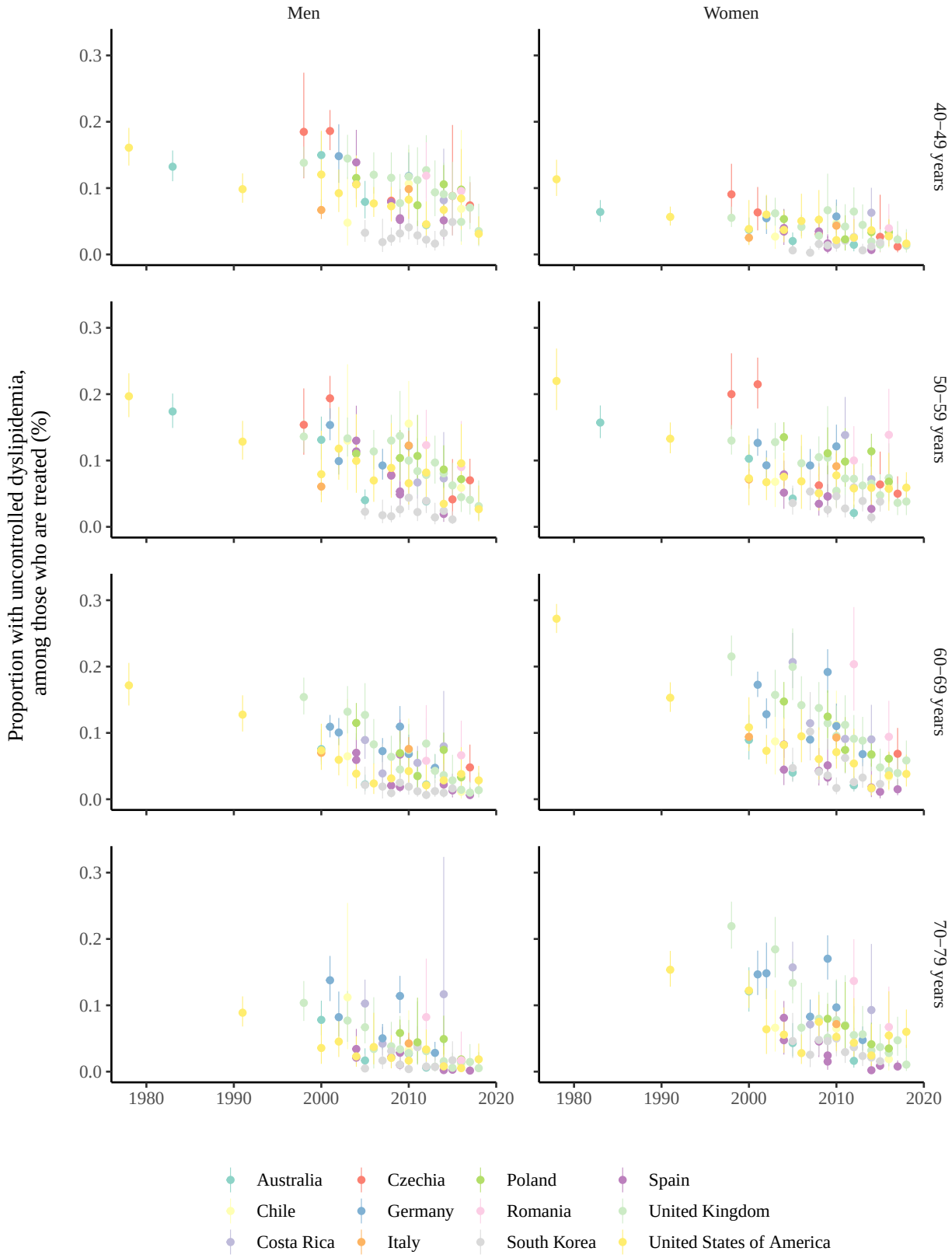


Figure 5: Trends in uncontrolled dyslipidemia among those on treatment, by country, sex, and age group.

# References


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# A Appendix

## A.1 Data sources

Using the NCDRisC database, we assembled data from 90 national health examination surveys completed between 1978 and 2018 in 12 high and middle-income countries: Australia, Chile, Costa Rica, Czech Republic, Germany, Italy, Poland, Romania, South Korea, Spain, United Kingdom, United States of America. These surveys included a lipid panel for a random sample of the general population. A list of surveys used and information about their design, including the age range and number of participants, whether LDL-C was calculated, and the devices used, is included in Table A.1.

Table A1: Data sources from 12 high-income countries with laboratory lipid values

| | | | | | Age range | | Sample size | |
|---|---|---|---|---|---|---|---|---|
| | Country | Start | End | Survey name | Women | Men | Women | Men |
| 1 | Australia | 1980 | 1980 | Risk Factor Prevalence Study (RFPS) | 25-64 | 25-64 | 2756 | 2739 |
| 2 | Australia | 1983 | 1983 | Risk Factor Prevalence Study (RFPS) | 25-64 | 25-64 | 3732 | 3655 |
| 3 | Australia | 1989 | 1989 | Risk Factor Prevalence Study (RFPS) | 20-69 | 20-69 | 4611 | 4501 |
| 4 | Australia | 1999 | 2000 | The Australian Diabetes, Obesity and Lifestyle Study 1999-2000 (AusDiab) | 25+ | 25+ | 6138 | 5047 |
| 5 | Australia | 2004 | 2005 | The Australian Diabetes, Obesity and Lifestyle Study 2004-2005 (AusDiab) | 30+ | 30+ | 3444 | 2852 |
| 6 | Australia | 2012 | 2012 | The Australian Diabetes, Obesity and Lifestyle Study 2012 (AusDiab) | 37+ | 37+ | 2535 | 2046 |
| 7 | Chile | 2003 | 2003 | Encuesta Nacional de Salud (ENS) | 17+ | 17+ | 1067 | 909 |
| 8 | Chile | 2009 | 2010 | Encuesta Nacional de Salud (ENS) | 15+ | 15+ | 1600 | 1122 |
| 9 | Chile | 2016 | 2017 | Encuesta Nacional de Salud (ENS) | 15+ | 15+ | 2349 | 1366 |
| 10 | Costa Rica | 2004 | 2006 | Costa Rican Longevity and Healthy Aging Study Pre-1945 Cohort Wave 1 (CRELES) | 60+ | 60+ | 1448 | 1208 |
| 11 | Costa Rica | 2006 | 2008 | Costa Rican Longevity and Healthy Aging Study Pre-1945 Cohort Wave 2 (CRELES) | 62+ | 62+ | 1215 | 1018 |
| 12 | Costa Rica | 2010 | 2011 | Costa Rican Longevity and Healthy Aging Study 1945-1955 Cohort Wave 1 (CRELES) | 54-66 | 54-66 | 1590 | 1029 |
| 13 | Costa Rica | 2010 | 2010 | Costa Rican National Cardiovascular Risk Factors Survey, 2010 (CRFS) | 20+ | 20+ | 1937 | 725 |
| 14 | Costa Rica | 2014 | 2014 | Costa Rican National Cardiovascular Risk Factors Survey, 2014 (CRFS) | 20+ | 20+ | 1671 | 706 |
| 15 | Czech Republic | 1992 | 1992 | MONICA, Czech Republic | 25-64 | 25-64 | 1189 | 1127 |
| 16 | Czech Republic | 1997 | 1998 | Czech post-MONICA (postMONICA) | 25-64 | 25-64 | 1664 | 1527 |
| 17 | Czech Republic | 2000 | 2001 | Czech post-MONICA (postMONICA) | 25-64 | 25-64 | 1661 | 1612 |
| 18 | Czech Republic | 2006 | 2009 | Czech post-MONICA (postMONICA) | 25-64 | 25-64 | 1860 | 1718 |
| 19 | Czech Republic | 2014 | 2015 | European Heath Examination Survey (EHES) | 25-64 | 25-64 | 681 | 472 |
| 20 | Czech Republic | 2015 | 2018 | MONICA | 25-65 | 25-65 | 1361 | 1239 |
| 21 | Germany | 2000 | 2002 | ESTHER | 50-75 | 50-75 | 5270 | 4340 |
| 22 | Germany | 2000 | 2003 | Heinz Nixdorf Recall Study (HNRS) | 45-75 | 45-75 | 2402 | 2381 |
| 23 | Germany | 2005 | 2008 | Heinz Nixdorf Recall Study (HNRS) | 50-80 | 50-80 | 2082 | 2045 |
| 24 | Germany | 2008 | 2011 | ESTHER | 58-84 | 58-84 | 2488 | 2082 |
| 25 | Germany | 2008 | 2012 | Study of Health in Pomerania, second cohort (SHIP-TREND) | 20-79 | 20-79 | 2233 | 2098 |
| 26 | Germany | 2011 | 2014 | Heinz Nixdorf Recall Study (HNRS) | 56-85 | 56-85 | 1557 | 1492 |
| 27 | Italy | 1998 | 2002 | Osservatorio Epidemiologico Cardiovascolare (OEC) | 35-74 | 35-74 | 4705 | 4831 |
| 28 | Italy | 2008 | 2012 | Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey (OEC) | 35-80 | 35-80 | 4302 | 4331 |
| 29 | Poland | 2003 | 2005 | National Multicenter Health Survey in Poland. Project WOBASZ | 20-74 | 20-74 | 6809 | 6119 |
| 30 | Poland | 2004 | 2004 | LIPIDOGRAM2004 Study | 30+ | 30+ | 9920 | 6672 |
| 31 | Poland | 2006 | 2006 | LIPIDOGRAM2006 Study | 32+ | 32+ | 10640 | 6440 |
| 32 | Poland | 2007 | 2011 | Medical, psychological and socioeconomic aspects of aging in Poland (PolSenior) | 55+ | 55+ | 2306 | 2427 |
| 33 | Poland | 2011 | 2011 | NATPOL | 18-79 | 18-79 | 1213 | 1147 |
| 34 | Poland | 2013 | 2014 | National Multicenter Health Survey in Poland. Project WOBASZ II | 20+ | 20+ | 3233 | 2633 |
| 35 | Poland | 2015 | 2016 | LIPIDOGRAM2015 & LIPIDOGEN2015 Study | 18+ | 18+ | 8688 | 5032 |
| 36 | Romania | 2011 | 2012 | SEPHAR II | 18-80 | 18-80 | 1037 | 931 |
| 37 | Romania | 2015 | 2016 | SEPHAR III | 18-80 | 18-80 | 1033 | 935 |
| 38 | South Korea | 2005 | 2005 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3475 | 2755 |
| 39 | South Korea | 2007 | 2007 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 1813 | 1388 |
| 40 | South Korea | 2008 | 2008 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 4142 | 3203 |

