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ORIGINAL RESEARCH

Effects of COVID-19 Pandemic and Lockdown on Monitoring and Treatment Balance of Finnish Coronary Heart Disease and Type 2 Diabetes Patients

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Purpose: We aimed to examine the effect of the COVID-19 pandemic and lockdown on monitoring and treatment balance of Finnish coronary heart disease (CHD) and type 2 diabetes (T2D) patients.

Patients and Methods: We used data from the electronic health records on 1604 CHD and 10,136 T2D patients aged 18–85 years in Eastern Finland. Measurement and levels of low-density lipoprotein cholesterol (LDL) of CHD patients and glycated haemoglobin (HbA1c) of T2D patients were assessed monthly during January 2019–June 2021. Interrupted time-series analysis design was utilized to examine the effect of the lockdown on proportion of patients monitored and treatment balance.

Results: Reductions in frequencies of LDL testing of CHD and HbA1c testing of T2D patients were observed during the national lockdown. Downward trend in average LDL was observed from January 2019 until June 2021. Average HbA1c values increased from January 2019 to March 2020 with an additional increase by 2.04 mmol/mol (0.80 to 3.29) in April 2020. However, there was a downward trend in monthly average HbA1c during the lockdown until June 2021 with an additional change in level by 0.61 mmol/mol (95% CI 0.06 to 1.16) in July 2020.

Conclusion: The lockdown decreased the frequency of monitoring among both CHD and T2D patients. Meanwhile, monthly average LDL had a steadily improving pattern in CHD patients during the follow-up while temporary worsening in HbA1c in patients with T2D was observed at the time of the lockdown. The lockdown may have introduced selection in patients who had their treatment outcomes monitored. Better self-management of risk factors among patients is also possible.

Keywords: HbA1c, LDL, interrupted time-series, electronic health records

Introduction

The first ever confirmed COVID-19 case in Finland was reported on 29 January 2020. Due to the rapid onset of the COVID-19 pandemic, the Finnish government declared a state of emergency due to COVID-19 with a national lockdown under the Emergency Powers Act on 16 March 2020. Among other things, less critical activity in social and healthcare was partly run down to ensure sufficient capacity for the care of COVID-19 cases.[1] Furthermore, inhabitants over 70 years old were recommended to decrease social contacts to a minimum and to live in circumstances corresponding to quarantine. The government gradually loosened the restrictions from mid-May on. The lockdown lasted until 15 June 2020 when the state of emergency was declared to end, the restrictions were cancelled, and the society was re-opened. However, the recommendation for inhabitants over 70 years remained in action.

In the North Karelia region in Eastern Finland having 166,000 inhabitants, 18% of the scheduled appointments to physicians and nurses and 25% of all visits were cancelled among persons aged 55 years or older between March and

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November 2020.[2] The first SARS-CoV-2 infection occurred in the region on 9 March 2020.[3] Early on at the end of April 2020, when it was seen that the health system was not overloaded with COVID-19 patients, the health authorities of North Karelia advised patients to use the remote services to take care of non-urgent matters. If the matter could not be handled remotely, patients were advised to visit the facility in person as facilities implemented additional safety precautions to reduce the risk of COVID-19 infection among patients and personnel.[4]

In our previous study, 9% reduction in diabetes-related primary healthcare service usage was observed among type 2 diabetes (T2D) patients in the North Karelia region in 2020 when compared with 2019 with most significant reductions occurring during the lockdown.[5] Also, a 9% reduction in the proportion of patients with any contacts was detected. In this study, we aimed to examine more specifically the effect of the national lockdown on disease monitoring and treatment balance of Finnish coronary heart disease (CHD) and T2D patients. In addition, we were also interested in variation by age and treatment balance before the lockdown.

Materials and Methods

Study Setting

In Finland, municipalities fund and organize healthcare for all their residents by themselves or together with other municipalities. In the North Karelia region, Finland, Siun sote – Joint municipal authority of North Karelia social and health services was established in 2017 to produce healthcare services for 13 municipalities of the area. Since its implementation in 2010–2011, an electronic health register (EHR) called Mediatri has been in use in the Siun Sote region. In this study, we utilized EHRs data on primary and secondary care as well as on laboratory assays.

Study Design

Two cohorts were formed from the EHR data. The first cohort included patients diagnosed with incident CHD in 2014–2018 as identified with ICD-10 code I20.0 or I21 or procedure code indicating acute medical procedure related to CHD (percutaneous coronary intervention or coronary artery bypass graft) without previous history of CHD for whom the active follow-up and good low-density lipoprotein cholesterol (LDL) management is essential. The second cohort consisted of patients having T2D as diagnosed with ICD-10 code E11 prior to 2019 who should be regularly followed up and controlled for hemoglobin A1c (HbA1c). We restricted both cohorts to patients aged 18–85 years-old at the end of the follow-up on 30 June 2021. Patients older than 85 years were excluded because of the increased risk of institutionalization that may cause uncertain and incomprehensive recordings on health centre visits and examinations. In addition, patients had to be alive and living in the North Karelia region at the end of the study on 30 June 2021 (CHD n = 1604; T2D n = 10,136).

