Supplementary material

Supplement to: Premysl Velek, Marije J. Splinter, M. Kamran Ikram, M. Arfan Ikram, Maarten J.G. Leening, Johan van der Lei, Tim olde Hartman, Lilian L. Peters, Huibert Tange, Frans H. Rutten, Henk van Weert, Frank J. Wolters, Patrick J.E. Bindels, Silvan Licher, Evelien I.T. de Schepper, Changes in the diagnosis of stroke and cardiovascular conditions in primary care during first two COVID-19 waves in the Netherlands

eTable 1: ICPC codes used to extract relevant data

Outcome	ICPC-1 codes
Any cardiovascular or cerebrovascular diagnosis or symptoms	All codes starting with the letter "K".
Cardiovascular risk factors	
Hypertension	K85.00 (Elevated blood pressure) K86.00 (Hypertension, uncomplicated) K87.00 (Hypertension, complicated)
Type 2 Diabetes	T90.00 (Diabetes mellitus) T90.02 (Diabetes mellitus type 2)
Lipid disorders	T93.00 (Lipid disorder) T93.01 (Hypercholesterolemia) T93.02 (Hypertriglyceridemia) T93.03 (Mixed hyperlipidaemia) T93.04 (Familial hypercholesterolemia / lipidemia)
Cardiovascular events	
Angina	K74.00 (Ischaemic heart disease with angina) K74.02 (Stable angina) K74.01 (Unstable angina)
Atrial fibrillation	K78.00 (Atrial fibrillation / flutter)
Transient ischemic attack	K89.00 (Transient cerebral ischemia / TIA)
Myocardial infarction	K75.00 (Acute myocardial infarction)
Stroke	K90.00 (Stroke / cerebrovascular accident) K90.01 (Subarachnoid haemorrhage) K90.02 (Intracerebral haemorrhage) K90.03 (Cerebral infarction)

eTable 1: ICPC codes used to extract relevant data

eAppendix 1: Model specification

To estimate and quantify the effect of the pandemic and its control measures on the number of first diagnoses for each specific cardiovascular condition, we used a segmented time series analysis with two segments. The period before March 2020 was without restrictions, the period between March and May 2020 was considered as the period of the spring 2020 lockdown, all months afterwards corresponded to the post-lockdown period. The model is defined below:

GP consultations related to any cardiovascular disease or symptom:

$$\log(y_i) = \beta_0 + \beta_1 T_i + \beta_2 M + \beta_3 R_i + \beta_4 A_i + \log(n_i)$$

Number of first diagnoses for individual cardiovascular diagnosis:

$$\log(y_{di}) = \beta_0 + \beta_1 T_i + \beta_2 M + \beta_3 R_i + \beta_4 A_i + \log(n_{di})$$

Where:

Y_i: The count of GP consultations or the diagnoses d in month i

T_i: Number of months from the start of the study period to month i

M: Calendar month of the month i (as categorical variable)

R_i: Dummy variable indicating the second time series segment. R = 0 for all months in the in the study, except for the period of the spring lockdown. R = 1 for April 2020, R = 0.7 for March and May 2020. The estimate of β_3 is the estimate of the reduction in a specific outcome during the first wave of the pandemic.

A_i: Dummy variable indicating the third time series segment. R = 0 for all months before June 2020, R = 1 for all months after (and including) June 2020. The estimate of β_4 is the estimate of the reduction in a specific outcome during the post-lockdown period after the first wave of the pandemic.

n_i: Overall population size for the GP consultation rate (all eligible patients older than 30)

n_{di}: Population size for diagnosis d in month i

We fitted the data to both negative binomial or Poisson generalised linear regression, with the log link function. To compare the two models and test for overdispersion in the data, we performed a

likelihood ratio test with alpha level of 0.05. The negative binomial model was selected whenever the negative binomial model gave a significantly better fit to the data than the Poisson model, i.e. whenever the dispersion parameter θ in the negative binomial model was significantly different from zero assumed by the Poisson model).

