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Changes in the Diagnosis of Stroke and Cardiovascular Conditions in Primary Care During First 2 COVID-19 Waves in the Netherlands

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Abstract

Background and objectives

Although there is evidence of disruption in acute cerebrovascular and cardiovascular care during the COVID-19 pandemic, its downstream effect in primary care is less clear. We investigated how the pandemic affected utilization of cerebrovascular and cardiovascular care in general practices (GPs) and determined changes in GP-recorded diagnoses of selected cerebrovascular and cardiovascular outcomes.

Methods

From electronic health records of 166,929 primary care patients aged 30 or over within the Rotterdam region, the Netherlands, we extracted the number of consultations related to cerebrovascular and cardiovascular care, and first diagnoses of selected cerebrovascular and cardiovascular risk factors (hypertension, diabetes, lipid disorders), conditions and events (angina, atrial fibrillation, TIA, myocardial infarction, stroke). We quantified changes in those outcomes during the first COVID-19 wave (March-May 2020) and thereafter (June-December 2020) by comparing them to the same period in 2016-2019. We also estimated the number of potentially missed diagnoses for each outcome.

Results

The number of GP consultations related to cerebrovascular and cardiovascular care declined by 38% (0.62, 95% CI: 0.56-0.68) during the first wave, as compared to expected counts based on pre-pandemic levels. Substantial declines in the number of new diagnoses were observed for cerebrovascular events: 37% for TIA (0.63, 0.41-0.96), and 29% for stroke (0.71, 0.59 to 0.84), while no significant changes were observed for cardiovascular events (myocardial infarction (0.91, 0.74-1.14), angina (0.77, 0.48-1.25)). The counts across individual diagnoses recovered following June 2020, but the number of GP consultations related to cerebrovascular and cardiovascular care remained lower than expected also throughout the June-December period (0.93, 0.88-0.98).

Discussion

While new diagnoses of acute cardiovascular events remained stable during the COVID19 pandemic, diagnoses of cerebrovascular events declined substantially compared to pre-pandemic levels, possibly due to incorrect perception of risk by patients. These findings emphasize the need to improve symptom recognition of cerebrovascular events among the general public and to encourage urgent presentation despite any physical distancing measures.

Introduction

There has been considerable interest in the impact of COVID-19 on specialised cerebrovascular and cardiovascular healthcare. There was a global decline of 11.5% in stroke hospital admissions¹, the number of hospital admissions for acute coronary syndromes in England fell by 40% in March 2020². Besides acute care, the pandemic is likely to have long-lasting and serious implications also for primary care. As healthcare resources were allocated to COVID-19 care, the use and provision of non-COVID-19 primary care were inevitably affected. In addition, people may have delayed seeking help, either for fear of infection by SARS-CoV-2 or to avoid burdening health care providers. The risk of severe health complications due to delays or failure in seeking medical attention increases when risk factors or warning signs of underlying diseases are left unheeded.³ This is particularly relevant for preventive care, or for symptoms that have been considered unimportant by patients due to incorrect perception of risk, as seems particularly the case for transient cerebrovascular symptoms.⁴

This population-based study complements the existing evidence on acute care and examines how the COVID-19 pandemic affected utilization of cerebrovascular and cardiovascular care in general practices (GPs). We leveraged data from primary care consultations to quantify the overall changes in cerebrovascular and cardiovascular care during the COVID-19 pandemic and accompanying physical distancing measures taken by national governments. We also determined changes in the number of diagnoses of individual cerebrovascular and cardiovascular risk factors and events as registered by general practitioners. Finally, we estimated the number of cerebrovascular and cardiovascular diagnoses among community-dwelling individuals that may have been missed during the pandemic.