Outcomes

With a standardized method and analysis across the North Karelia Region, LDL samples were analysed with the photometric direct enzymatic method and HbA1c values with the turbidimetric inhibition immunoassay method (TINIA) in the Eastern Finland laboratory (ISLAB, https://www.islab.fi). Both LDL and HbA1c values were standardized to the International Federation of Clinical Chemistry (IFCC) units. LDL measurements for CHD patients and HbA1c measurements for T2D patients were extracted from January 2019 to June 2021.

Other Variables

For both cohorts, background data on sex and age were retrieved. Age was calculated at the time of the start of the lockdown on 16 March 2020 and was categorized to patients ≤70 years and >70 years old following the governmental special recommendation.

Statistical Analyses

Characteristics of patients were described with frequencies and proportions for categorical variables and with means and standard deviations for continuous variables.

Interrupted time-series (ITS) design was utilized to examine the effect of the lockdown on the treatment monitoring.[6] For this, the follow-up was divided into three phases. The lockdown was expected to have an immediate effect on the number of patients monitored because less critical activity in social and healthcare was partly run down. That is, monthly data was divided into 14 months before the lockdown (1 Jan 2019–28 February 2020), 3 months during the lockdown (1 March 2020–31 May 2020) and 13 months after the lockdown (1 June 2020–30 June 2021). This resulted in 30 repeated measurements in total. If several measurements were taken per participant, the latest one was selected as a monthly value. We used segmented autoregressive error models[7] for aggregated data on proportion (%) of patients monitored p at month t to model the ITS design. The estimated models were of the form:

$$p_t = \beta_0 + \beta_1\, time_t + \beta_2\, LD_t + \beta_3\, time\ after\ LD_t + \beta_4\, end\ of\ LD_t +$$

$$\beta_5\, time\ after\ end\ of\ LD_t + \beta_6\, January_t + \beta_7\, June_t +$$

$$\beta_8\, July_t + \beta_9\, December_t + \vartheta_t$$

$$\vartheta_t = -\varphi_1\, \vartheta_{t-1} - \ldots - \varphi_{13}\, \vartheta_{t-13} + \varepsilon_t$$

$$\varepsilon_t \sim IN\left(0, \sigma^2\right),$$

where β_0 is the proportion of patients with measurements at baseline in January 2019, β_1 is the monthly time trend before the lockdown (LD), β_2 is the immediate effect of the lockdown on level on March 2020, β_3 is the change in trend in March 2020, β_4 is the level change after the end of the lockdown in June 2020 and β_5 is the trend change after the lockdown in June 2020. In addition, models were adjusted for seasonal effects of January (β_6), June (β_7), July (β_8), and December (β_9) because of reduced monitoring due to seasonal vacations and its effects on health care services as well as on behaviour of the patients. The model was corrected for autocorrelation of error terms if it was diagnosed with generalized Durbin–Watson test. Autoregressive parameters up to 13 months were included in the model. In the presented model, ϑ_t is an error term consisting of an autoregressive error part $-\varphi_1\, \vartheta_{t-1} - \ldots - \varphi_{13}\, \vartheta_{t-13}$ and a random error part ε_t. Models were fitted with stepwise method where statistically non-significant parameters were manually removed one-by-one.

Effects of the lockdown on treatment balances measured with LDL and HbA1c were estimated under ITS design with linear mixed models[8] utilizing individual level data. In these analyses, the lockdown was expected to have a gradual effect on the treatment balances because HbA1c represents average blood glucose levels over past 2–8 weeks[9] and it takes few weeks also for LDL levels to adjust for the effects of diet or medication.[10] Therefore, the effect of the lockdown was lagged to start from April 2020 and last until the end of June 2020. That is, monthly data was divided into 15 months before the lockdown (1 Jan 2019–31 March 2020), 3 months during the lockdown (1 April 2020–30 June 2020) and 12 months after the lockdown (1 July 2020–30 June 2021). The fitted models were of the form:

$$TB_{it} = (\beta_0 + v_{i0}) + (\beta_1 + v_{i1})\, time_{it} + \beta_2\, LD_{it} + \beta_3\, time\ after\ LD_{it} + \beta_4\, end\ of\ LD_{it} + \beta_5\, time\ after\ end\ of\ LD_{it}$$
$$+ \beta_6\, January_{it} + \beta_7\, June_{it} + \beta_8\, July_{it} + \beta_9\, December_{it} + \beta_{10}\, Gender_i + \beta_{11}\, Age_i + \varepsilon_{it}$$

$$v_{i0} \sim N\left(0, \sigma_0^2\right),$$

$$v_{i1} \sim N\left(0, \sigma_1^2\right),$$

$$\varepsilon_{it} \sim N\left(0, \sigma_e^2\right),$$

where β_0–β_9 are fixed effects like in the models for treatment monitoring. In addition, models for treatment balance (TB) were adjusted for gender (β_{10}) and age (β_{11}). The models included random intercept v_{i0} and random slope v_{i1} growth factors to account for correlations between individual's i repeated measurements. Based on Akaike Information Criterions, unstructured covariance matrix was the best structure to describe correlations between random effects in both LDL and HbA1c models. The models assumed missing at random for missing LDL and HbA1c values, and they were estimated with restricted maximum likelihood method. Models were fitted with stepwise method where statistically non-significant parameters were manually removed one-by-one.