Table A1: Data sources from 12 high-income countries with laboratory lipid values *(continued)*

| | Country | Start | End | Survey name | Women | Men | Women | Men |
|---|---|---|---|---|---|---|---|---|
| 41 | South Korea | 2009 | 2009 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 4438 | 3606 |
| 42 | South Korea | 2010 | 2010 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3661 | 2976 |
| 43 | South Korea | 2011 | 2011 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3670 | 2888 |
| 44 | South Korea | 2012 | 2012 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3461 | 2691 |
| 45 | South Korea | 2013 | 2013 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3219 | 2635 |
| 46 | South Korea | 2014 | 2014 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3025 | 2365 |
| 47 | South Korea | 2015 | 2015 | Korea National Health and Nutrition Examination Survey (KNHANES) | 10+ | 10+ | 3080 | 2568 |
| 48 | Spain | 1991 | 1993 | Cardiovascular Risk Factors Survey in Murcia (CVDRF) | 18-69 | 18-69 | 1268 | 1151 |
| 49 | Spain | 2003 | 2005 | Registre Gironi del Cor (REGICOR) | 35-79 | 35-79 | 3280 | 2951 |
| 50 | Spain | 2004 | 2006 | PREVICTUS | 60+ | 60+ | 3834 | 3350 |
| 51 | Spain | 2004 | 2004 | Cardiovascular Risk Study in Castilla y León (RECCyL) | 15+ | 15+ | 2069 | 1897 |
| 52 | Spain | 2007 | 2009 | Harmonizing Equation of Risk in Mediterraneon countries EXtremadura (HERMEX) | 25-79 | 25-79 | 1498 | 1297 |
| 53 | Spain | 2008 | 2010 | Study on Nutrition and Cardiovascular Risk in Spain (ENRICA) | 18+ | 18+ | 6858 | 6193 |
| 54 | Spain | 2009 | 2009 | Cardiovascular Risk Study in Castilla y León (RECCyL) | 20+ | 20+ | 1572 | 1291 |
| 55 | Spain | 2014 | 2014 | Cardiovascular Risk Study in Castilla y León (RECCyL) | 20+ | 20+ | 1509 | 1220 |
| 56 | Spain | 2015 | 2015 | Study on Nutrition and Cardiovascular Risk in Spain (ENRICA) | 65+ | 65+ | 770 | 704 |
| 57 | United Kingdom | 1986 | 1987 | Dietary and Nutritional Survey of British Adults 1986-1987 (DNS) | 16-64 | 16-64 | 937 | 936 |
| 58 | United Kingdom | 1998 | 1998 | Health Survey for England (HSE) | 16+ | 16+ | 5565 | 5000 |
| 59 | United Kingdom | 2003 | 2003 | Health Survey for England (HSE) | 16+ | 16+ | 4460 | 3814 |
| 60 | United Kingdom | 2005 | 2005 | Health Survey for England (HSE) | 65+ | 65+ | 1190 | 1008 |
| 61 | United Kingdom | 2006 | 2006 | Health Survey for England (HSE) | 16+ | 16+ | 4061 | 3409 |
| 62 | United Kingdom | 2008 | 2008 | Health Survey for England (HSE) | 16+ | 16+ | 3922 | 3348 |
| 63 | United Kingdom | 2008 | 2012 | National Diet and Nutrition Survey (NDNS) | 10+ | 10+ | 1266 | 1008 |
| 64 | United Kingdom | 2009 | 2009 | Health Survey for England (HSE) | 16+ | 16+ | 1227 | 1075 |
| 65 | United Kingdom | 2010 | 2010 | Health Survey for England (HSE) | 16+ | 16+ | 2158 | 1720 |
| 66 | United Kingdom | 2011 | 2011 | Health Survey for England (HSE) | 16+ | 16+ | 2201 | 1738 |
| 67 | United Kingdom | 2012 | 2012 | Health Survey for England (HSE) | 16+ | 16+ | 2192 | 1745 |
| 68 | United Kingdom | 2013 | 2013 | Health Survey for England (HSE) | 16+ | 16+ | 2438 | 2080 |
| 69 | United Kingdom | 2013 | 2014 | National Diet and Nutrition Survey (NDNS) | 10+ | 10+ | 520 | 386 |
| 70 | United Kingdom | 2014 | 2014 | Health Survey for England (HSE) | 16+ | 16+ | 2085 | 1816 |
| 71 | United Kingdom | 2015 | 2015 | Health Survey for England (HSE) | 16+ | 16+ | 2130 | 1777 |
| 72 | United Kingdom | 2015 | 2016 | National Diet and Nutrition Survey (NDNS) | 10+ | 10+ | 485 | 391 |
| 73 | United Kingdom | 2016 | 2016 | Health Survey for England (HSE) | 16+ | 16+ | 2083 | 1682 |
| 74 | United Kingdom | 2016 | 2017 | National Diet and Nutrition Survey (NDNS) | 10+ | 10+ | 204 | 174 |
| 75 | United Kingdom | 2017 | 2017 | Health Survey for England (HSE) | 16+ | 16+ | 2160 | 1711 |
| 76 | United Kingdom | 2018 | 2018 | Health Survey for England (HSE) | 16+ | 16+ | 1947 | 1600 |
| 77 | United States of America | 1976 | 1980 | US NHANES II | 20-74 | 20-74 | 6245 | 5601 |
| 78 | United States of America | 1988 | 1994 | US NHANES III | 10+ | 10+ | 10275 | 9408 |
| 79 | United States of America | 1999 | 2000 | US NHANES 1999-2000 | 10+ | 10+ | 3123 | 3150 |
| 80 | United States of America | 2001 | 2002 | US NHANES 2001-2002 | 10+ | 10+ | 3402 | 3496 |
| 81 | United States of America | 2003 | 2004 | US NHANES 2003-2004 | 10+ | 10+ | 3202 | 3361 |
| 82 | United States of America | 2005 | 2006 | US NHANES 2005-2006 | 10+ | 10+ | 3128 | 3302 |
| 83 | United States of America | 2007 | 2008 | US NHANES 2007-2008 | 10+ | 10+ | 3333 | 3367 |
| 84 | United States of America | 2009 | 2010 | US NHANES 2009-2010 | 10+ | 10+ | 3599 | 3558 |
| 85 | United States of America | 2011 | 2012 | US NHANES 2011-2012 | 10+ | 10+ | 3131 | 3155 |
| 86 | United States of America | 2013 | 2014 | US NHANES 2013-2014 | 10+ | 10+ | 3535 | 3350 |

Table A1: Data sources from 12 high-income countries with laboratory lipid values *(continued)*

| | Country | Start | End | Survey name | Women | Men | Women | Men |
|---|---|---|---|---|---|---|---|---|
| 87 | United States of America | 2015 | 2016 | US NHANES 2015-2016 | 10+ | 10+ | 3320 | 3218 |
| 88 | United States of America | 2017 | 2018 | US NHANES 2017-2018 | 10+ | 10+ | 3153 | 3011 |

## A.2 Data cleaning

Given the heterogeneity in the data collection procedures and cleaning across surveys, we implemented a secondary data cleaning protocol, developed for NCD-RisC, and applied it to the pooled data from all 90 surveys. The basic steps were as follows, we evaluated:

1. univariate plausibility ranges
2. multivariate plausibility constraints
3. multivariate outlier detection

### A.2.1 Univariate plausibility ranges

We removed values of certain laboratory and examination measurements that were outside the range of biological plausibility, as determined by expert consensus. Table A2 below shows the plausiblity ranges used for each variable.

Table A2: Univariate plausibility ranges for select variables from national surveys.

| Variable | Ages | Plausibility range |
|---|---|---|
| height (cm) | 5 to 9 years | 60 - 180 |
| height (cm) | 10 to 14 years | 80 - 200 |
| height (cm) | ≥15 years | 100 - 250 |
| weight (kg) | 5 to 9 years | 5 - 90 |
| weight (kg) | 10 to 14 years | 8 - 150 |
| weight (kg) | ≥15 years | 12 - 300 |
| BMI ($kg/m^2$) | 5 to 9 years | 6 - 40 |
| BMI ($kg/m^2$) | 10 to 14 years | 8 - 60 |
| BMI ($kg/m^2$) | ≥15 years | 10 - 80 |
| SBP (mmHg) | all | 70 - 270 |
| DBP (mmHg) | all | 30 - 150 |
| TC (mmol/L) | all | 1.75 - 20 |
| LDL (mmol/L) | all | 0.5 - 10 |
| HDL (mmol/L) | all | 0.4 - 5 |
| Triglycerides (mmol/L) | all | 0.2 - 20 |

### A.2.2 Multivariate plausibility constraints

After removing data outside the univariate plausibilty ranges, we also apply logical multivariate biological plausibility constraints such as checking that the reported systolic blood

pressure measurement is greater than the diastolic measurement. We evaluated the following constraints:

- SBP > DBP (before calculating average BP)
- TC > LDL
- TC > HDL
- TC – (LDL + HDL) ≥ margin of error[1]

Table A3 below shows the number of implausible observations identified and set to missing.

Table A3: Implausible values detected using mulitvariate biological plausibility constraints.

| Constraint | Evaluated (N) | Implausible (N) | % |
|---|---|---|---|
| DBP > SPB | 478,407 | 8 | 0.002 |
| LDL > TC | 274,214 | 36 | 0.013 |
| HDL > TC | 459,919 | 4 | 0.001 |
| TC – (LDL + HDL) ≥ margin of error | 273,547 | 209 | 0.076 |

### A.2.3 Multivariate outlier detection

Finally, we identify multivariate outliers across pairwise combinations of risk factors based on the Mahalanobis distance. That is for vectors of observations for variables $\mathbf{x}$ and $\mathbf{y}$ we calculate the distance

$$d(\mathbf{x}, \mathbf{y}) = \sqrt{(\mathbf{x} - \mathbf{y})^t \Sigma (\mathbf{x} - \mathbf{y})}$$

where $\Sigma$ is the covariance matrix, which gives a sense for how far a paired set of values is from the multivariate center. For skewed variables we apply a log transformation prior to the calculation of the Mahalanobis distance. To identify potentially implausible combinations of values, we use a cut-off based on quantiles of the $\chi^2$ distribution, corresponding to a combination being more the 6 standard deviations from the center. Figure A1 below plots the pairwise distributions and highlights the possible outliers identified.

[1] "margin of error" is determined by using the Cholesterol Reference Method Laboratory Network permitted measurement error limits for TC (8.9%), HDL (13%) and LDL (12%) as follows: Calculate errors in worst case scenario, i.e., TC underestimated, and HDL/LDL overestimated, each by the largest error permitted.

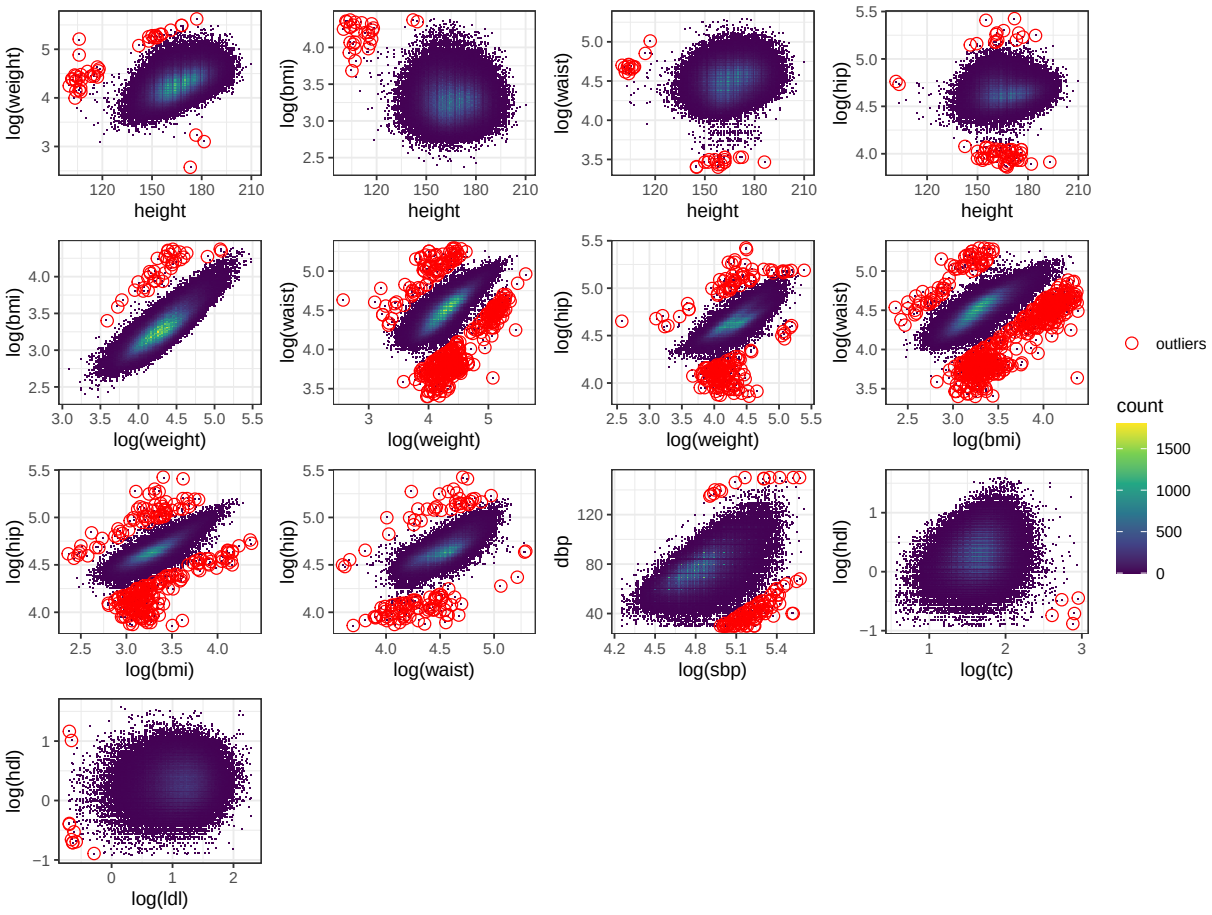


Figure A1: Pairwise outliers based on Mahalanobis distance

Table A4: Pairwise outliers detected using Mahalanobis distance.