Methods

Data sources and study population

We conducted a population-based cohort study using the Rijnmond Primary Care database, a region-specific derivative of the Integrated Primary Care Information database⁵, managed by the Department of General Practice of the Erasmus MC - University Medical Centre Rotterdam. The data covers information about approximately 18% of the population of the greater Rotterdam area in the Netherlands, equally distributed across the region. It contains information about patients and episodes of care routinely collected by general practitioners: diagnoses, symptoms, clinical findings, test results, drug prescriptions, and other relevant information. The Rotterdam region is a dense urban area, 36% of the residents have non-Dutch background, of which 70% have non-Western background.⁶ The average distance to the nearest GP practice is 0.6 kilometers (0.37 miles).⁷ The study period started on 1 January 2016 and ended on 31 December 2020.

We included all patients aged 30 years and over. A patient's period of eligibility started either on 1 January 2016, 1 year from registration within a general practice, date of turning 30 years of age, or from the date of the inclusion of the general practice in Rijnmond Primary Care database (whichever came later). The eligibility period ended either by patient's death, transferring to another practice, the end of data collection from their practice, or on 31 December 2020 (whichever came first).

The study was carried out following the RECORD guidelines⁸.

Outcomes and procedures

We focused on two types of outcomes: (a) the overall number of GP consultations related to cerebrovascular and cardiovascular care, and (b) new diagnoses of specific risk factors (hypertension, type 2 diabetes, and lipid disorders); and cerebrovascular and cardiovascular events (myocardial infarction, angina pectoris, atrial fibrillation, stroke and TIA).⁹

A GP consultation was defined as any contact between a GP and a patient (in person, by phone, or online), in which symptoms, complaints, diagnosis, or treatment were discussed. The first diagnosis was defined as a GP consultation, for which a GP entered a new diagnosis in the patient's record, previously not recorded in the patient's history. To include also patients who were diagnosed in hospital or during out-of-hours services of primary care, we also included diagnoses records based on correspondence between GPs and specialist care providers.

The selected diagnoses were identified in the patients' records based on a country-specific version of the International Classification of Primary Care. The classification is managed by the Dutch College of General Practitioners¹⁰ and is adopted by all Dutch GPs (see Supplementary materials. eTable 1).

Data analysis

The analysis were conducted in four steps. First, we extracted the total number of GP consultations related to all cerebrovascular and cardiovascular diagnoses and symptoms for each month in the study period, and the monthly number of new diagnoses for each individual outcome of interest. The sample size was calculated for each month and each individual outcome (the start date of the eligibility period was set on the first day of the month following the exact start date, the end date was set on the last day of the month in which the eligibility period ended). Patients who were already diagnosed with one of the selected outcomes were excluded from the corresponding analyses following their date of diagnosis. Patients with a history of any of the outcomes of interest before study entry were excluded from the sample for this particular outcome.

Second, we fitted a negative binomial regression model to the monthly counts of GP consultations and separately to monthly counts of first diagnosis for each outcome of interest. We tested for overdispersion in our data and used Poisson regression for outcomes in which we did not detect statistically significant overdispersion. The seasonal pattern of the data was modelled with a

categorical variable indicating a calendar month for each data point; a possible long-term linear trend in the outcomes was modelled with a covariate indicating the number of months since the start of the study.