The 95% confidence intervals for the reduction and recovery rates were calculated on the linear predictor scale and converted to 95% intervals on the response scale.

To predict the expected counts in a hypothetical scenario in which the pandemic did not happen in 2020, we set the parameters R and A to zero for all months. The fitted values of the model then present point estimates of the mean expected counts in 2020. The 95% confidence intervals were first calculated on the linear scale and then converted to the scale of the dependent variable.

# eFigure 1.1: Observed counts in 2020 vs historical averages: Cardiovascular and cerebrovascular events

Observed counts of first diagnoses of cardiovascular and cerebrovascular events during the pandemic period plotted against those observed during the pre-pandemic period, averaged over two pre-pandemic periods: 2018-2019 and 2016-2019.
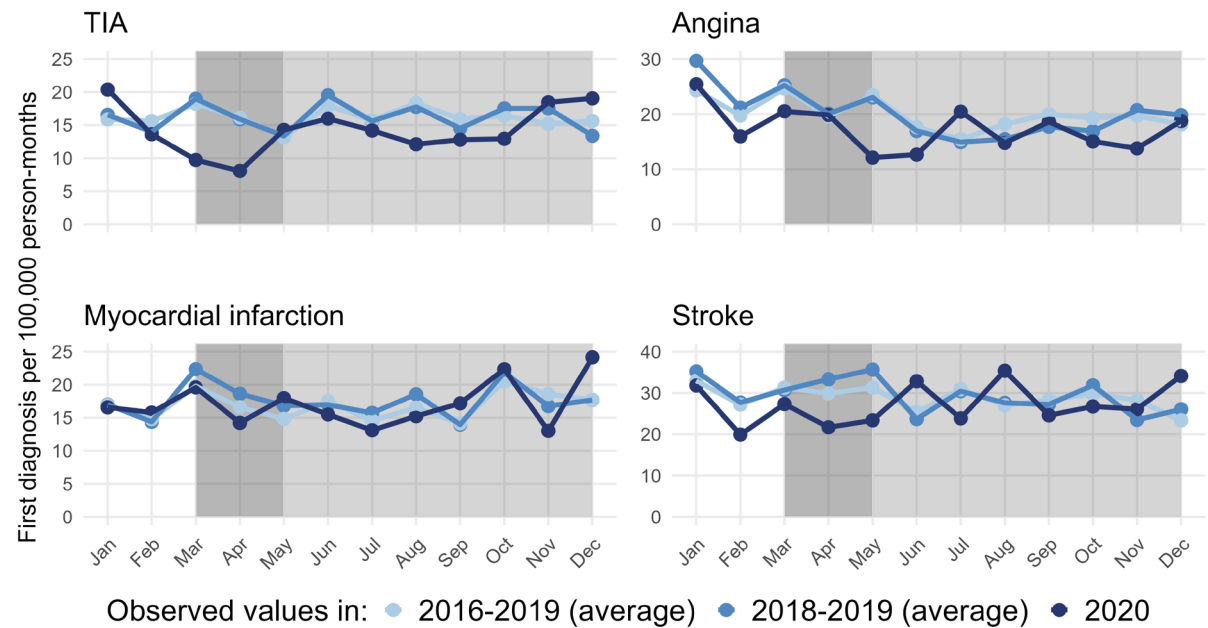
eFigure 1.2: Observed counts in 2020 vs historical averages: Cardiovascular and cerebrovascular risk factors