| Variable Pair | Evaluated (N) | Outliers (N) | % |
|---|---|---|---|
| HEIGHT vs. WEIGHT | 530,247 | 45 | 0.0084 |
| HEIGHT vs. BMI | 530,223 | 32 | 0.0060 |
| HEIGHT vs. WAIST | 441,684 | 32 | 0.0072 |
| HEIGHT vs. HIP | 259,229 | 71 | 0.0273 |
| WEIGHT vs. BMI | 530,223 | 36 | 0.0067 |
| WEIGHT vs. WAIST | 441,837 | 410 | 0.0927 |
| WEIGHT vs. HIP | 259,232 | 179 | 0.0690 |
| BMI vs. WAIST | 439,276 | 493 | 0.1122 |
| BMI vs. HIP | 257,094 | 246 | 0.0956 |
| WAIST vs. HIP | 265,771 | 115 | 0.0432 |
| SBP vs. DBP | 476,122 | 100 | 0.0210 |
| TC vs. HDL | 459,027 | 6 | 0.0013 |
| LDL vs. HDL | 273,370 | 13 | 0.0047 |

## A.3 Exclusion criteria

The flow diagram below shows how we arrived at our final analytic sample. First, we excluded 191,912 subjects outside our target age range of 40-79 years of age, as this population is generally the focus of cholesterol treatment guidelines for primary and secondary prevention. Next, we excluded 9,120 subjects in 10-year age groups from surveys in which we had less than 5 of the 10 ages observed. Finally, we excluded 77,165 subjects with missing data on cholesterol levels and 58,999 subjects with missing data on key risk factors for calculating risk thresholds, leaving a final sample of 255,369.

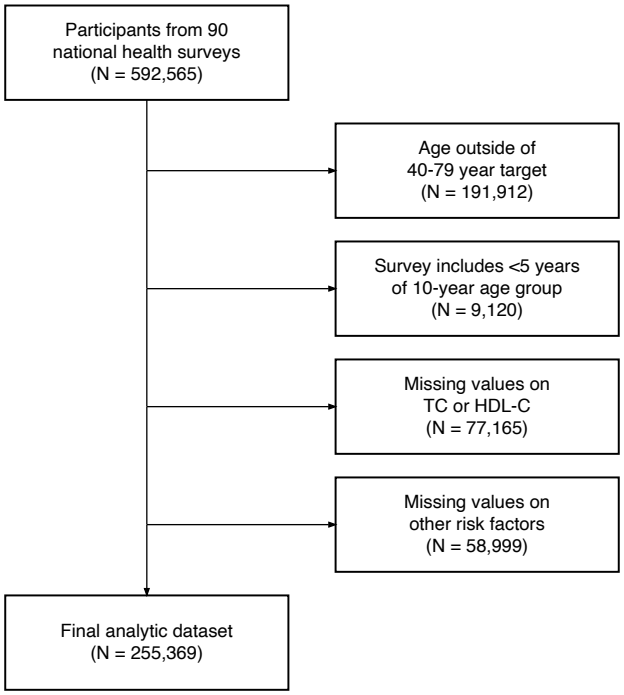


Figure A2: Exclusion criteria.

## A.4 Cholesterol Treatment Guidelines

We compiled a list of cholesterol treatment guidelines from official sources that have been published and discussed in the academic literature. Most of these come from a review conducted by the World Heart Foundation in 2019. They will be used, possibly, as criteria for determining who should be on treatment in assembled surveys. Note that many of these same sources have guidance about control as well (i.e. ideal reductions in LDL or absolute level attained while on treatment). Table A5 below summarizes the specific treatment guidance from the US, Europe, the UK, Canada, China, Brazil, South Africa, and the WHO.

Table A5: Cholesterol treatment guidelines and recommendations for primary prevention.

| Source | Year | Treatment recommendation | Goal of therapy |
|---|---|---|---|
| NHLBI NCEP ATP III [1] | 2013 | LDL $\geq$ 100 mg/dL and 10-year risk$^{*}$ $\geq$ 20% | LDL $<$ 100 mg/dL |
| | | LDL $\geq$ 130 mg/dL and 10-year risk$^{*}$ $\geq$ 10% (2+ risk factors) | LDL $<$ 130 mg/dL |
| | | LDL $\geq$ 160 mg/dL and 10-year risk$^{*}$ $<$ 10% (2+ risk factors) | LDL $<$ 130 mg/dL |
| | | LDL $\geq$ 190 mg/dL (0-1 risk factors) | LDL $<$ 160 mg/dL |
| AHA/ACC Statement [2] | 2018 | LDL $\geq$ 190 mg/dL (severe hypercholesterolemia) | LDL $<$ 100 mg/dL |
| | | LDL $\geq$ 70 mg/dL and 10-year risk$^{*}$ $\geq$ 7.5% | LDL reduced 30% to 49% |
| | | LDL $\geq$ 70 mg/dL and 10-year risk$^{*}$ $\geq$ 20% | LDL reduced $\geq$ 50% |
| | | LDL $\geq$ 70 mg/dL and diabetes mellitus | LDL reduced $\geq$ 50% |
| ESC/EAS Guidelines [3] | 2019 | LDL $\geq$ 70 mg/dL and 10-year risk$^{\dagger}$ $\geq$ 10% (very-high) | LDL reduced $\geq$ 50% or $<$ 55 mg/dL |
| | | LDL $\geq$ 100 mg/dL and 10-year risk$^{\dagger}$ $\geq$ 5% (high) | LDL reduced $\geq$ 50% or $<$ 70 mg/dL |
| | | LDL $\geq$ 190 mg/dL and 10-year risk$^{\dagger}$ $\geq$ 1% (moderate) | LDL $<$ 100 mg/dL |
| | | LDL $\geq$ 190 mg/dL and 10-year risk$^{\dagger}$ $<$ 1% (low) | LDL $<$ 116 mg/dL |
| NICE Guidelines [4] | 2014 | 10-year risk$^{\ddagger}$ $\geq$ 10% or CKD | |
| | | diabetes mellitus (type-2) and 10-year risk$^{\ddagger}$ $\geq$ 10% | |
| | | diabetes mellitus (type-1), >40 years-old, duration >10 years | |
| CCS Guidelines [5] | 2012 | LDL $\geq$ 75 mg/dL and 10-year risk$^{\S}$ $\geq$ 20% | LDL $<$ 75 mg/dL |
| | | LDL $\geq$ 130 mg/dL and 10-year risk$^{\S}$ $\geq$ 10% | LDL $<$ 130 mg/dL |
| | | LDL $\geq$ 130 mg/dL and 10-year risk$^{\S}$ $\geq$ 5% (optional) | LDL $<$ 190 mg/dL |
| | | LDL $\geq$ 190 mg/dL and 10-year risk$^{\S}$ $<$ 1% | LDL $<$ 190 mg/dL |
| China Guidelines [5] | 2016 | 10-year risk$^{||}$ $\geq$ 10% | LDL $<$ 130 mg/dL |
| | | 10-year risk$^{||}$ $\geq$ 5% | LDL $<$ 130 mg/dL |
| | | diabetes mellitus and LDL $\geq$ 70 mg/dL or TC $\geq$ 120 | LDL $<$ 100 mg/dL |
| | | LDL $\geq$ 190 mg/dL or TC $\geq$ 280 | LDL $<$ 100 mg/dL |
| Brazil Guidelines [5] | 2013 | 10-year risk$^{\S}$ $\geq$ 10% (women) $\geq$ 20% (men) | LDL $<$ 100 mg/dL |
| | | diabetes mellitus or CKD or FH | LDL $<$ 70 mg/dL |
| South Africa Guidelines [5] | 2012 | 10-year risk$^{\S}$ $\geq$ 30% (very high) | LDL $<$ 70 mg/dL |
| | | LDL $\geq$ 100 mg/dL and 10-year risk$^{\S}$ $\geq$ 15% (high) | LDL $<$ 100 mg/dL |
| | | diabetes mellitus or CKD or FH | LDL $<$ 70 mg/dL |
| WHO Guidelines [5] | 2007 | TC $\geq$ 320 mg/dL or LDL $\geq$ 240 mg/dL or TC/HDL ratio $>$ 8 | LDL $<$ 77 mg/dL or TC $<$ 152 mg/dL |
| | | diabetes mellitus | LDL $<$ 77 mg/dL or TC $<$ 152 mg/d |
| | | 10-year risk$^{\P}$ $\geq$ 30% | LDL $<$ 77 mg/dL or TC $<$ 152 mg/dL |
| | | LDL $\geq$ 115 mg/dL or TC $\geq$ 193 mg/dL and 10-year risk$^{\P}$ $\geq$ 20% | LDL $<$ 100 mg/dL |

$^{*}$ Based on Pooled Cohort Equations
$^{\dagger}$ Based on SCORE
$^{\ddagger}$ Based on QRISK2
$^{\S}$ Based on Framingham Risk Score
$^{||}$ Based on CMCS re-callibration
$^{\P}$ Based on WHO/ISH risk charts

## A.5 Calibrating Non-HDL-C to LDL-C

In this study, we use non-HDL-C to define those who are elligible for treatment with lipid-lowering drugs as well as those whose serum cholesterol levels are "controlled". However, most national guidelines use LDL-C targets rather than non-HDL-C. We chose to use non-HDL-C because many surveys, especially those conducted several decades ago, did not measure LDL-C or did not measure the necessary components[2] to calculate LDL-C. In the main text, we use a correction factor to convert LDL-C targets in guidelines to non-HDL-C derived from more recent guidelines in Europe and North America.

Here we validate this correction factor in our sample by looking at the relationship between non-HDL-C and LDL-C among studies in which both were measured (N = 198,761 observations). Figure A3 below plots non-HDL-C levels versus LDL-C levels. We fit both a linear as well as a more flexbile GAM regression model to the data and find evidence that the relationship is linear across the full range. We find a high degree of linear correlation between non-HDL-C and LDL-C ($\rho = 0.916$) with an estimated bias/correction factor of 0.65 mmol/L (25.2 mg/dL) which compares favorably with the one in the literature of 0.78 mmol/L (30 mg/dL).

[2]Roughly speaking total cholesterol is composed of HDL-C, LDL-C, and Triglycerides