Third, we conducted segmented time series analyses to quantify the level change following the implementation of governmental COVID-19 control measures. We included two with-restriction variables in the model that divided the data into three segments: the pre-COVID-19 period (January 2016 to February 2020), the period of the first lockdown in the Netherlands (March to May 2020), and the period after the first lockdown (June to December 2020). The first variable defined the period of the first lockdown and was set to 0 for all months in the study, except for March, April, and May 2020. Since the nation-wide lockdown in the Netherlands was introduced on March 11 and ended on May 10 2020, these two months were considered a transition periods with only a partial impact of the pandemic. The first with-restriction value was therefore set to 1 for April, and to 0.7 for March and May 2020. The value of 0.7 provided the best fit to the data, based on the root square error, across all outcomes. The second with-restriction variable defined the period following the spring lockdown; it was set to 0 for all months before June 2020 and to 1 for all months afterwards (June-December 2020). The estimated coefficients of the two with-restriction variables defined the effect of the pandemic throughout 2020: the first with-restriction coefficient represents the relative decline in the monthly counts as a proportion of expected counts during the first COVID-19 wave, the second with-restriction coefficient estimated the relative decline in the monthly counts in the period after the first COVID-19 wave. (Values less than 1 indicate a decline and values greater than 1 indicate an increase.) To account for heteroscedasticity and autocorrelation in the error terms, the standard errors of the estimates and the coefficients were calculated using heteroscedasticity and autocorrelation consistent covariance matrix estimation.¹¹ The natural logarithm of the sample size was used as an offset to control for the changing sample size throughout the study period. Detailed specification of the model is available in the Supplementary material (eAppendix 1).

Fourth, to estimate the absolute effect on the number of new diagnoses, we fitted the same model again, but with the two with-restriction variables set to zero for all months. The fitted values of the model for March through December 2020 thus represented the expected counts in the counterfactual scenario where no pandemic and no restrictions took place. By comparing these expected counts with

observed counts for each calendar month from March to December 2020, we estimated the cumulative number of potentially missed or delayed diagnoses.

To show how the observed counts during the pandemic period differed from those observed during the pre-pandemic period, we plotted the observed counts for each calendar month in 2020 against observed counts averaged over two pre-pandemic periods: 2018-2019 and 2016-2019 (eFigure 1.1 and eFigure 1.2, Supplementary material).

We conducted a sensitivity analysis to assess the robustness of our findings. We re-analyzed the data in which we set the first with-restriction value for March and May 2020 to 0.2, 0.4, 0.6 and 0.8 in order to account for potential variation of the lockdown impact on the main results.

Data extraction and analyses were carried out in R (version 4.0.0)¹², data was prepared and plotted using the tidyverse collection of packages¹³, and the negative binomial regression model was fitted using the MASS package¹⁴.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Governance Board of Rijnmond Primary Care (project number 2020.012). All patient data are de-identified for research purposes, no patient consent was therefore required.

Data availability

Due to legal restraints, data are not made publicly available in a repository. Access to the data will be provided upon reasonable request and subject to approval by the Governance Board of Rijnmond Primary Care.

Results

Population characteristics

The total study population (patients over 30 years) grew from 122,302 patients in January 2016 to 166,929 in December 2020, as more GP practices were included in the database. The average age of the patients was 55.7 years, 51 % of the population were females. The population characteristics

remained stable throughout the study period. Detailed characteristics of the study population and the relevant subgroups are available in the Supplementary material (eTable 2, eTable 3).

The Netherlands experienced two COVID-19 waves in 2020, the first wave peaked on 27 March 2020 with 620 daily hospital admissions (3.56 per 100,000 people), the second wave had two peaks, the first on 2 November 2020 with 399 daily hospital admissions (2.29 per 100,000 people), the second peak was on 28 December 2020 with 469 daily hospital admissions (2.69 per 100,000 people).¹⁵ The Rotterdam region recorded 47 daily hospital admissions (3.21 per 100,000 people) at the peak of the first wave, 53 daily admissions at the first peak of the second wave (3.62 per 100,000 people), and 37 daily admissions at the second peak (2.53 per 100,000 people).¹⁶

Changes in the total number of GP consultations related to cerebrovascular and cardiovascular care

Immediately after the start of the first national lockdown in the Netherlands, the number of GP consultations related to cerebrovascular and cardiovascular care declined to 62% of the expected count (0.62, 95% CI: 0.56 to 0.68). After the initial steep decline, the number of consultations returned closer to pre-pandemic level, but remained lower than the expected number throughout the rest of 2020 (0.93, 0.88 to 0.98) (**Figure 1**).