Sub-group analyses were conducted by age (≤70 years/>70 years) and treatment balance. LDL level of a patient at the start of the lockdown was defined according to the latest measured value before "week 9" of the year 2020. Although the treatment target of LDL for very high-risk CHD patients is ≤1.4 mmol/l, we used cut-offs of LDL ≤1.8 mmol/l for good treatment balance and LDL >1.8 mmol/l for poor treatment balance before the lockdown because of low number of patients with LDL ≤1.4 mmol/l (n = 250).[10,11] HbA1c level of the patient at the start of the lockdown was defined according to the latest measured HbA1c value before week 9 of the year 2020. Treatment balance was dichotomized to those with good treatment balance,[9] HbA1c ≤53 mmol/mol, and to those with poor treatment balance, HbA1c >53 mmol/mol, before the lockdown.

All analyses were conducted with SAS 9.4 (SAS Institute Inc., Cary, North Carolina). Two-sided P values <0.05 were considered statistically significant.

Ethics Statement

Use of the data was approved by the Ethics Committee of the Northern Savonia Hospital District (diary number 81/2012) that considers all applications within its university hospital catchment area. The study protocol was also approved by the register administrator, Siun sote – Joint municipal authority for North Karelia social and health services. We utilized only de-identified register-based data and individuals in the registers were not contacted. In accordance with Finnish legislation, no written consent from the patients was required. The study complies with the Declaration of Helsinki.

Results

Characteristics of CHD and T2D patients in total and stratified by the latest treatment outcome prior to the lockdown are presented in Table 1.

Table 1 Characteristics of CHD and T2D Patients in Total and Stratified by the Latest Treatment Outcome Prior to the Lockdown

	All CHD Patients	LDL <1.8 mmol/l	LDL ≥1.8 mmol/l	All T2D Patients	HbA1c ≤53 mmol/mol	HbA1c >53 mmol/mol
Total, n (%)	1604 (100)	–	–	10,136 (100)	–	–
Mean age, years (SD)	68.8 (9.5)	–	–	68.0 (10.3)	–	–
≤70 years	687 (42.8)	–	–	5306 (52.35)	–	–
>70 years	917 (57.2)	–	–	4830 (47.65)	–	–
Female	597 (37.2)	–	–	4398 (43.4)	–	–
With at least 1 outcome measure, n (%)	1481 (100)	685 (46.3)	796 (53.7)	8459 (100)	5742 (67.9)	2717 (32.1)
Mean age, years (SD)	71.0 (9.4)	71.8 (9.0)	70.3 (9.6)	68.5 (10.1)	68.8 (10.0)	67.9 (10.4)
≤70 years	631 (42.6)	269 (39.3)	362 (45.5)	4235 (50.1)	2823 (49.2)	1412 (52.0)
>70 years	850 (57.4)	416 (60.7)	434 (54.5)	4224 (49.9)	2919 (50.8)	1305 (48.0)
Female	550 (37.1)	233 (34.0)	317 (39.8)	3702 (43.8)	2604 (45.4)	1098 (40.4)

Note: Numbers are frequencies (proportions) unless otherwise stated.
Abbreviations: CHD, coronary heart disease; LDL, low-density lipoprotein; T2D, type 2 diabetes.

Effects Among Coronary Heart Disease Patients

Of the 1604 CHD patients, 1481 (92.3%) had LDL measured before the lockdown. In total, 3440 LDL measurements were taken during the follow-up with on average 2.3 (SD 1.3, range 1–11) measurements per patient (Supplementary Table 1). In total, 1063 measurements were taken during January–June 2019, whereas 597 (56.2% of the corresponding frequency in 2019) measurements were taken during January–June 2020, and 439 during January–June 2021. During March–May 2019, there were 511 measurements, whereas during March–May 2020 a total of 223 measurements were taken and 225 during March–May 2021.

Effects on Monitoring

On January 2019, on average 10.8% of CHD patients were monitored (Table 2, Figure 1A). The monitoring rate decreased by −0.13%-units (95% confidence interval, CI, −0.21 to −0.04) per month from January 2019 to February 2020. An immediate decrease by −2.85%-units (95% CI −4.34 to −1.35) in the proportion of CHD patients measured occurred in March 2020. Thereafter, the change in monthly rate of monitoring was the same as before the lockdown. Similar results were obtained in subgroup analyses when stratified by age (Table 2, Figure 1B) and treatment balance (Table 2, Figure 1C).