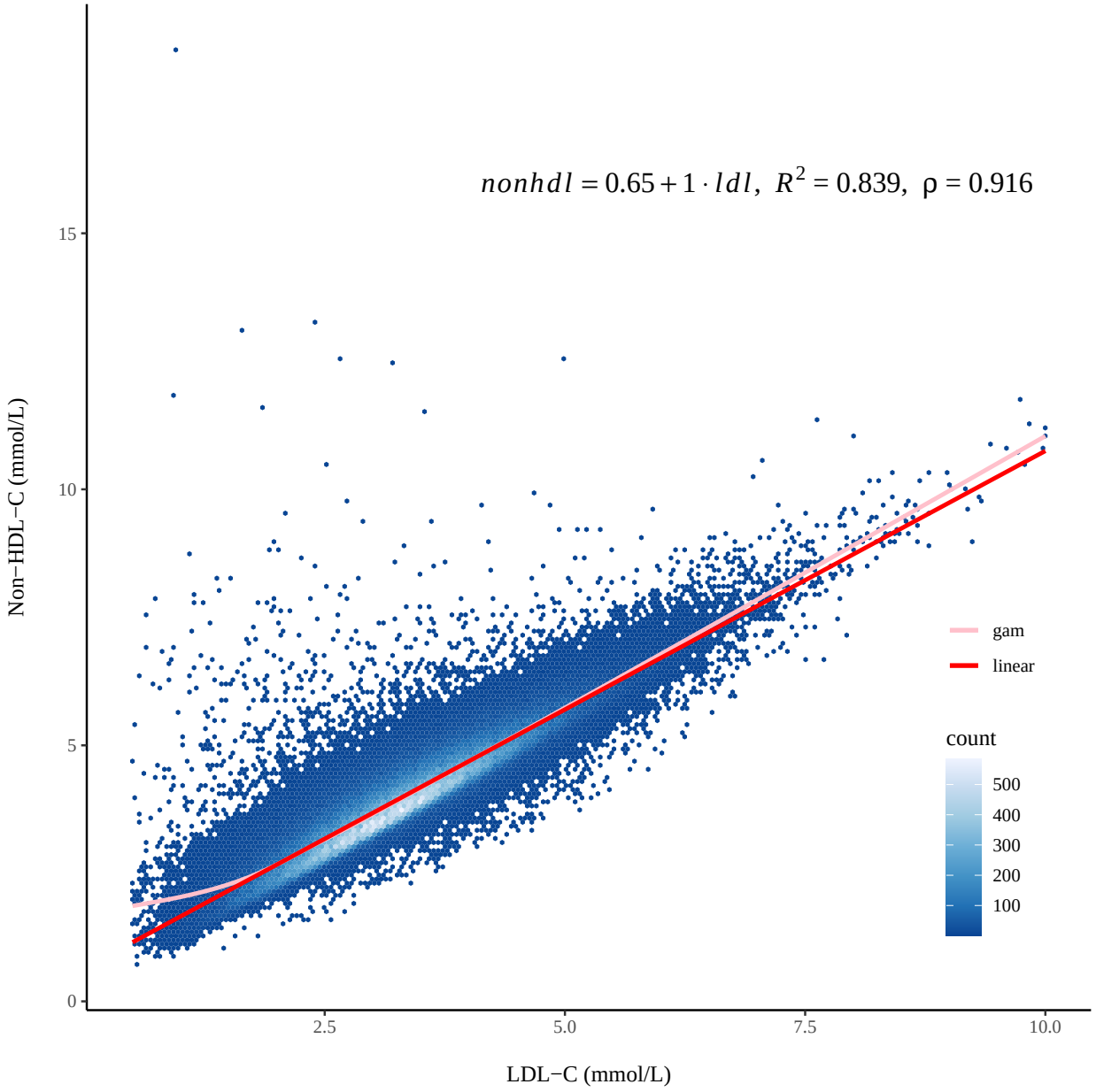


Figure A3: Callibrating non-HDL-C levels with LDL-C among those surveys which collected data on both.

## A.6 Calculation of risk scores

For risk-based guidelines about treatment eligibility, we used Globorisk [6] to calculate risk scores for all individuals with complete risk factor data. Globorisk is a cardiovascual disease risk prediction equation that can be recalibrated and updated for use in different countries with routinely available information. Currently it supports risk estimates for 182 countries from 2000 to 2020 [7]. Coefficients were estimated in original study using Cox propostional hazards model with age as the time scale. Thus the risk equation is of the form:

$$
\begin{aligned}
h(t \mid sex, sbp, tc, dm, smk) = h_0(t) \exp\big\{ & \\
& \beta_1(sbp - \overline{sbp}) + \beta_2(tc - \overline{tc}) + \beta_3(dm - \overline{dm}) + \beta_4(smk - \overline{smk}) + \beta_5(dm - \overline{dm}) \times sex \\
& + \beta_6(smk - \overline{smk}) \times sex + \beta_7(sbp - \overline{sbp}) \times t + \beta_8(tc - \overline{tc}) \times t + \beta_9(dm - \overline{dm}) \times t \\
& + \beta_{10}(smk - \overline{smk}) \times t \\
\big\} &
\end{aligned}
$$

where $(\beta_1, \ldots, \beta_{10})$ are constant across countries but the mean risk factor levels $(\overline{sbp}, \ldots, \overline{smk})$ and baseline hazard $h_0(t)$ are country-specific and thus can be re-callibrated to local conditions. The values of $(\beta_1, \ldots, \beta_{10})$ are provided in table below.

Table A6: Coefficient values for Globorisk risk equations.

| Coefficient | Estimate |
|---|---|
| $\beta_1$ | 0.3070129 |
| $\beta_2$ | 0.6149061 |
| $\beta_3$ | 1.475305 |
| $\beta_4$ | 1.846684 |
| $\beta_5$ | 0.4050458 |
| $\beta_6$ | 0.3253832 |
| $\beta_7$ | -0.002247118 |
| $\beta_8$ | -0.006865652 |
| $\beta_9$ | -0.01320953 |
| $\beta_{10}$ | -0.02205285 |

Country-specific risk factor values and baseline hazards were the same as those used in a prior study [7]. The estimated risk for each subject is calculated as 10-year cumulative

incidence based on the formula

$$CI = 1 - \prod_{t=0}^{T} \exp\{h(t \mid sex, sbp, tc, dm, smk)\}.$$

All calculations were performed using the `globorisk` package [8] in R. For reference, below are the trends in mean risk score by country, sex, and age group.

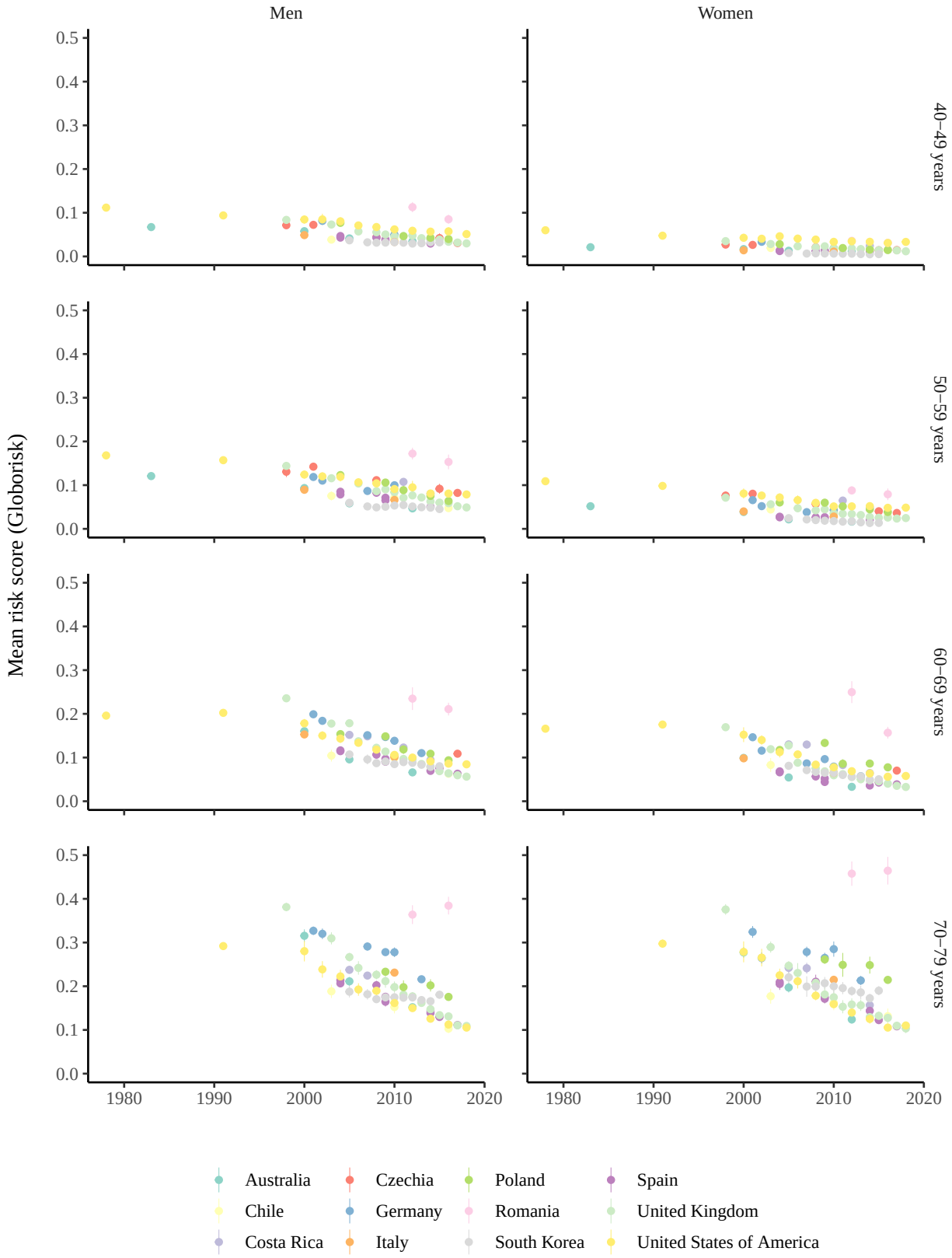


Figure A4: Trends in mean risk score by country, sex, and age group.

## A.7 Linear trends

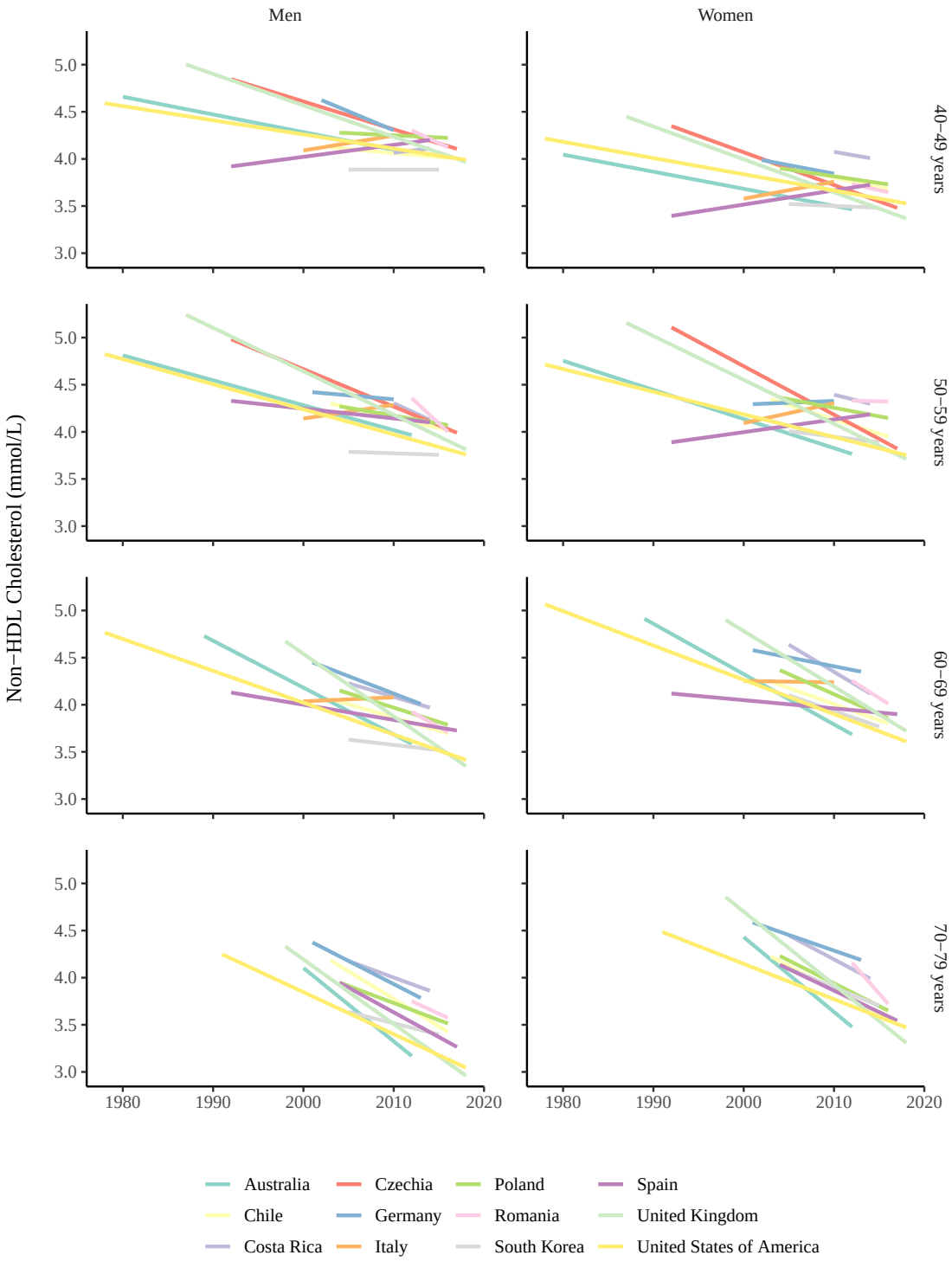


Figure A5: Linear trends in mean Non-HDL-C level by country, age, and sex.