The decline in GP consultations was higher for females than for males: 0.59, (0.54 to 0.66) versus 0.64 (0.59 to 0.71). Greater declines were observed for older adults: the largest relative decline was observed for people between 66 to 75 years (0.58, 0.52 to 0.65); the smallest decline was observed for the youngest group in this study (31 to 45 years) (0.74, 0.65 to 0.85). The youngest group is the only age group for which we observed a statistically significant increase in the number of consultations in the second half of 2020 (1.08, 1.00 to 1.17) as compared to the expected counts (see Supplementary material, eFigure 2, eFigure 3).

Changes in the number of new diagnoses across cerebrovascular, cardiovascular events and risk factors

While the number of first diagnoses for cerebrovascular events declined at the start of the spring lockdown in the Netherlands (TIA: 0.63 (0.41 to 0.96), stroke: 0.71 (0.59 to 0.84)), the number of first diagnoses for cardiovascular events did not change significantly (myocardial infarction: 0.91 (0.73 to 1.13), angina pectoris: 0.71 (0.59 to 0.84)). Significant changes were also observed for risk factors

(hypertension: 0.47 (0.38 to 0.57), type 2 diabetes: 0.74 (0.59 to 0.92), lipid disorders: 0.54 (0.35 to 0.82)), and for atrial fibrillation (0.77, 0.48 to 1.25)). The observed monthly numbers of new diagnoses for each outcome in 2020, compared to the estimated mean expected numbers per 100,000 person-months is represented in **Figure 2** and **Figure 3**. The relative decline for each outcome as compared to expected levels is presented in **Figure 4A**. Sensitivity analysis using varying values for the first with-restriction variable for the two transition months (March and May 2020) provided consistent results for all outcomes (see Supplementary material, eTable 4).

From June 2020 onwards, the monthly counts of first diagnoses increased and returned to their pre-COVID-19 levels, but – with the exception of lipid disorders – did not exceed the expected counts. The rate of new diagnosis for lipid disorders exceeded significantly the expected rate for all months from June 2020 onwards, with a rate of change of 1.57 (1.43 to 1.74) (**Figure 4B**).

Atrial fibrillation and stroke were the only diagnoses with differences between males and females during the lockdown in March, April, and May 2020. A decline was observed among females for atrial fibrillation (0.53, 0.41 to 0.68), whereas no significant change was observed among males (0.82, 0.64 to 1.06). For stroke, the change for females was 0.52 (0.42-0.66) and 0.88 (0.62-1.26) for males (see Supplementary material, eFigure 4.1).

Number of potentially missed cerebrovascular and cardiovascular diagnoses in primary care

The impact of the COVID-19 pandemic on cerebrovascular and cardiovascular care in terms of number of potentially missed cases for each diagnosis is presented in **Table 1**. These numbers reflect the difference between the observed number of first diagnoses during the COVID-19 pandemic and the predicted number of first diagnoses, based on our model estimates. The highest number of potentially missed cases was for hypertension with 303 fewer diagnoses in the study population from March to December 2020 (328 diagnoses per 100,000 person-years). There were 39 fewer diagnoses of stroke and 35 fewer diagnoses of TIA in the study population (25 and 26 diagnoses per 100,000 person-years, respectively). Contrary to all the other outcomes, the number of new diagnoses of lipid disorders increased by over 100 diagnoses per 100,000 person-years as compared to the expected counts.

