Impact of COVID-19 and Associated Preventive Measures on Cardiometabolic Risk Factors in South Korea: An Observational Study

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Abstract

Background: During the COVID-19 pandemic, people have been required to follow preventive measures such as social distancing or staying at home, which can lead to an unhealthy lifestyle. We investigated the effect of these preventive measures on metabolic parameters in individuals with cardiometabolic risk factors.

Methods: Using data for patients who visited a tertiary hospital in South Korea at least twice a year for the past 4 years, changes in clinical and biochemical data from the COVID-19 pandemic (2019−2020) were compared with changes in the same data at the same annual time points during the three previous seasons of 2016−2019.

Results: Among 7,094 patients, data for 1,485 were included. Systolic blood pressure increased by 2.6 ± 18.2 mmHg in the COVID-19 pandemic period compared with the 2018−2019, 2017−2018, and 2016−2017 seasons: −1.4 ± 16.5 mmHg, −2.8 ± 14.3 mmHg, and −0.7 ± 14.3 mmHg, respectively; all p < 0.05. The body mass index increased by 0.09 ± 1.16 kg/m^2 in the 2019−2020 pandemic season whereas it changed by −0.39 ± 3.03 kg/m^2 in 2018−2019 and by −0.34 ± 2.18 kg/m^2 in 2017−2018 (both p <0.05). Total cholesterol, triglycerides, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol levels worsened in the pandemic season compared with the previous three. Fasting glucose and glycated hemoglobin levels also showed increasing tendencies during the pandemic, but without significance. During the COVID-19 pandemic, the number of patients whose metabolic syndrome worsened increased significantly by 21% compared with the 2018−2019 season. The 10-year coronary heart disease risk calculated using the Framingham risk score also increased significantly.

Conclusions: Comorbidity and mortality arising from cardiometabolic disorders as collateral damage during COVID-19 infections and preventive procedures could have major impacts on human health in the future. Nationwide strategies to reverse the aggravation of cardiometabolic health during a pandemic should be implemented in countries attempting to cope with it.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), and 65,899,432 confirmed cases of COVID-19 have been reported, including 1,518,668 deaths, as of December 5, 2020 [1]. SARS-CoV-2 induces mild symptoms in the initial stage but has the potential to result in severe illness, including a systemic inflammatory response syndrome, acute respiratory distress syndrome, multiorgan involvement, and shock [2].The fatality-to-infection ratio for COVID-19 has been estimated to be 0.5−3.7% [3, 4].

In South Korea, the COVID-19 pandemic broke out on February 22, 2020 (Fig. 1a), and the government raised the crisis alert level to "severe," the highest, for the second time, which was first actioned during the influenza outbreak in 2009 (Fig. 1b) [5]. The infectious disease prevention and control measures included shutting down public facilities such as libraries and sports centers, and suspending school attendance. The public was requested to stay home, refrain from going outside, and avoid crowded environments at work [6]. Thus, public movement decreased by 38.1% during the early period of the COVID-19 outbreak compared with before the outbreak [7]. Thanks to these preventive measures and cooperation from the general public, the number of daily new domestic infections in South Korea fell dramatically [8]. People have become accustomed to distancing themselves by acknowledging its importance, which has been reflected in the increase in online shopping [9]. The daily number of new COVID-19 cases in South Korea has dropped to fewer than 100 up to the end of October, but unfortunately, it has rebounded to over 500 recently [8]. This might have been because the Korean government eased the quarantine level: people could get together and became less rigorous in following preventive principles. The Korean government has now raised the crisis alert level, which means stricter observation of social distancing, and a ban on staying not only in public places but also in indoor health facilities, cafés, bars, and any places that people can get together, and is now prohibiting large-scale gatherings again (see http://ncov.mohw.go.kr/en).