Effects on Treatment Balance

Monthly mean LDL values are presented in Supplementary Table 2. Steadily decreasing trend of −0.02 mmol/l (95% CI −0.01 to −0.02) per month was observed in average LDL level throughout the follow-up. No immediate effects of the lockdown were seen on average LDL level of CHD patients (Table 2, Figure 1D).

Table 2 Impact of the Lockdown on Monitoring and Average LDL Values (mmol/l) in All CHD Patients and Stratified by Age and Treatment Balance

Monitoring	**All CHD Patients (n=1604)**	**≤70 Years (n=687)**	**>70 Years (n=917)**	**LDL <1.8 mmol/l (n=685)***	**LDL ≥1.8 mmol/l (n=796)***
	Est. (95% CI)	**Est. (95% CI)**	**Est. (95% CI)**	**Est. (95% CI)**	**Est. (95% CI)**
Baseline level at 01/2019	10.80 (9.94 to 11.65)	11.22 (10.45 to 12.00)	10.46 (9.35 to 11.57)	10.99 (10.21 to 11.76)	13.00 (11.73 to 14.29)
Trend since 01/2019, per month	−0.13 (−0.21 to −0.04)	−0.10 (−0.19 to −0.01)	−0.14 (−0.25 to −0.03)	–	−0.34 (−0.46 to −0.23)
Level change in 03/2020	−2.85 (−4.34 to −1.35)	−3.65 (−5.18 to −2.12)	−2.20 (−4.14 to −0.26)	−6.20 (−7.23 to −5.18)	−3.19 (−4.51 to −1.87)
Trend change since 03/2020, per month	–	–	–	–	0.32 (0.18 to 0.46)
Average LDL (mmol/l)	**All Patients (n=1481)**	**≤70 Years (n=689)**	**>70 Years (n=857)**	**LDL <1.8 mmol/l (n=685)**	**LDL ≥1.8 mmol/l (n=796)**
	Est. (95% CI)	**Est. (95% CI)**	**Est. (95% CI)**	**Est. (95% CI)**	**Est. (95% CI)**
Trend since 01/2019, per month	−0.02 (−0.02 to −0.01)	−0.02 (−0.02 to −0.01)	−0.02 (−0.02 to −0.01)	−0.02 (−0.03 to −0.01)	–
Level change in 04/2020	–	–	–	0.17 (0.08 to 0.27)	–
Trend change since 04/2020, per month	–	–	–	–	−0.14 (−0.17 to −0.10)
Level change in 07/2020	–	–	–	–	–
Trend change since 07/2020, per month	–	–	–	0.01 (0.00 to 0.02)	0.13 (0.08 to 0.18)

Notes: Analyses were adjusted for seasonal effects of January, June, July, and December. Average LDL levels were adjusted for age and gender, in addition. Only statistically significant coefficients were kept in the model. *Estimated among those who had at least one LDL measurement before the lockdown.

Abbreviations: CHD, coronary heart disease; LDL, low-density lipoprotein.