Discussion

The overall number of GP consultations related to cerebrovascular and cardiovascular care dropped by 38% during the first lockdown and remained below pre-pandemic levels in the second half of the year. More importantly, the number of new diagnoses of cerebrovascular events declined substantially, in contrast with the number of new diagnoses of acute cardiovascular events which remained stable. This suggests that patients may be less alarmed by symptoms suggestive of TIA or stroke (as compared to myocardial infarction) and therefore less likely to contact their GPs⁴. This behavior might be further reinforced during lockdowns when people with cerebrovascular symptoms may avoid seeking care due to fear of COVID-19 and related complications, especially when public authorities urge them to stay home.¹⁷

Previous studies

Previous studies showed a substantial decline in GP consultations across a range of diagnoses and health conditions during the first half of 2020, including acute cerebrovascular and cardiovascular events.¹⁸⁻²⁰ Qualitative studies also documented disruption to primary care across a range of European countries.²¹

A global observational study found 11.5% decline in stroke admissions (including TIA) during the initial four months of the pandemic (March-June 2020)¹, which is in line with our finding. A UK-wide study focusing on missed GP contacts for acute events found decline by 0.63 in the number of contacts for TIA in March 2020 and 0.59 for strokes. Contrary to our study, they also observed a substantial decline in the number of GP contacts for myocardial infarction, unstable angina, and diabetes emergencies.²⁰

Clinical implications

The number of potentially missed diagnosis of stroke, TIA, atrial fibrillation, and risk factors may lead to increased health complications. The risk of recurrent stroke for people after their first stroke is estimated to be 11% within 1 year and 26% within 5 years.²² It has been suggested that timely secondary preventive measures can reduce the risk of recurrent cardiovascular events by up to 70%²³,³. Patients who did not seek medical attention during the pandemic for cerebrovascular symptoms, and hence did not start risk lowering treatment, may therefore be at increased risk of repeat neurological

events and death. The composite risk of stroke, acute coronary syndrome, or death from cardiovascular causes at 5 years after TIA is estimated to be nearly twice as high for people without any risk-reduction measures.³

The high number of potentially missed diagnoses of cerebrovascular and cardiovascular risk factors and atrial fibrillation is worrying, given the established benefits of preventive interventions to reduce the risk of cerebrovascular and cardiovascular events and mortality.^{24, 25} Hypertension is the only outcome we studied in which the impact of the pandemic was detectable at the level of individual GPs: the total potentially missed diagnoses of hypertension equaled around 8 cases per year per general practitioner (with an average number of patients per GP in the Netherlands being 2,300)²⁶.

Limitations and strengths

Limitations of our study firstly include possible inconsistent recording practices among GPs. Furthermore, interventions at the level of individual GP practices might have influenced our data and our results. We also did not include recurrent events which may follow different pattern of health seeking behaviour as those who have already experienced a cerebrovascular or cardiovascular event might be more likely to recognize their symptoms. We also could not distinguish between patients diagnosed by GPs and patients diagnosed in hospital/emergency departments (who were later referred to their GP). It is possible that the effect of the pandemic was different for these two groups of patients. Finally, we did not have access to the data on education levels, smoking and other lifestyle indicators, which might have provided greater insight into the healthcare avoidance patterns.

A key strength of this study is that we assessed the impact of COVID-19 on primary care by the inclusion of a broad spectrum of cerebrovascular and cardiovascular conditions, also including risk factors. As our data covered the full year of 2020, we were also able to examine changes in health care seeking behavior over a longer time span.

Conclusions

The COVID-19 pandemic has a potentially long-lasting impact on the prognosis of cerebrovascular and cardiovascular diseases due to missing or delayed diagnosing of risk factors and most notably cerebrovascular events. Even though the number of new diagnoses returned to the expected levels in the second half of 2020, the number of potentially missed diagnoses during the first wave were not

recuperated. The decline in the number of first diagnoses of stroke and TIA calls for improvement of symptom recognition of cerebrovascular events among the general public and for awareness campaign to encourage urgent presentation despite any existing physical distancing measures.

The challenge for the near future is to identify patients who avoided healthcare and develop strategies for cerebrovascular and cardiovascular primary care that will minimize the consequences of undiagnosed risk factors and events during the COVID-19 pandemic. A critical question is to assess whether this disruption in primary care will lead to increased cerebrovascular and cardiovascular morbidity and mortality in the future.