As we recently reviewed [10], old age, diabetes mellitus (DM), cardiovascular disease (CVD), hypertension, and obesity are determining factors for fatal outcomes of COVID-19. People with coronary heart disease (CHD) or DM had a higher chance of being admitted to intensive care units, needing mechanical ventilation, or of dying [11, 12]. According to a case-control study in South Korea (7,341 COVID-19 cases among 219,961 patients), DM, hypertension, and chronic renal failure including end-stage renal disease were associated with increased disease severity in [13].

Because elevated glucose levels directly promote SARS-CoV-2 replication, which essentially requires glycolysis in the host [14], patients with uncontrolled DM are expected to experience a more rapid progression of COVID-19. A recent study reported that increased glucose concentrations significantly predicted mortality in those with COVID-19, regardless of the presence of DM [15]. Conversely, inactivity associated with social and physical distancing for COVID-19 might impair metabolic control. Thus, the COVID-19 pandemic is likely to have a negative influence on public lifestyle and behaviors [16], which could adversely affect cardiometabolic health [17, 18]. So far, the exact

effects of COVID-19 prevention and control measures including social distancing, movement restriction, and limitations of gathering on the impact of such chronic diseases have not yet been evaluated. Here, we hypothesized that the COVID-19 pandemic and associated unhealthy lifestyles have produced negative influences on metabolic parameters in individuals with cardiometabolic risk factors.

Methods

Study design and population

This was a single-center, retrospective, observational cohort study conducted at Seoul National University Bundang Hospital (SNUBH) in South Korea. The study was approved by our independent Ethics Committee/Institutional Review Board (SNUBH: B-2008/630 – 102).

The study population was adults aged over 19 years with diagnosed cardiometabolic risk factors including impaired glucose metabolism, hypertension, dyslipidemia, or obesity who visited the outpatients' clinic at the Department of Endocrinology and Metabolism at SNUBH. Patients who visited from September 1, 2016 to May 31, 2020 at least twice a year, before and after February, the time of South Korea's COVID-19 outbreak, were further selected. In all, 7,094 patients were identified to have International Classification of Diseases Tenth Edition (ICD-10) diagnostic codes of E10–14 for DM, I10 and I15 for hypertension, E78 for dyslipidemia, and E66 for obesity using the hospital database, clinical data warehouse (CDW) [19].

Patients who were hospitalized for a major illness or major surgery, and who received dialysis during the study period were excluded (Fig. 2). Major surgery was defined as surgery performed for neoplasms, severe diseases in the circulatory or digestive systems, and injuries determined by ICD-10 codes starting with C, D, I, K, and S. The number of patients hospitalized in the endocrinology unit did not differ between years, but they were excluded from the study analysis because hospitalization for intensive glucose-lowering therapy might have hindered identifying the impact of pandemic preventive measures.

Collection of clinical parameters

The Korean government reinforced the national public health emergency response by emphasizing the need to maintain social distance on February 29, 2020. Therefore, we divided the clinical data according to the date of examination: (i) from September 2019 to November 2019 ("fall"); (ii) from December 2019 to February 2020 ("winter"), and (iii) from March 2020 to May ("spring"), and compared the clinical parameters in each season with those of the previous years (2016–2017, 2017–2018, and 2018–2019; Fig. 1c).

Patients' outpatient care information, admission information, clinical laboratory values, anthropometric measurements, and prescription information were retrieved from the CDW. Body weight, body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP, respectively), and metabolic profiles such as the levels of fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), total cholesterol, triglyceride (TG), high-density lipoprotein-cholesterol (HDL-c), and low-density lipoprotein-cholesterol (LDL-c) in each season were analyzed as means for each individual. Data cleaning was performed for manually inputted anthropometrics into the system at the time of care. Thus, obviously inaccurate values, recorded as ranges or as typographic errors, physically impossible values such as height > 300 cm and DBP > SBP, were discarded. Height was converted to a 4-year mean measure for each patient. Then, the BMI was recalculated as mass (in kilograms) divided by height (in meters) squared. The use of medications for DM, hypertension, and dyslipidemia was also investigated.