## A.8 Example distributional changes

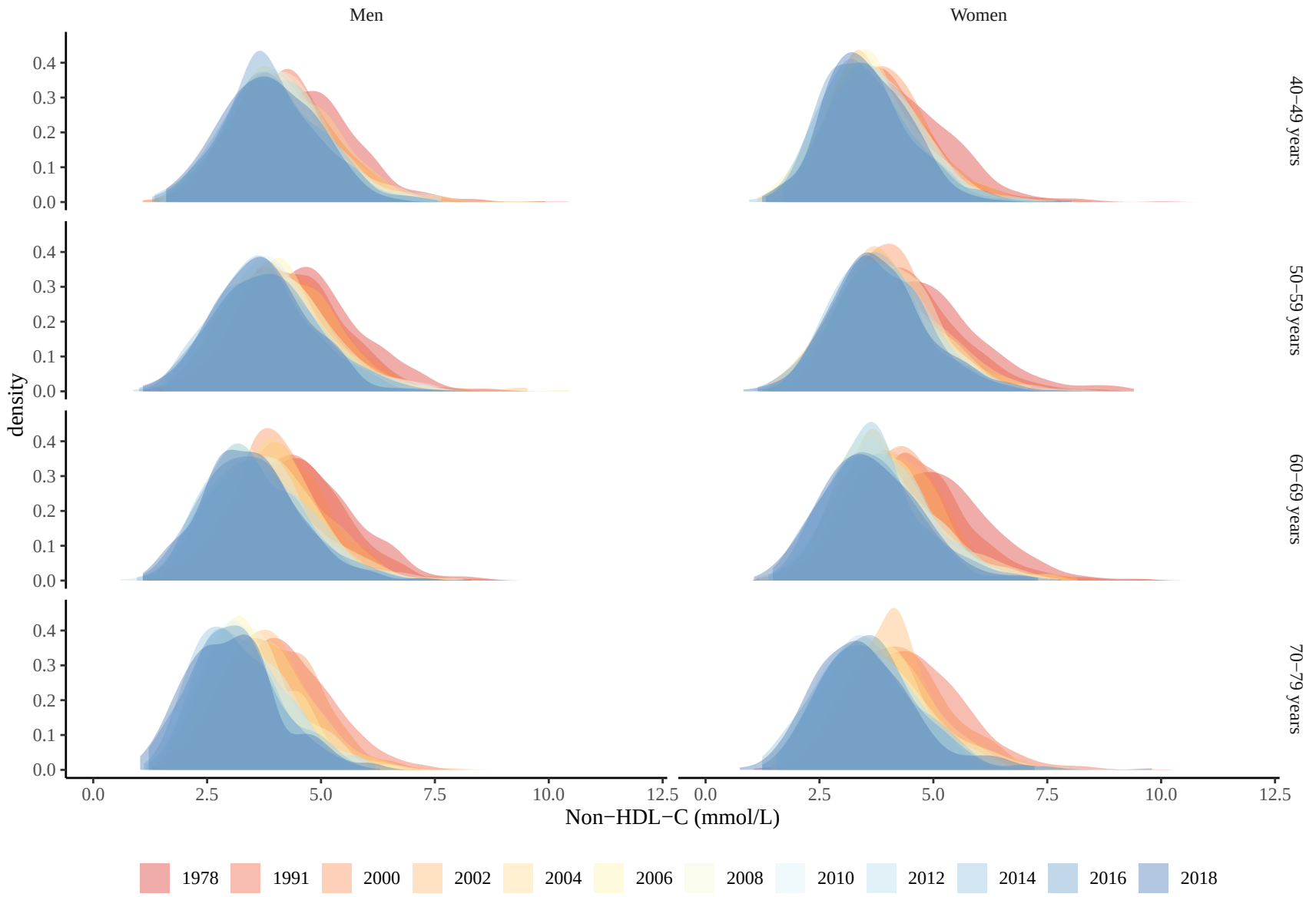


Figure A6: Changes in distribution of Non-HDL-C in United States by sex and age group.