Observed counts of first diagnoses of cardiovascular and cerebrovascular risk factors during the pandemic period plotted against those observed during the pre-pandemic period, averaged over two pre-pandemic periods: 2018-2019 and 2016-2019.
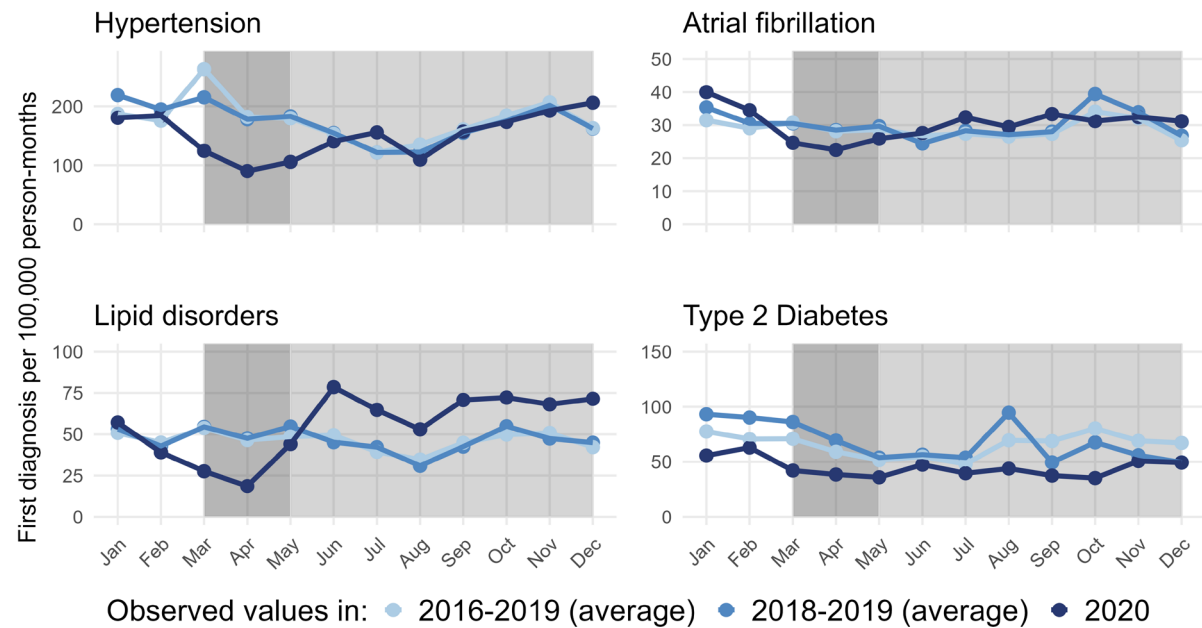
eTable 2: Study population size and mean age

Size and mean age of the study population. Measured in January, April, August and December in each year of the study period. (Age of the participants were rounded to the nearest multiple of five.)

|	Size	Age (mean)	Age (sd)	Age (IQR)	Sex ratio
January 2016	122,302	55.20	15.10	43.0-66.5	0.52
April 2016	134,103	55.20	15.08	43.0-66.5	0.52
August 2016	135,328	55.29	15.13	43.5-66.5	0.52
December 2016	137,600	55.32	15.15	43.0-66.5	0.52
January 2017	139,871	55.39	15.11	43.5-66.5	0.52
April 2017	148,303	55.48	15.09	43.5-67.0	0.52
August 2017	149,359	55.49	15.14	43.5-67.0	0.52
December 2017	160,186	55.79	15.24	43.5-67.5	0.52
January 2018	156,795	55.89	15.21	44.0-67.5	0.52
April 2018	156,887	55.91	15.18	44.0-67.5	0.52
August 2018	157,890	55.93	15.25	43.5-67.5	0.52
December 2018	158,509	56.02	15.28	44.0-67.5	0.52
January 2019	159,409	56.02	15.31	43.5-67.5	0.52
April 2019	164,052	56.05	15.29	44.0-67.5	0.52
August 2019	159,476	56.08	15.32	43.5-67.5	0.52
December 2019	162,756	56.13	15.35	43.5-68.0	0.53
January 2020	155,980	56.18	15.40	43.5-68.0	0.53
April 2020	152,703	56.22	15.39	44.0-68.0	0.53
August 2020	169,547	55.74	15.42	43.0-67.5	0.53
December 2020	166,929	55.73	15.46	43.0-67.5	0.53

eTable 3: Size of the study population by age

Size of the study population by age, as measured in January, April, August and December in each year of the study period. (Age of the participants were rounded to the nearest multiple of five when assigning to the age brackets.)