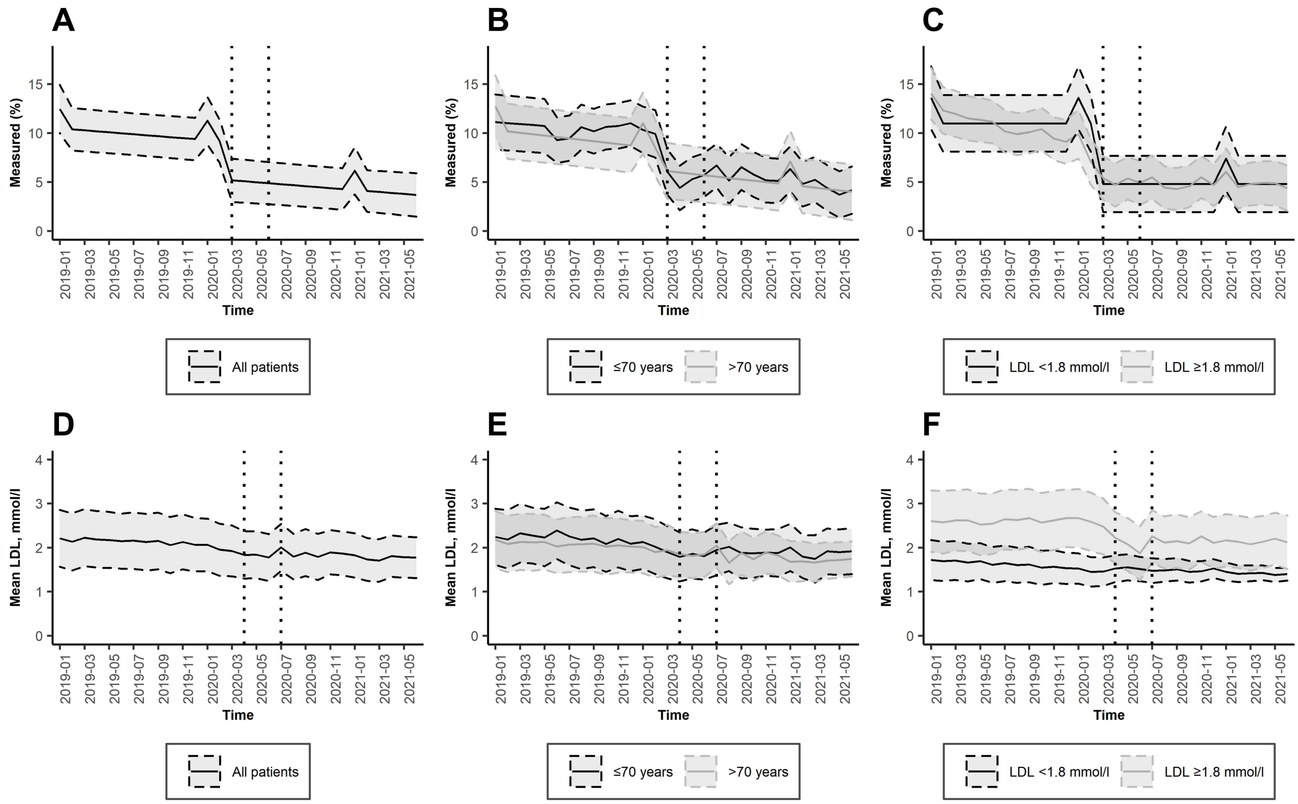

Figure 1 (**A**) Estimated monthly proportions (95% confidence interval) of monitored CHD patients. (**B**) Estimated monthly proportions (95% confidence interval) of monitored CHD patients by age groups. (**C**) Estimated monthly proportions (%, 95% confidence interval) of monitored CHD patients by LDL level before the lockdown. (**D**) Estimated monthly mean LDL levels (95% confidence intervals) among all CHD patients. (**E**) Estimated monthly mean LDL levels (95% confidence intervals) by age groups. (**F**) Estimated monthly mean LDL levels (95% confidence intervals) by LDL level before the lockdown.

In stratified analyses, no differences between age groups were observed (Table 2, Figure 1E). When the analyses were stratified by treatment balance, average LDL decreased by −0.02 mmol/l (95% CI −0.03 to −0.01) until the end of March 2020 among patients with LDL <1.8 mmol/l before the lockdown (Table 2, Figure 1F). In April 2020, a sudden increase in average LDL by 0.17 mmol/l (95% CI 0.08 to 0.27) was detected but the decreasing trend remained thereafter. After the end of the lockdown in July 2020, decrease in average monthly LDL level started to decelerate (change in trend by 0.01 mmol/l [95% CI 0.00 to 0.02] per month) until the end of June 2021. However, among patients with LDL ≥1.8 mmol/l before the lockdown, constant LDL was observed until the lockdown. Average monthly LDL had downward trend during the lockdown (−0.14 mmol/l per month [95% CI −0.17 to −0.10]) but the trend changed back to almost stable in June 2020 (change in trend after the lockdown 0.13 mmol/l [95% CI 0.08 to 0.18]).

Effects Among Type 2 Diabetes Patients

Of the 10,136 T2D patients, 8459 (83.5%) had HbA1c measured before the lockdown. In total, 27,691 HbA1c measurements were taken during the follow-up (Supplementary Table 3). On average, 3.3 (SD 1.9, range 1–24) measurements were taken per patient. In total, 11,860 HbA1c measurements were taken in 2019 whereas 9698 measurements were taken in 2020 making it 81.8% of the corresponding amount in 2019. During January–June 2019, there were 6102 measurements, whereas during January–June 2020, a total of 4945 measurements were taken and 6133 during January–June 2021. During March–May 2019, there were 3061 measurements, whereas during March–May 2020 a total of 2269 measurements were taken and 3256 during March–May 2021.

Effects on Monitoring

In total, 9.97% of T2D patients were monitored in January 2019 and the level stayed stable until the lockdown (Table 3, Figure 2A). An immediate decrease of −2.78%-units (95% CI −3.91 to −1.65) in monitoring rate was observed in March 2020

Table 3 Impact of the Lockdown on the Proportion of Monitored T2D Patients and on Average HbA1c (mmol/Mol) Levels