## A.9 Country-by-country results

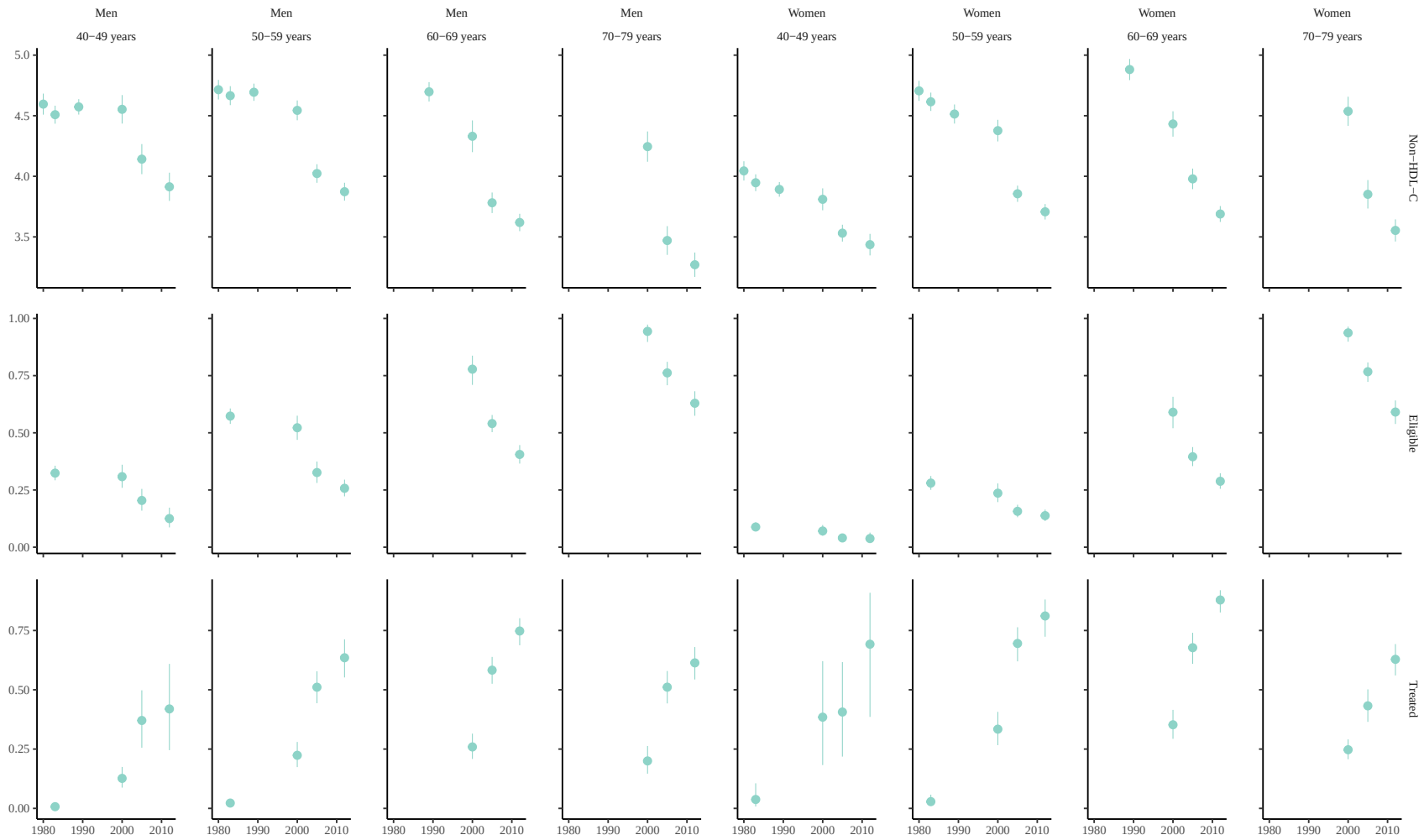


Figure A7: Australia

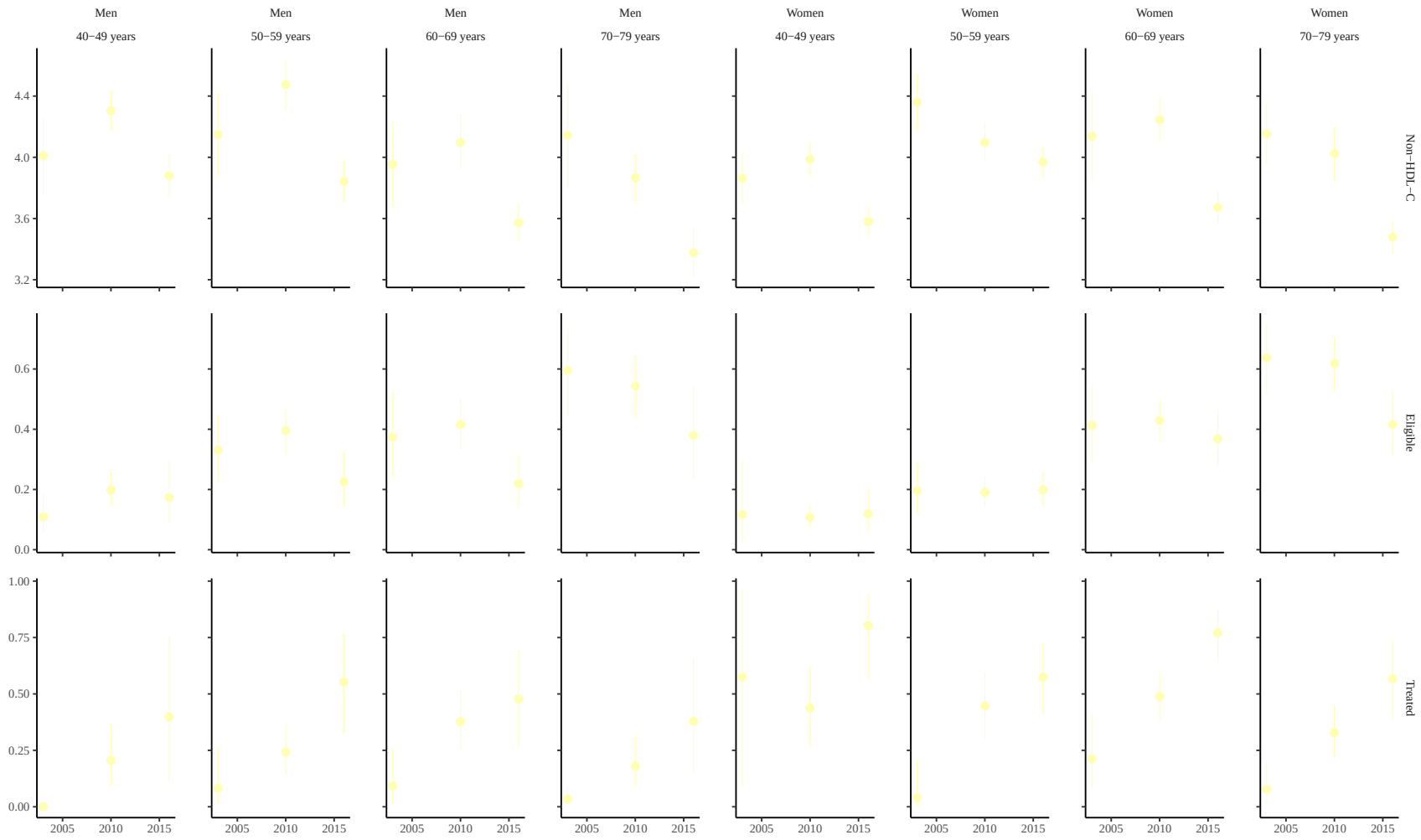


Figure A8: Chile

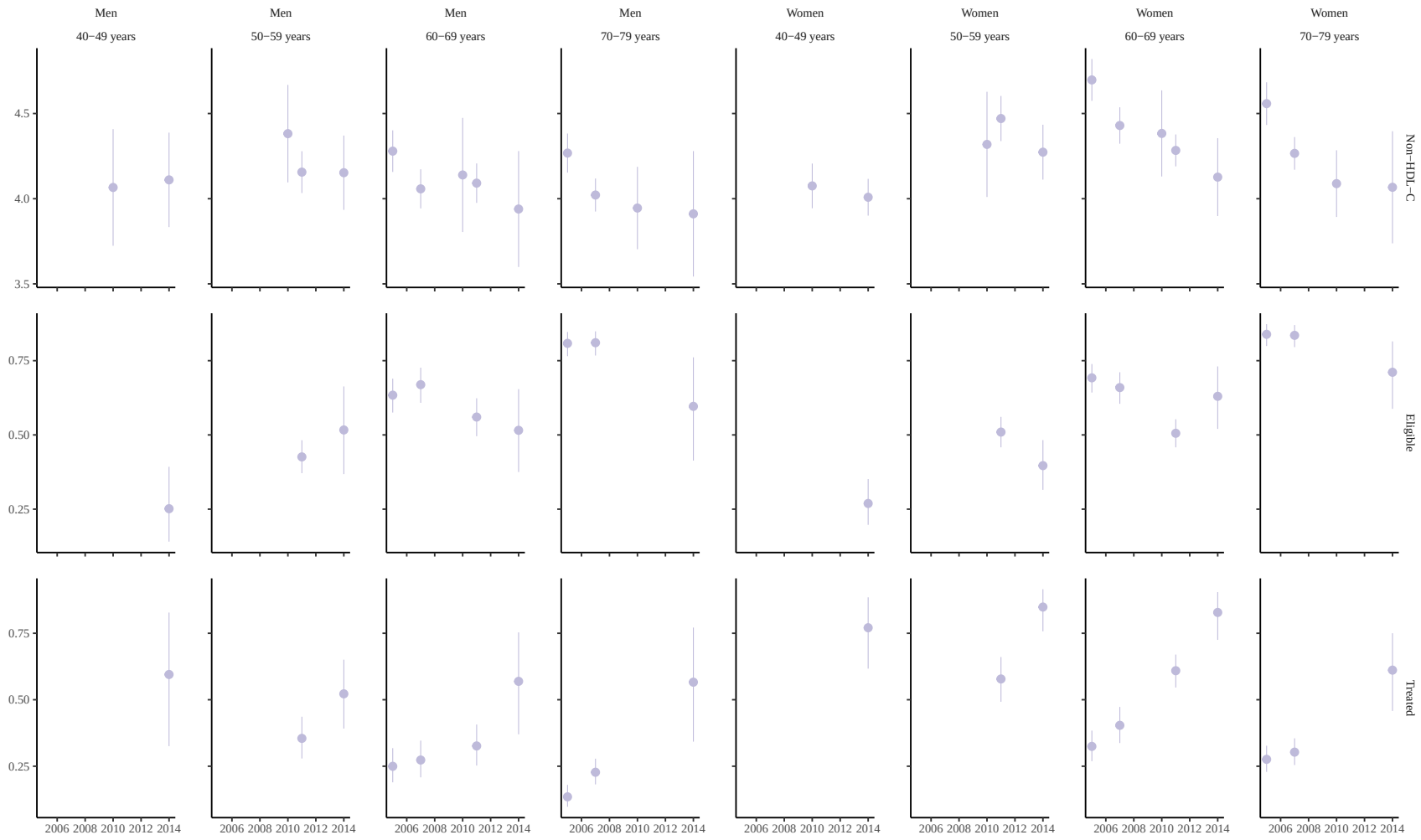


Figure A9: Costa Rica

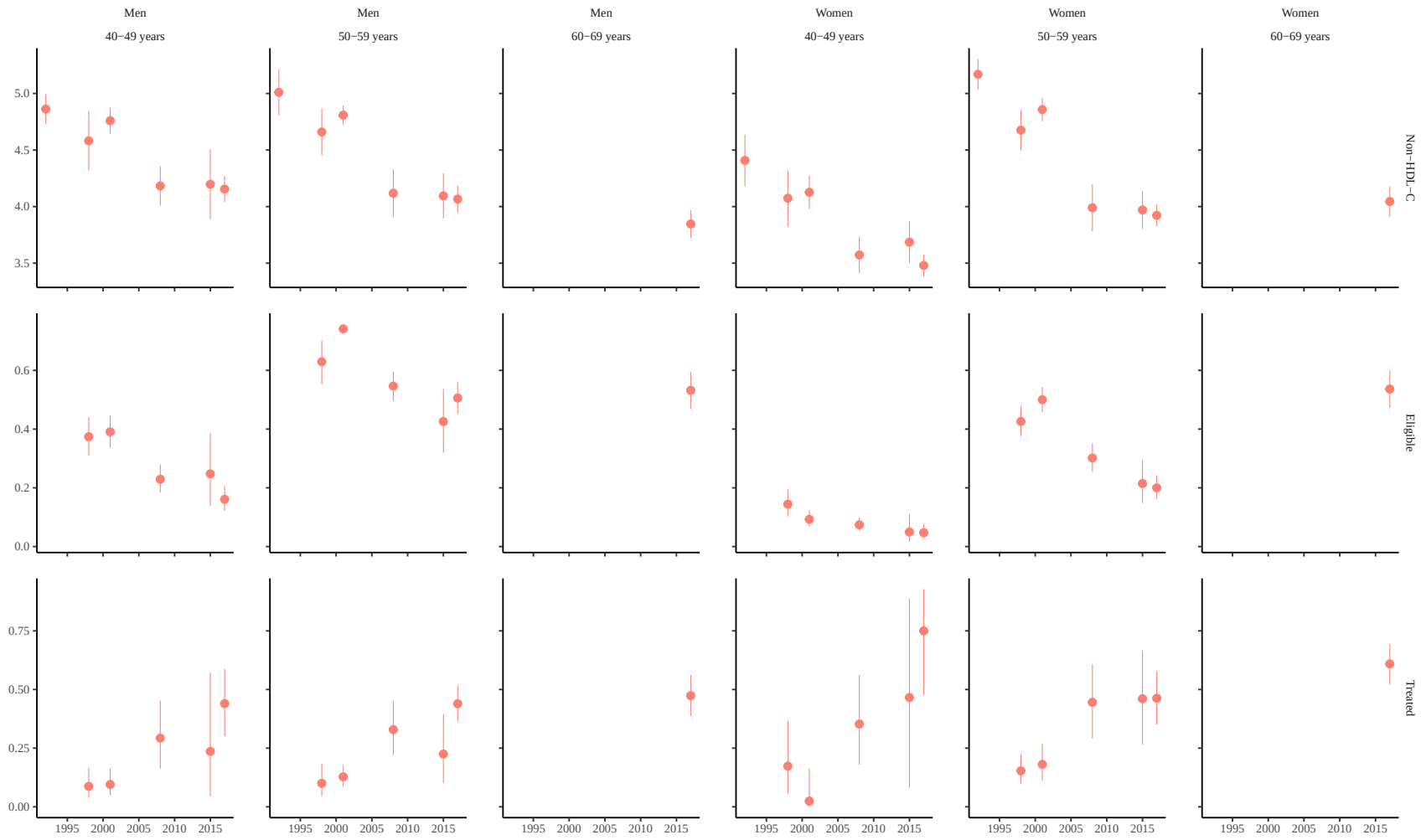