	30-45	46-65	66-75	>75
January 2016	36,353	52,888	18,953	14,108
April 2016	39,904	58,051	20,816	15,332
August 2016	39,641	58,671	21,255	15,761
December 2016	40,269	59,677	21,728	15,926
January 2017	40,605	60,916	22,060	16,290
April 2017	42,844	64,573	23,682	17,204
August 2017	42,842	64,966	24,034	17,517
December 2017	45,501	69,013	26,266	19,406
January 2018	43,850	67,857	25,961	19,127
April 2018	43,935	67,965	26,030	18,957
August 2018	44,071	68,065	26,346	19,408
December 2018	44,376	68,137	26,438	19,558
January 2019	44,628	68,393	26,524	19,864
April 2019	45,825	70,485	27,406	20,336
August 2019	44,333	68,368	26,739	20,036
December 2019	45,488	69,542	27,253	20,473
January 2020	43,418	65,084	24,137	20,038
April 2020	42,546	65,119	24,201	19,507
August 2020	49,259	67,850	25,780	21,039
December 2020	48,916	69,013	26,266	20,581

eTable 3: Size of the study population by age

eFigure 2: Observed vs. expected monthly number of cardiovascular and cerebrovascular GP consultations by age
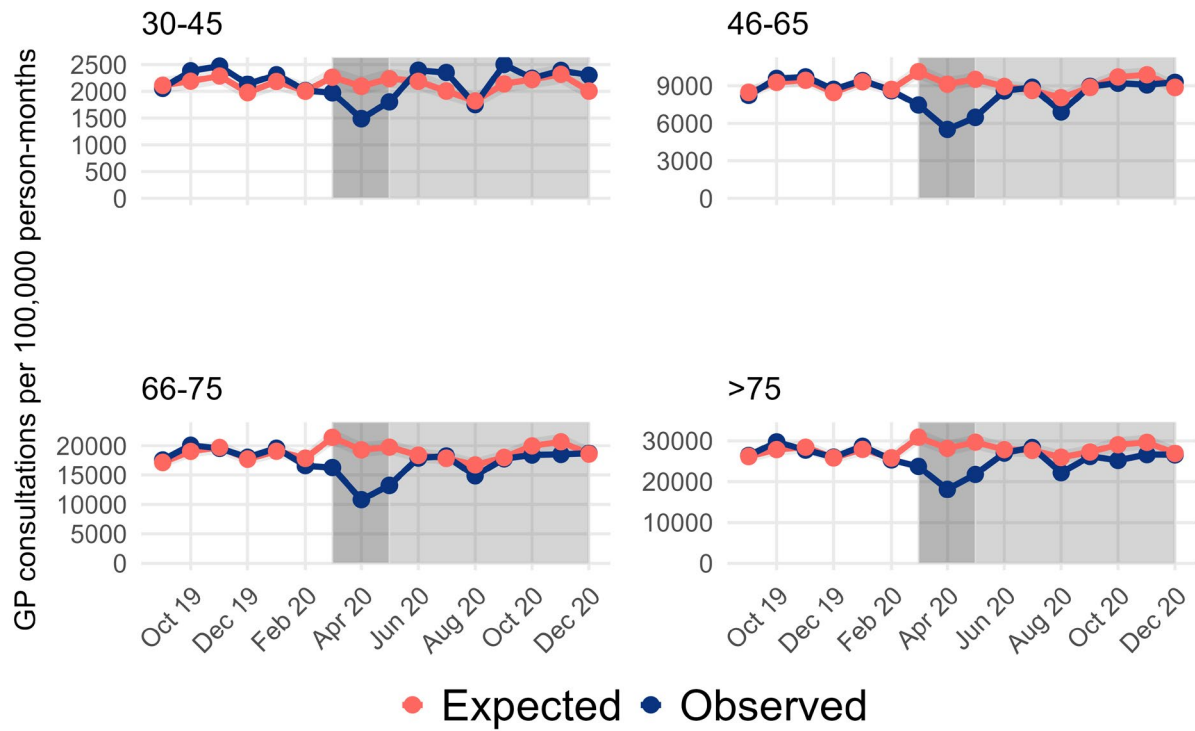
eFigure 3: Observed vs. expected monthly number of cardiovascular and cerebrovascular GP consultations by sex
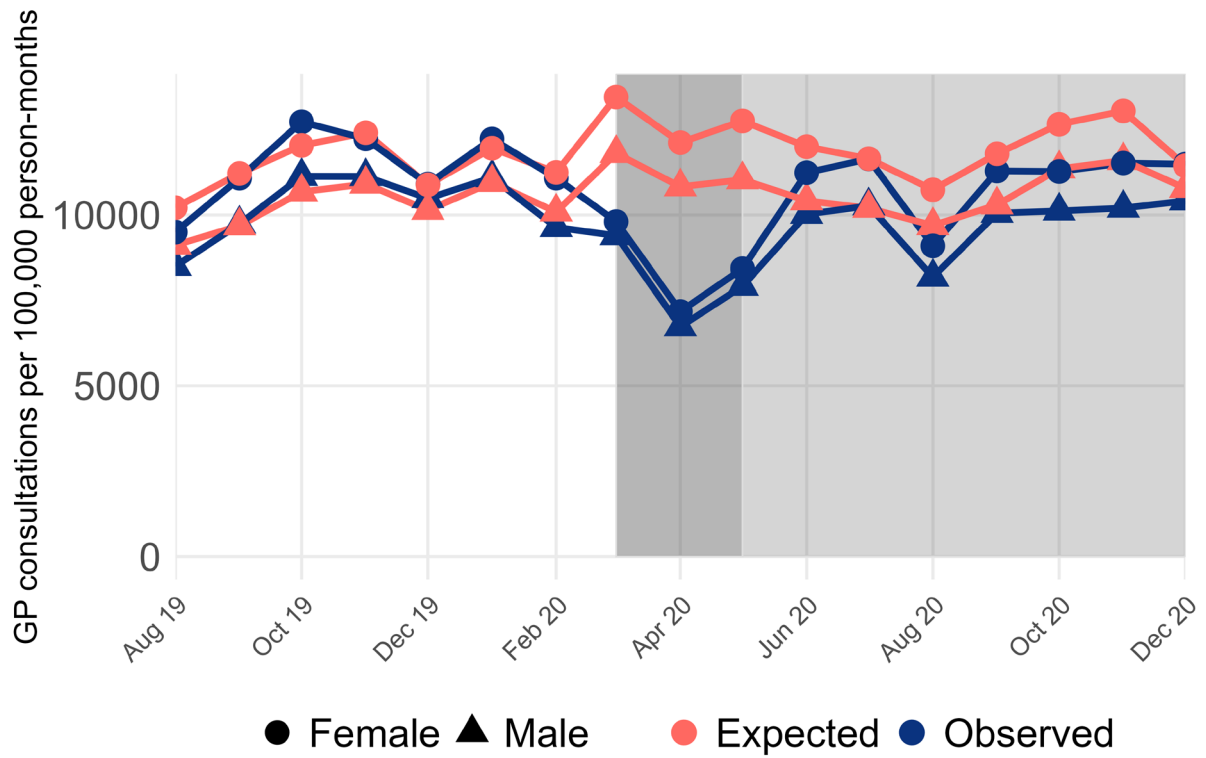
eTable 4: Estimated relative declines for our outcomes with varying values for the first with restriction variable set for March and May 2020.

We tested the sensitivity of our findings to the different specifications of our impact model. We repeated the analysis with different values for the first with-restriction variable set for March and May 2020, the two transition months. We tested our results with values 0.4, 0.6 and 0.8.