Monitoring	All T2D Patients (n=10,136)	≤70 Years (n=5306)	>70 Years (n=4830)	HbA1c ≤53 mmol/mol (n=5742)*	HbA1c >53 mmol/mol (n=2717)*
	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)
Baseline level at 01/2019	9.93 (9.40 to 10.46)	9.36 (8.88 to 9.85)	10.52 (9.93 to 11.11)	10.77 (10.14 to 11.41)	14.35 (13.84 to 14.85)
Level change in 03/2020	−2.79 (−3.92 to −1.67)	−2.00 (−3.04 to −0.97)	−2.09 (−3.35 to −0.82)	−2.59 (−3.72 to −1.46)	−3.93 (−5.12 to −2.73)
Trend change since 03/2020, per month	0.20 (0.10 to 0.30)	0.16 (0.06 to 0.25)	0.16 (0.04 to 0.27)	0.24 (0.11 to 0.37)	0.28 (0.16 to 0.39)
Average HbA1c (mmol/mol)	**All T2D Patients (n=8459)**	**≤70 Years (n=4235)**	**>70 Years (n=4224)**	**HbA1c ≤53 mmol/mol (n=5742)**	**HbA1c >53 mmol/mol (n=2717)**
	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)	Est. (95% CI)
Trend since 01/2019, per month	0.14 (0.11 to 0.17)	0.14 (0.10 to 0.18)	0.13 (0.09 to 0.17)	0.07 (0.04 to 0.09)	0.25 (0.19 to 0.31)
Level change in 04/2020	2.04 (0.80 to 3.29)	–	2.08 (0.52 to 3.64)	2.73 (1.56 to 3.90)	–
Trend change since 04/2020, per month	−1.45 (−2.15 to −0.75)	−0.22 (−0.29 to −0.16)	−1.21 (−2.02 to −0.39)	−1.31 (−1.96 to −0.66)	−1.31 (−1.67 to −0.96)
Level change in 07/2020	0.61 (0.06 to 1.16)	–	–	1.70 (1.19 to 2.20)	–
Trend change since 07/2020, per month	1.23 (0.53 to 1.93)	–	1.04 (0.21 to 1.87)	0.93 (0.28 to 1.58)	1.31 (0.94 to 1.67)

Notes: Adjusted for age, gender and seasonal effects of January, June, July, and December. *Calculated among those who had at least one HbA1c measurement during 1 Jan 2019–15 March 2020.
Abbreviations: HbA1c, glycated haemoglobin A1c; T2D, type 2 diabetes.

when the lockdown started. Thereafter, the proportion of monitored patients started to increase steadily by 0.21%-units (95% CI 0.10 to 0.31) per month until June 2021. Similar effects of the lockdown were seen when stratified by age group (Table 3, Figure 2B) or treatment balance among those who had HbA1c measurement during the follow-up (Table 3, Figure 2C).

Effects on Treatment Balance

Monthly mean HbA1c values are presented in Supplementary Table 4. Increase in average HbA1c values by 0.14 mmol/mol (95% CI 0.11–0.17) per month was observed during January 2019 – March 2020 (Table 3, Figure 2D). An immediate additional increase of 2.04 mmol/mol (0.80 to 3.29) was seen in April 2020 after the lockdown becoming into effect in March. During the lagged lockdown in April–June 2020, trend of average HbA1c changed from upward direction to downward direction (trend change −1.45 mmol/mol [95% CI −2.15 to −0.75] when compared with the trend before the lockdown). At the end of the lockdown in July 2020, an immediate increase of 0.61 mmol/mol (95% CI 0.06 to 1.16) in average HbA1c was observed. Thereafter, the downward trend in HbA1c level remained (change in trend 1.23 mmol/mol [95% CI 0.53–1.93] when compared with the trend during the lockdown).

In subgroup analyses by age, similar results as for the total population were seen among >70-year-old T2D patients (Table 3, Figure 2E). In younger patients ≤70 years old, no immediate effect of the lockdown was detected and the increasing trend in average HbA1c in January 2019 – March 2020 changed to slightly decreasing trend (−0.08 mmol/mol per month) in April 2020. When stratified by treatment balance before the lockdown, additional level change was observed also patients with HbA1c <53 mmol/mol before the lockdown but not among patients with poor treatment balance (Table 3, Figure 2F).

Discussion

Reductions in LDL testing of CHD and HbA1c testing of T2D patients were observed during the national lockdown related to the COVID-19 pandemic in Finland. Among T2D patients, an increase in monthly mean HbA1c values was observed immediately after the start of the lockdown but, after all, there was a downward trend during the lockdown. On the contrary, no effects of the