Figure A10: Czechia

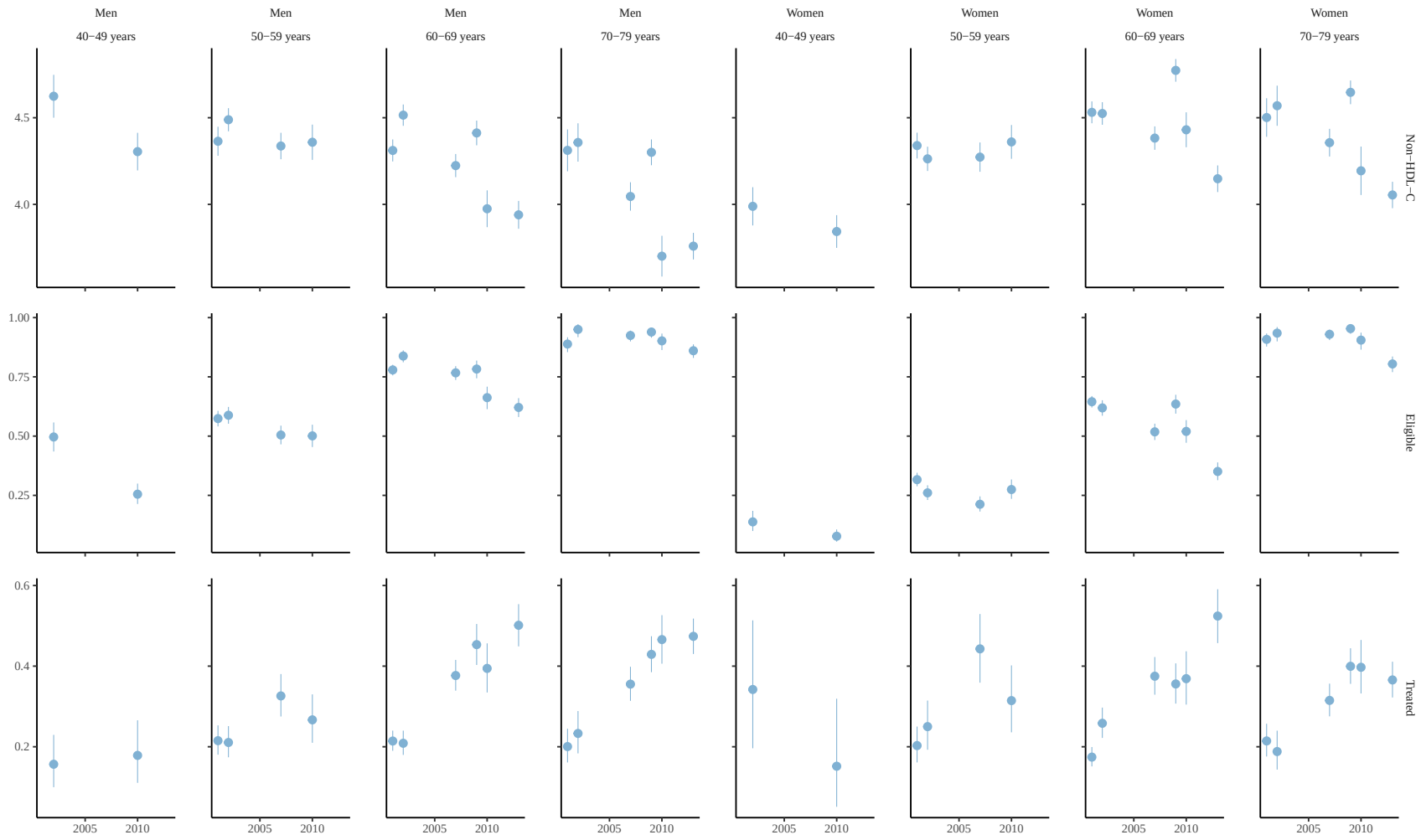


Figure A11: Germany

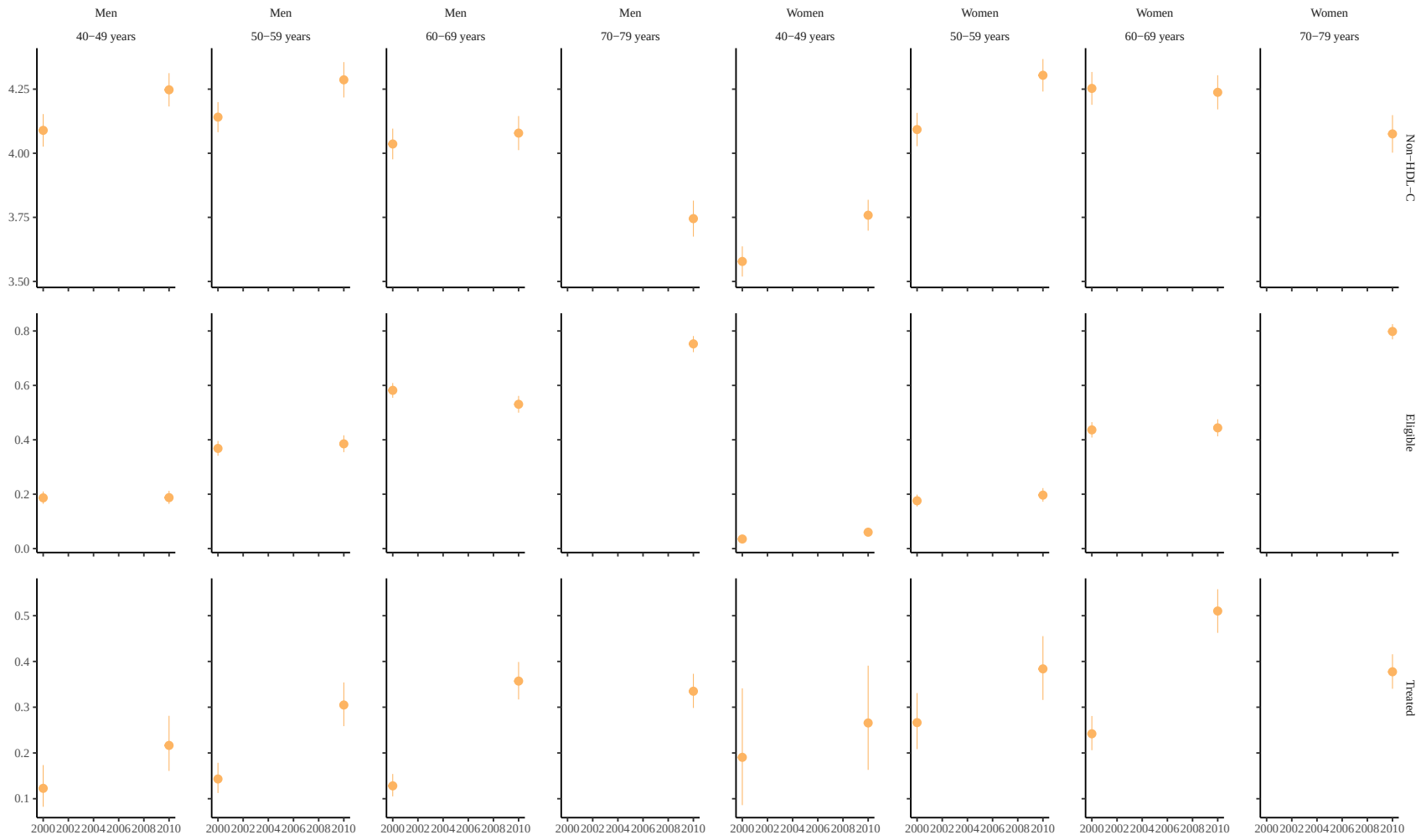


Figure A12: Italy

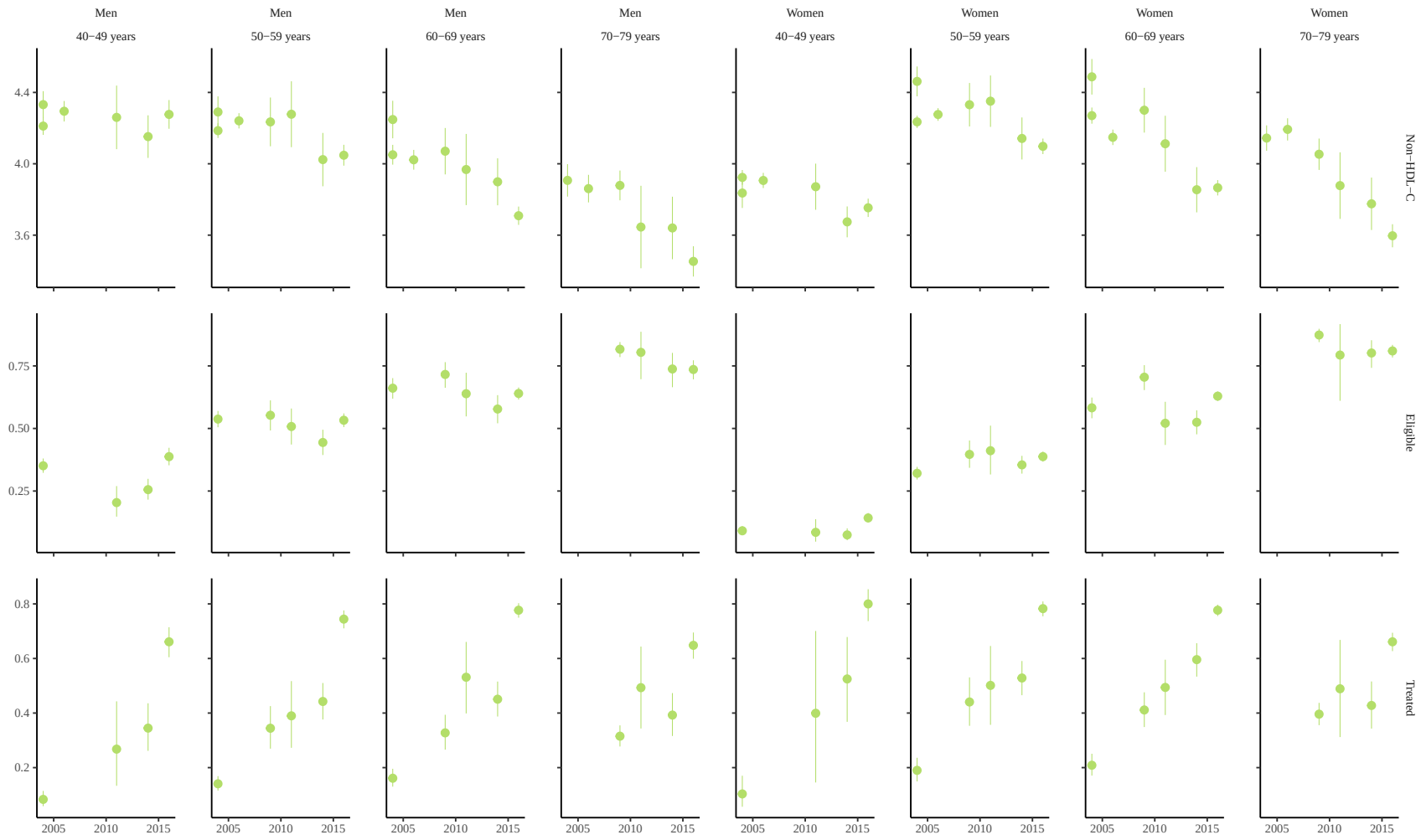


Figure A13: Poland

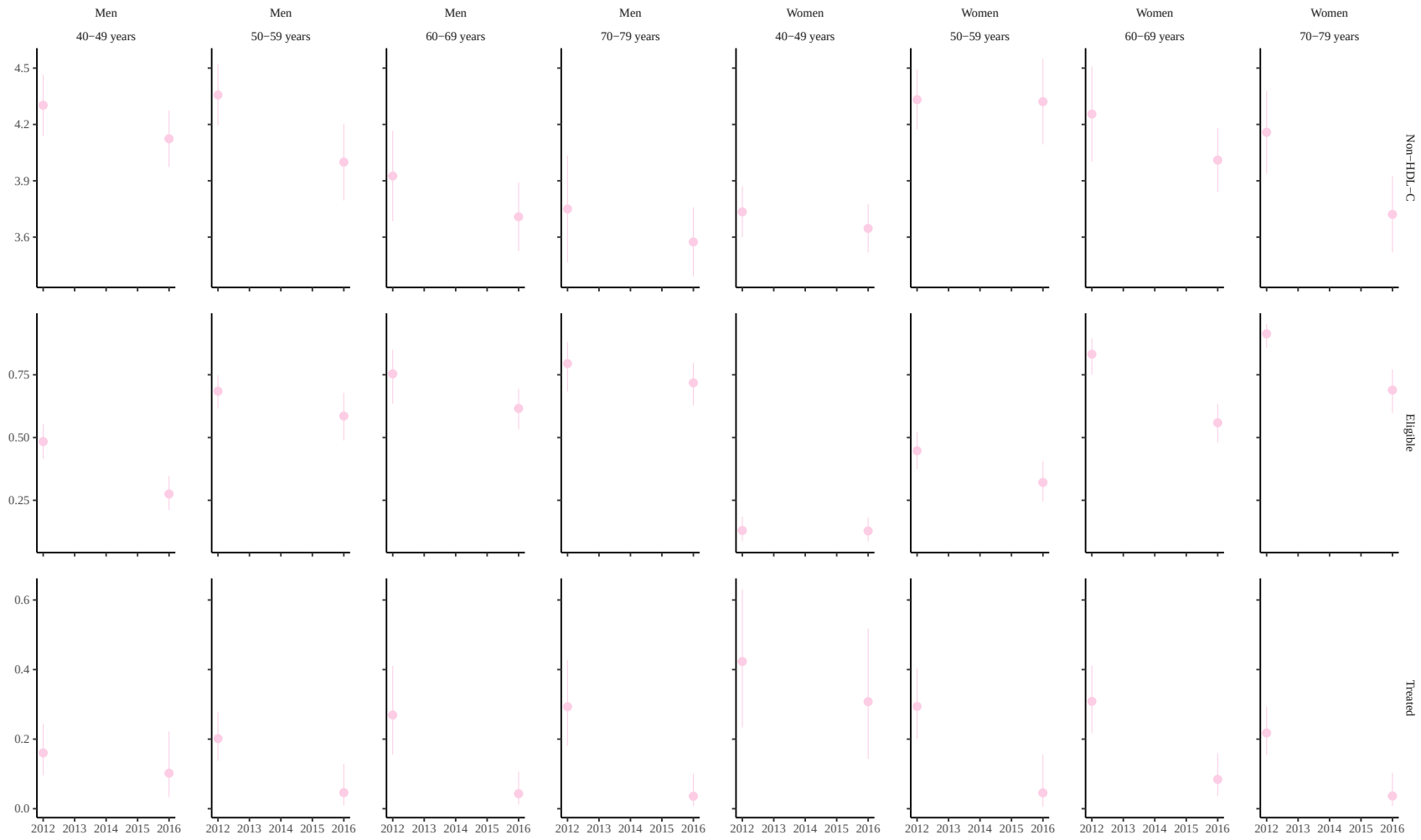


Figure A14: Romania