[AZ 10.27.2021] 175406 Supplement --- <http://links.lww.com/WNL/B688>

References

1. Nogueira RG, Qureshi MM, Abdalkader M, et al. Global Impact of COVID-19 on Stroke Care and Intravenous Thrombolysis. *Neurology* 2021.
2. Mafham MM, Spata E, Goldacre R, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. *The Lancet* 2020;396:381-389.
3. Amarenco P, Lavallée PC, Monteiro Tavares L, et al. Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke. *N Engl J Med* 2018;378:2182-2190.
4. Wolters FJ, Li L, Gutnikov SA, Mehta Z, Rothwell PM. Medical Attention Seeking After Transient Ischemic Attack and Minor Stroke Before and After the UK Face, Arm, Speech, Time (FAST) Public Education Campaign: Results From the Oxford Vascular Study. *JAMA Neurol* 2018;75:1225-1233.
5. Vlug AE, van der Lei J, Mosseveld BM, et al. Postmarketing surveillance based on electronic patient records: the IPCI project. *Methods Inf Med* 1999;38:339-344.

6. Bevolking; leeftijd, migratieachtergrond, geslacht, regio, 1 jan. 1996-2020 [online]. Available at: <https://opendata.cbs.nl/#/CBS/nl/dataset/37713/table>. Accessed 30/09/2021.
7. StatLine: Huisarts in 2019 gemiddeld op 1 kilometer afstand [online]. Available at: <https://www.cbs.nl/nl-nl/nieuws/2020/17/huisarts-in-2019-gemiddeld-op-1-kilometer-afstand>. Accessed 30/09/2021.
8. Benchimol EI, Smeeth L, Guttman A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLOS Medicine* 2015;12:e1001885.
9. Leening MJ, Kavousi M, Heeringa J, et al. Methods of data collection and definitions of cardiac outcomes in the Rotterdam Study. *Eur J Epidemiol* 2012;27:173-185.
10. Genootschap NH. NHG-Tabel 24-ICPC-versie 8. 2020.
11. Zeileis A. Object-oriented Computation of Sandwich Estimators. *Journal of Statistical Software*; Vol 1, Issue 9 (2006) 2006.
12. R: A language and environment for statistical computing. R Foundation for Statistical Computing [computer program]. Vienna, Austria: 2020.
13. Wickham H, Averick M, Bryan J, et al. Welcome to the Tidyverse. *Journal of Open Source Software* 2019; 4.
14. N. VW, D. RB. *Modern Applied Statistics with S*. Fourth Edition., Fourth ed. New York, USA: Springer, 2002.
15. Ontwikkeling COVID-19 in grafieken [online]. Available at: <https://www.rivm.nl/coronavirus-covid-19/grafieken>. Accessed 30/09/2021.

16. Gemeld aantal ziekenhuisopnames op één dag van inwoners van veiligheidsregio Rotterdam-Rijnmond [online]. Available at: <https://coronadashboard.rijksoverheid.nl/veiligheidsregio/VR17/ziekenhuis-opnames>. Accessed 30/09/2021.
17. Henrique D, Pedro SCM, Sheila COM, et al. Decrease in Hospital Admissions for Transient Ischemic Attack, Mild, and Moderate Stroke During the COVID-19 Era. *Stroke* 2020;51:2315-2321.
18. Williams R, Jenkins DA, Ashcroft DM, et al. Diagnosis of physical and mental health conditions in primary care during the COVID-19 pandemic: a retrospective cohort study. *Lancet Public Health* 2020;5:e543-e550.
19. Carr MJ, Steeg S, Webb RT, et al. Effects of the COVID-19 pandemic on primary care-recorded mental illness and self-harm episodes in the UK: a population-based cohort study. *The Lancet Public Health* 2021;6:e124-e135.
20. Mansfield KE, Mathur R, Tazare J, et al. Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: a population-based study. *The Lancet Digital Health* 2021;3:e217-e230.
21. Wanat M, Hoste M, Gobat N, et al. Transformation of primary care during the COVID-19 pandemic: experiences of healthcare professionals in eight European countries. *British Journal of General Practice* 2021:BJGP.2020.1112.
22. Keerthi MM, Charles DAW, Anthony GR, Peter UH, Peter LK-R, Andrew PG. Risk and Cumulative Risk of Stroke Recurrence. *Stroke* 2011;42:1489-1494.
23. Pedersen RA, Petursson H, Hetlevik I. Stroke follow-up in primary care: a prospective cohort study on guideline adherence. *BMC Family Practice* 2018;19:179.