Anthropometric and biochemical parameters

Anthropometric and biochemical parameters were measured in SNUBH as reported previously [20]. Height and body weight were measured using standard methods with the subjects in light clothing. The FPG concentration was measured using the glucose oxidase method (747 Clinical Chemistry Analyzer; Hitachi, Tokyo, Japan). HbA1c levels were measured using a Bio-Rad Variant II Turbo High-Performance Liquid Chromatography Analyzer (Bio-Rad, Hercules, CA, USA) in a National Glycohemoglobin Standardization Program level II certified laboratory. Total cholesterol, TG, HDL-c, and LDL-c levels were measured using a 747 Clinical Chemistry Analyzer (Hitachi).

Metabolic syndrome was defined using modified Adult Treatment Panel III criteria [21]. Because the waist circumference data were limited, the BMI was used instead as suggested by the World Health Organization [22]; metabolic syndrome was diagnosed as the existence of at least three abnormal components of: (i) BMI ≥ 23 kg/m^2 and/or taking anti-obesity agents; (ii) SBP ≥ 130 mmHg, DBP ≥ 85 mmHg, and/or taking antihypertensive agents; (iii) TG ≥ 150 mg/dL and/or taking lipid-lowering agents; (iv) HDL-c ≤ 40 mg/dL in men and HDL-c ≤ 50 mg/dL in women, and (v) FPG ≥ 100 mg/dL and/or taking antidiabetic agents. Patients with HbA1c $\geq 6.5\%$ and/or taking antidiabetic agents were classified according to the state of DM treatment.

The 10-year CHD risk was calculated using the Framingham risk score (FRS) [23]. The correlation of calculated CHD risk with actual 10-year CHD was shown to be stronger when using total cholesterol levels than when using LDL-c scoring in Korean subjects [24]. Therefore, the FRS with total cholesterol scoring was used here.

Statistical analysis

Continuous variables are summarized as the mean ± standard deviation (SD) and categorical variables are shown as the numbers and percentages of subjects. Normality of data distribution was evaluated using the Shapiro−Wilk test and by histograms [25], which showed all variables to be normally distributed with bell-shaped symmetric graphs. Student's t tests for continuous variables and chi-squared tests for categorical variables were used for comparisons. The changes of values from winter 2019 to spring 2020 (2019−2020 season) were compared with that of previous seasons, 2018−2019, 2017−2018, and 2016−2017 seasons, using paired Student's t tests. Because the patient follow-up period was up to 6 months, not all the patients had complete seasonal data. To reduce the bias of visiting patient's characteristics, the dataset was imputed using multiple imputation by chained equations for the missing values from patients who did not have complete test results [26]. The imputed data were used to analyze changes in values. Relative risk (RR) was calculated as the number of patients who showed worse metabolic syndrome components in the 2019−2020 season than those in the 2018−2019 season, expressed as RR with a 95% confidence interval (CI). Statistical significance was considered at a two-sided p value < 0.05. All analyses were performed using R software version 4.0.2 (R Development Core Team, Vienna, Austria) and RStudio version 1.3.1056 (RStudio, Inc., Boston, MA, USA).

Results

Patient characteristics

A total of 1,485 patients were included in this study, with a mean age of 61.8 ± 11.7 years in September 2016. The proportions of men and women were almost equal among the study participants. All of them had at least one chronic cardiometabolic impairment such as DM, hypertension, dyslipidemia, or obesity at baseline (Table 1). The number of comorbid diseases tended to increase with time. The total use of antidiabetic agents increased in 2019 compared with 2016. The total use of antiobesity agents increased in 2019−2020 compared with the previous 3 years. The usage of recently approved antidiabetic drugs, sodium−glucose co-transporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs), increased in 2019−2020.