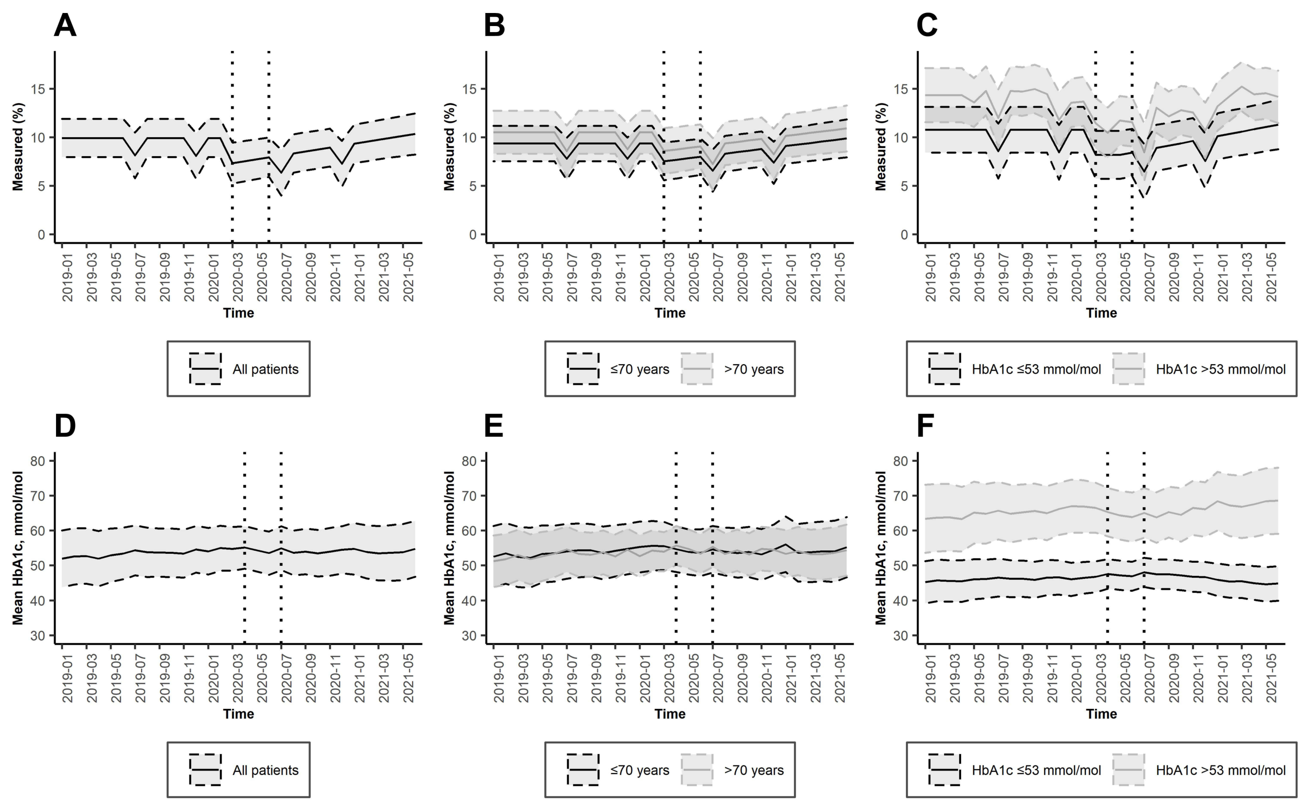

Figure 2 (**A**) Estimated monthly proportions (95% confidence interval) of monitored T2D patients. (**B**) Estimated monthly proportions (95% confidence interval) of monitored T2D patients by age group. (**C**) Estimated monthly proportions (95% confidence interval) of monitored T2D patients by HbA1c level before the lockdown. (**D**) Estimated monthly mean HbA1c values (95% confidence interval) among all T2D patients. (**E**) Estimated monthly mean HbA1c values (95% confidence interval) among all T2D patients stratified by age group. (**F**) Estimated monthly mean HbA1c values (95% confidence interval) among all T2D patients stratified by HbA1c level before the lockdown.

lockdown were seen in monthly mean LDL levels among CHD patients that had downward trend throughout the follow-up. However, an improvement in LDL values was detected among patients with LDL ≥1.8 mmol/l at the time of the lockdown in April–June 2020.

Both CHD and T2D are noncommunicable diseases that decrease the quality of life and cause chronic disabilities and mortality. CHD is the leading cause of death worldwide accounting for 16% of all deaths.[12] It affects around 126 million individuals with almost 11 million new cases occurring every year whereas an estimated 537 million people suffer from T2D worldwide.[13,14] Observed reductions in both LDL and HbA1c testing during the lockdown are alarming and similar results have been reported in previous studies for T2D.[15,16] Especially in T2D, in which treatment decisions are based almost only on HbA1c, postponed intensifications in medication may have effect on later complication risks that are also costly to care. However, the observed reduction of 19% in the number of T2D patients measured during Jan–June 2020 when compared with the same time-period in 2019 was temporary as the frequency of measurements recovered to the pre-COVID-19 level in 2021. Among CHD patients, the reduction in the number of patients measured was 44% in Jan–June 2020 compared with the same period in 2019 but the monthly proportion of monitored had a declining trend throughout the follow-up. This may partly be explained by a general decline in monitoring after the acute phase and partly by lost contacts to the service system because of the lockdown. The effect of the lockdown was seen as an additional 2.9%-units decrease in the proportion of monitored CHD patients. Generally, North Karelia region had lower incidence of COVID-19 cases and less severe pandemic situation than on average in Finland.[3] Therefore, reductions in LDL and HbA1c testing may be even higher in Finland as a whole.