Outcome	Values of the first with-restriction variable set for March and May 2020		
	0.4	**0.6**	**0.8**
GP consultations related to cardiovascular care	0.57 (0.50 to 0.64)	0.59 (0.54 to 0.66)	0.60 (0.54 to 0.66)
Transient ischemic attack	0.54 (0.36 to 0.80)	0.60 (0.39 to 0.91)	0.66 (0.43 to 1.00)
Stroke	0.66 (0.54 to 0.80)	0.69 (0.57 to 0.82)	0.72 (0.61 to 0.85)
Myocardial infarction	0.85 (0.69 to 1.04)	0.89 (0.72 to 1.11)	0.92 (0.75 to 1.14)
Angina	0.83 (0.46 to 1.50)	0.78 (0.46 to 1.33)	0.77 (0.50 to 1.18)
Hypertension	0.43 (0.33 to 0.56)	0.44 (0.35 to 0.56)	0.49 (0.40 to 0.59)
Atrial fibrillation	0.68 (0.55 to 0.85)	0.69 (0.58 to 0.82)	0.72 (0.62 to 0.83)
Lipid disorders	0.42 (0.29 to 0.62)	0.50 (0.32 to 0.77)	0.57 (0.37 to 0.87)
Diabetes type 2	0.72 (0.56 to 0.93)	0.73 (0.58 to 0.92)	0.70 (0.60 to 0.82)

eFigure 4.1: Observed vs. expected monthly number of cardiovascular and cerebrovascular events by sex
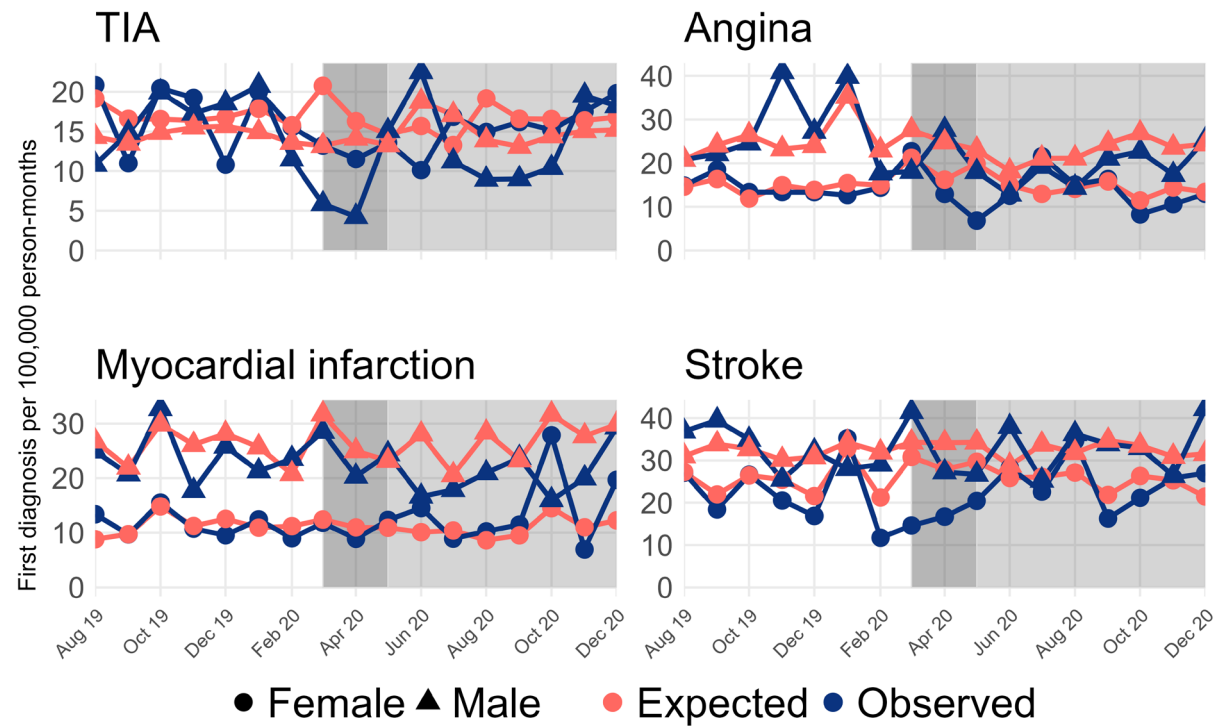
eFigure 4.2: Observed vs. expected monthly number of cardiovascular and cerebrovascular risk factors by sex