24. Blood Pressure Lowering Treatment Trialists C. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet* 2021;397:1625-1636.
25. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;383:955-962.
26. Kringos DS vRPJ, Boerma WGW. . The Netherlands. Building primary care in a changing Europe: Case studies, Observatory Studies Series, No. 40. 20 ed. Copenhagen, Denmark 2015.

Figures

Throughout the manuscript, the observed outcomes are represented in blue, the estimated expected outcomes are represented in red. Estimated expected outcomes are always presented with 95% confidence intervals – in grey around the point estimate.

The pandemic period in 2020 (March-December 2020) are highlighted in grey in all figures, the period of the first lockdown (March-May 2020) is represented in dark grey.

In Figures 3 and 4, the estimated relative decline for the number of GP consultations related to cardiovascular care is represented in red, cardiovascular risk factors are represented in grey and cardiovascular events in blue.

In the Supplementary material, when presented results stratified by sex, females are represented by a circle, males are represented by a triangle.

Figure 1. All GP consultations on cardiovascular conditions

(A): Number of GP consultations related to cardiovascular care in 2020 compared to historical averages. (B): Number of GP consultations related to cardiovascular care in 2020 compared to estimated expected number of GP consultations. The shaded area indicates the pandemic period with the period of the first lockdown in the Netherlands (15 March to 11 May 2020) highlighted.

Figure 2. Observed vs. expected monthly number of new diagnoses: Cardiovascular and cerebrovascular events

Number of new diagnoses of cerebrovascular ((A)TIA, (B) stroke) and cardiovascular events ((C) myocardial infarction, (D) angina): observed and expected counts of new diagnoses (August 2019 to December 2020). The shaded area indicates the pandemic period with the period of the first lockdown in the Netherlands (15 March to 11 May 2020) highlighted.

Figure 3. Observed vs. expected monthly number of new diagnoses: Risk factors

Number of new diagnoses for (A) hypertension, (B) atrial fibrillation, (C) type 2 diabetes, and (D) lipid disorders: observed and expected counts of new diagnoses (August 2019 to December 2020). The shaded area indicates the pandemic period with the period of the first lockdown in the Netherlands (15 March to 11 May 2020) highlighted.

Figure 4. Relative decline in the number of first diagnoses

Relative decline in the number of first diagnoses for all cerebrovascular and cardiovascular GP consultations, and for individual outcomes compared to expected numbers. (A) March to May 2020, (B) June to December 2020.

ACCEPTED

A. March–May 2020

B. June–December 2020

Tables

Table 1: Expected and observed numbers of first diagnoses and estimated differences in the number of new diagnoses for each outcome.

	Total expected number of first diagnoses in the study population (March-December 2020)	Total observed number of first diagnoses in the study population (March-December 2020)	Absolute difference between expected and observed in number of first diagnoses in the study population (March-December 2020)	Difference between expected and observed in number of first diagnoses in the study population (March-December 2020) per 100,000 person-years
Hypertension	1792	1489	-303	-274
Atrial fibrillation	471	415	-56	-43
Lipid disorders	595	737	+142	+108
Type 2 Diabetes	684	533	-151	-122
Transient ischemic attack	228	193	-35	-26
Angina	274	233	-41	-31
Stroke	427	388	-39	-25
Myocardial infarction	262	237	-25	-30

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