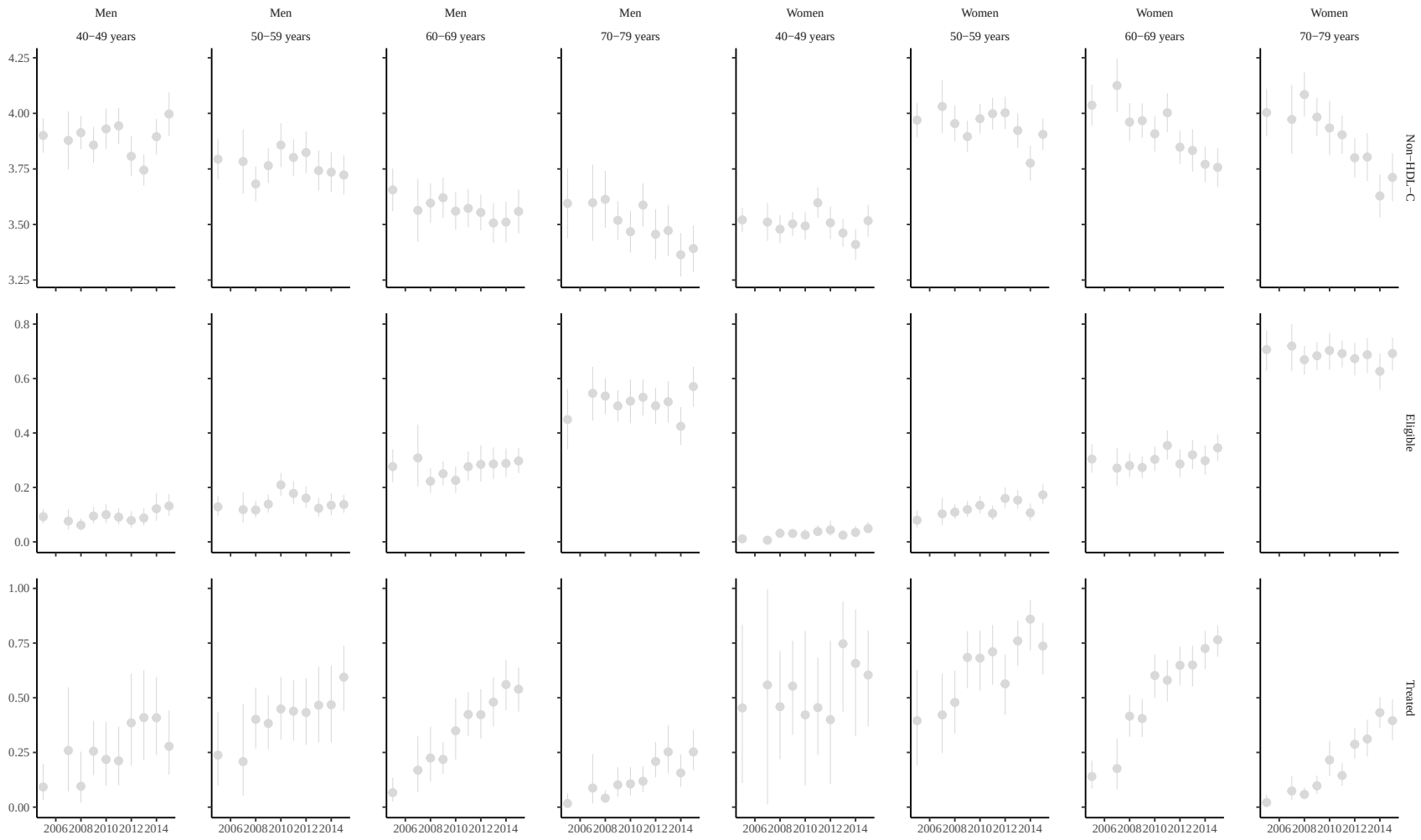


Figure A15: South Korea

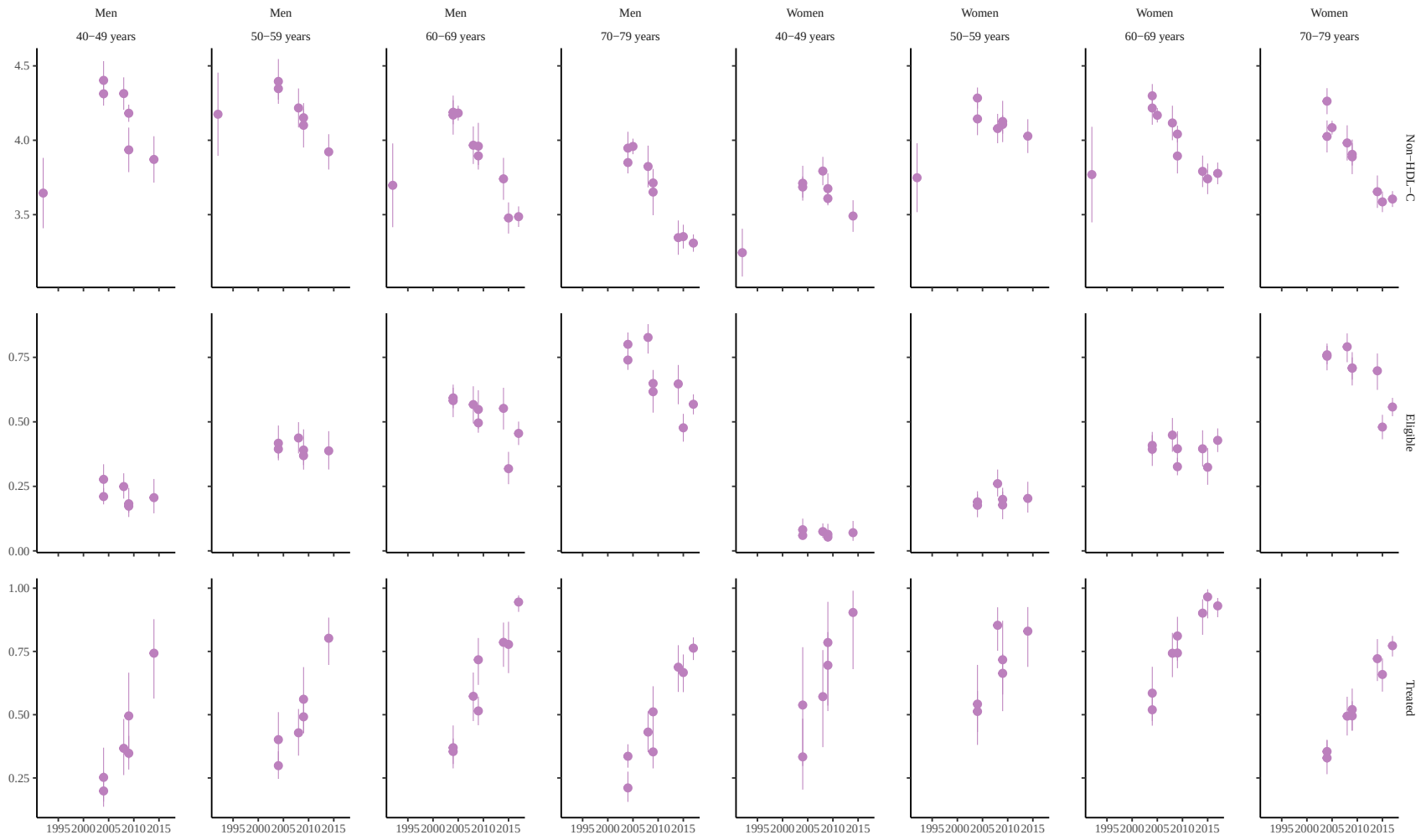


Figure A16: Spain

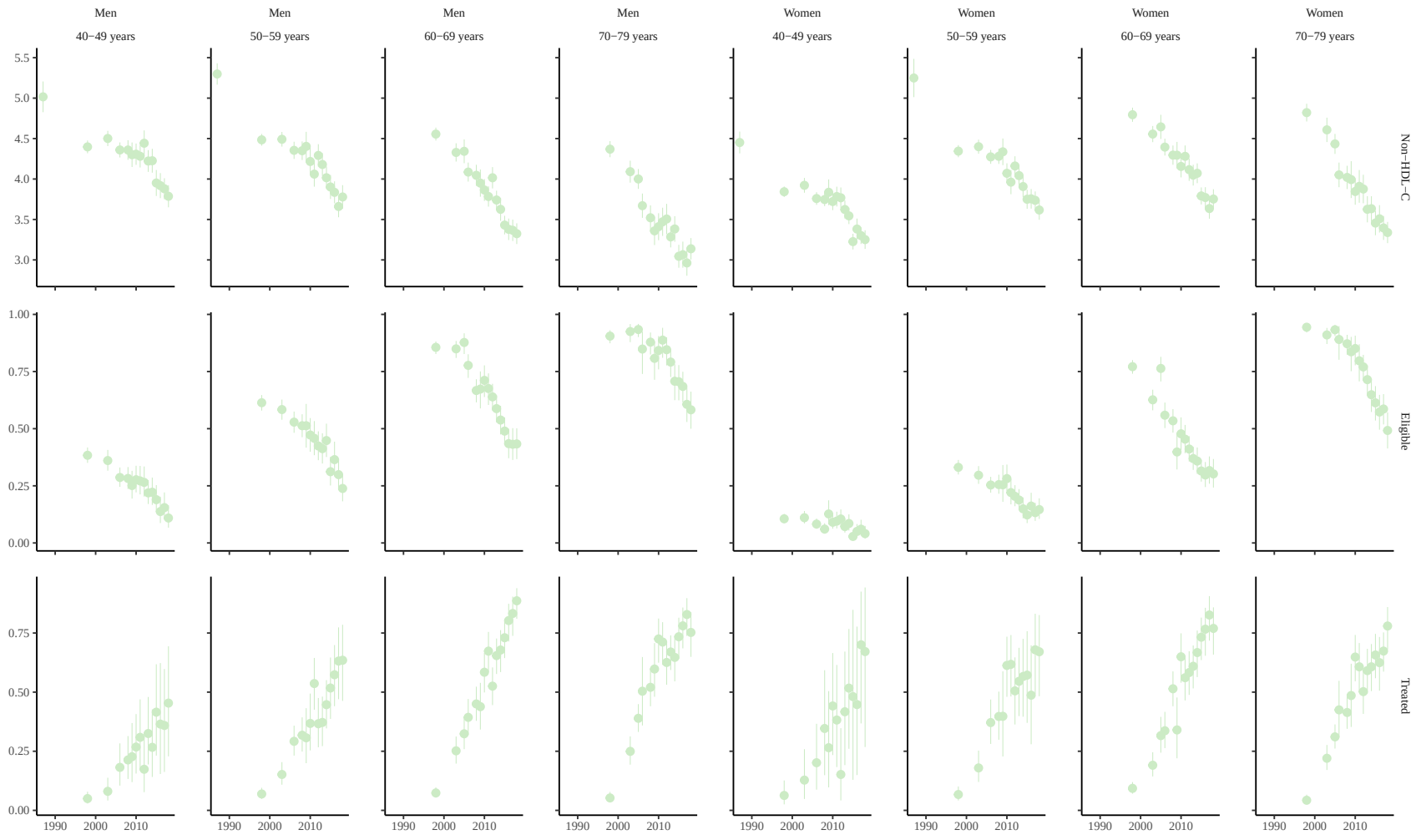


Figure A17: United Kingdom

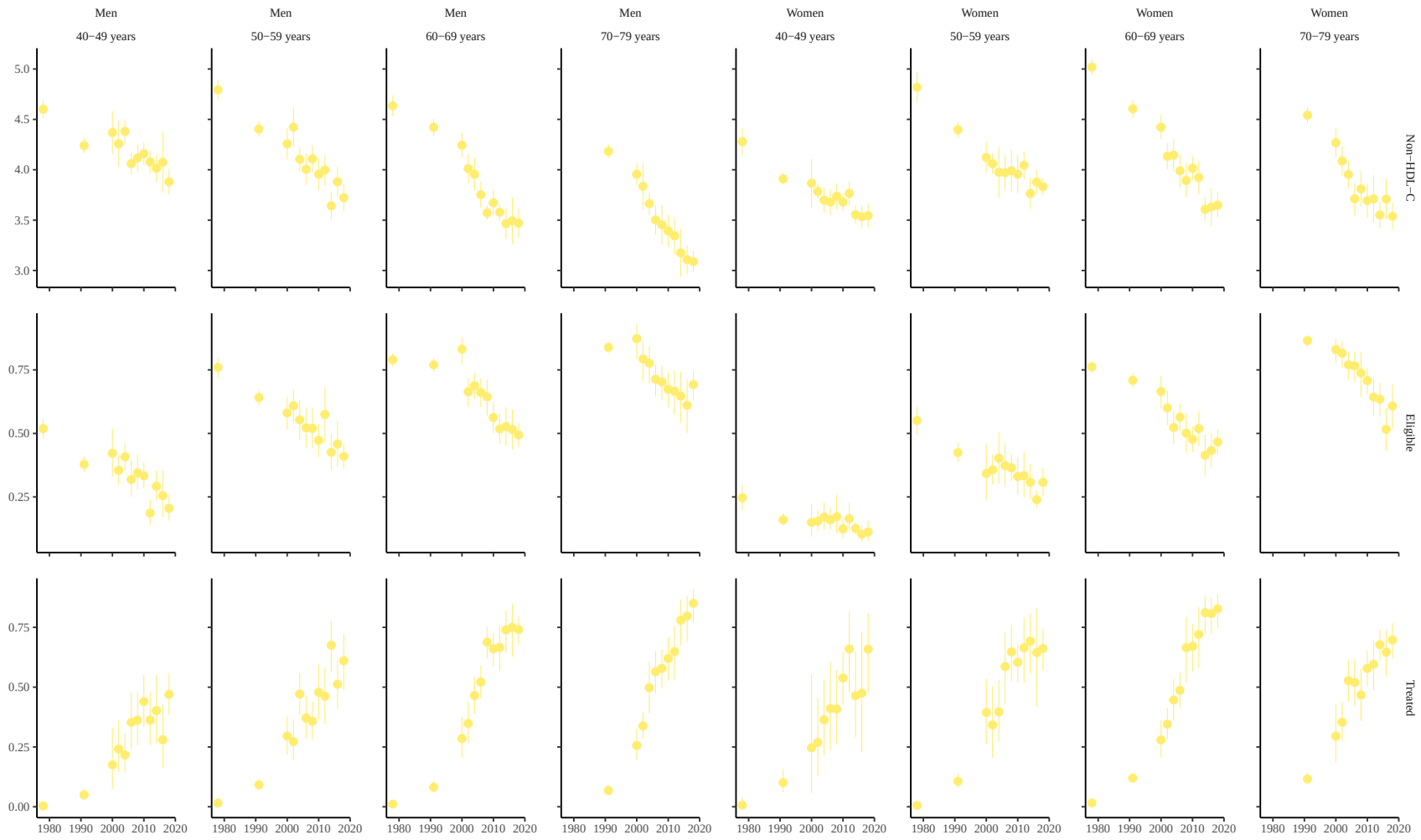


Figure A18: United States of America