Improvement in LDL values was observed at the time of the lockdown among CHD patients with LDL ≥1.8 mmol/l. To our knowledge, the current study is the first to examine the effect of the lockdown stratified by the LDL level at the time of the lockdown. The observed effect may be explained by the profile of patients who were monitored during the lockdown. It may be that patients with the lowest LDL values among patients with poor treatment balance had their values measured during the lockdown. Those patients may be more motivated to treat their LDL values than those with very poor LDL values. However, it is also possible that the observed reduction is a true reduction in values caused by better self-care during the lockdown. On the contrary to our results, a Spanish study reported LDL to have worsened among both ischemic heart disease and cerebrovascular accident patients as well as among patients with high cardiovascular risk during March and April 2020 compared with 2019.[17] Similarly, another Spanish study reported worsening of cardiovascular risk factors, including increased LDL and glucose levels, due to the lockdown among 6236 healthy adults.[18] However, in a meta-analysis of 4 studies, lipid levels showed tendencies of lowering during a lockdown, but the result was not consistent against sensitivity analysis of leaving out one study.[19] In Finland, patients may have better preconditions for self-care than elsewhere but also patients with better treatment balance may have been selected for treatment monitoring during the lockdown. In addition, the difference may be explained be a more intense lockdown in Spain than in Finland, for example, regarding curfew.

There is contradicting evidence on the effects of a lockdown on treatment balance among T2D patients. In a systematic review on 8 studies, worsening of HbA1c levels was observed in half of the studies, no change in 2 studies and modest improvement in 2 studies.[20] In a meta-analysis, lockdown was shown to increase HbA1c levels.[19] We observed an immediate increase in average HbA1c level by 2.0 mmol/mol (95% CI 0.8 to 3.3) in April 2020 after the start of the lockdown, but as stated with the LDL, that may be due to different population having their values measured, not the effect of the lockdown as such. To note, increases in HbA1c are associated with increases in the risk of microvascular and macrovascular complications.[21–23]

Further, the effects of the lockdown seem to vary by the treatment balance of a T2D patient at the time of a lockdown. A Dutch study observed HbA1c values to increase significantly in patients with low pre-lockdown values (5.4%–7.2%), remain at the same level in patients with moderate pre-lockdown values (7.2%–8.1%) and even decrease in patients with high pre-lockdown values (8.2%–12.7%).[24] Also, in a Korean study, HbA1c was observed to increase most in patients with good treatment balance (HbA1c <7.0%) and in patients <50 years.[25] In our study, the change in HbA1c level was observed only among patients with good treatment balance (≤53 mmol/mol or <7.0%) before the lockdown, but not among those with poor treatment balance (>53 mmol/mol). However, also an immediate decrease in the proportions of patients monitored was observed at the same time. This may suggest that patients with borderline optimal blood glucose values were more often screened during the lockdown than patients with clearly optimal or suboptimal values.

Previous studies have detected changes in nutritional habits and reductions in physical activity during the lockdown.[26–28] Furthermore, weight gain in obese persons during the lockdown has been reported.[29] These factors are also possible explanations for the observed changes in HbA1c together with inabilities to visit hospitals and pharmacies during the pandemic. However, these factors should also affect LDL levels but no remarkable changes during the lockdown were observed in LDL.

Our study has some strengths and limitations. A strength of our study is the inclusion of all patients from the area as identified from the EHRs. The area-specific recommendations for the COVID-19 pandemic and the lockdown were uniform for all inhabitants of the North Karelia region. As a limitation, we restricted this study to those patients who were alive on 30 June 2021 meaning that the most comorbid patients during the lockdown may be missing as they had died. They may have had greater effects of the lockdown on treatment balance.

Conclusion

In conclusion, effects of the national lockdown due to the COVID-19 pandemic were seen as temporary reductions in HbA1c testing and more permanent reductions in LDL testing. Monthly average LDL levels stayed stable in CHD patients during the follow-up but worsening in HbA1c was observed at the time of the lockdown. Observed effects may be explained by changes in self-monitoring of risk factors or selection of patients who had their values monitored. Future studies on long-term effects of the observed changes during the lockdown are needed.

Abbreviations

CHD, coronary heart disease; EHR, electronic health register; HbA1c, hemoglobin A1c; IFCC, International Federation of Clinical Chemistry; ITS, interrupted time-series; LD, lockdown; LDL, low-density lipoprotein cholesterol; T2D, type 2 diabetes; TB, treatment balance; TINIA, turbidimetric inhibition immunoassay method.

Data Sharing Statement

Access to data is regulated by the European Union and Finnish laws and therefore, sharing of sensitive data is not possible and data are not publicly available. An anonymized version of the data is available for researchers who meet the criteria as required by the European Union and Finnish laws for access to confidential data with a data permit of an appropriate authority. Contact information: aineistoneuvonta@siunsote.fi for data requests from the Siun sote – Joint municipal authority for North Karelia social and health services.

Ethics Approval and Informed Consent

Use of the data was approved by the Ethics Committee of the Northern Savonia Hospital District (diary number 81/2012). The study protocol was also approved by the register administrator, the Siun sote. Only register-based data were utilized and thus, consent from the patients was not needed.

Consent for Publication

All authors confirm that the details of any images, etc. can be published, and that the persons providing consent have been shown the article contents to be published.

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Disclosure

JM is a founding partner of ESiOR Oy and a board member of Siltana Oy. These companies were not involved in carrying out this research. PL, M-LL, TR, LI, and TL declare no conflicts of interest.

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