Table 1
Patients' characteristics

	Winter 2016	Winter 2017	Winter 2018	Winter 2019
Comorbid status				
Diabetes mellitus	1348 (90.8%)	1348 (90.8%)	1348 (90.8%)	1350 (90.9%)
Hypertension	814 (54.8%)	834 (56.2%)	840 (56.6%)	849 (57.2%)
Dyslipidemia	1162 (78.2%)	1158 (78.0%)	1163 (78.3%)	1169 (78.7%)
Obesity	50 (3.4%)	49 (3.3%)	51 (3.4%)	60 (4.0%)
Concomitant medications				
Antidiabetic agents, n (%)	1159 (78.0%)	1181 (79.5%)	1207 (81.3%)	1212 (81.6%)[a]
Insulin, n (%)	190 (12.8%)	192 (12.9%)	188 (12.7%)	218 (14.7%)
Metformin, n (%)	1087 (73.2%)	1100 (74.1%)	1123 (75.6%)	1113 (74.9%)
DPP4 inhibitors, n (%)	590 (39.7%)	570 (38.4%)	561 (37.8%)	557 (37.5%)
SGLT2 inhibitors, n (%)	79 (5.3%)	102 (6.9%)	174 (11.7%)	209 (14.1%)[a,b]
Sulfonylureas, n (%)	485 (32.7%)	511 (34.4%)	519 (34.9%)	520 (35.0%)
Thiazolidinediones, n (%)	92 (6.2%)	84 (5.7%)	73 (4.9%)	68 (4.6%)
α-glucosidase inhibitors, n (%)	6 (0.4%)	5 (0.3%)	5 (0.3%)	4 (0.3%)
GLP-1 RAs, n (%)	4 (0.3%)	6 (0.4%)	14 (0.9%)	14 (0.9%)[a]
Antihypertensive agents, n (%)	726 (48.9%)	753 (50.7%)	763 (51.4%)	767 (51.6%)
ACE inhibitors, n (%)	65 (4.4%)	64 (4.3%)	64 (4.3%)	58 (3.9%)
ARBs, n (%)	554 (37.3%)	556 (37.4%)	570 (38.4%)	580 (39.1%)
CCB, n (%)	398 (26.8%)	421 (28.4%)	429 (28.9%)	431 (29.0%)
Diuretics, n (%)	92 (6.2%)	101 (6.8%)	103 (6.9%)	109 (7.3%)
β-blockers, n (%)	90 (6.1%)	108 (7.3%)	108 (7.3%)	96 (6.5%)
Lipid-lowering agents, n (%)	887 (59.7%)	888 (59.8%)	891 (60.0%)	907 (61.1%)
Statins, n (%)	878 (59.1%)	877 (59.1%)	880 (59.3%)	893 (60.1%)
Ezetimibe, n (%)	160 (10.8%)	171 (11.5%)	186 (12.5%)	182 (12.3%)
PCSK9 inhibitors, n (%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Fibrates, n (%)	36 (2.4%)	57 (3.8%)	28 (1.9%)	33 (2.2%)[b]
Cholestyramine resin, n (%)	1 (0.1%)	0 (0%)	1 (0.1%)	1 (0.1%)
Nicotinic acid, n (%)	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)
Omega 3 fatty acid, n (%)	15 (1.0%)	12 (0.8%)	15 (1.0%)	21 (1.4%)
Anti-obesity agents, n (%)	1 (0.1%)	2 (0.1%)	7 (0.5%)	41 (2.8%)[a,b,c]
Liraglutide 3 mg, n (%)	0 (0%)	0 (0%)	7 (0.5%)	40 (2.7%)[a,b,c]
Orlistat, n (%)	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)
Phentermine/Topiramate, n (%)	0 (0%)	1 (0.1%)	0 (0%)	0 (0%)
Naltrexone/Bupropion, n (%)	0 (0%)	1 (0.1%)	0 (0%)	1 (0.1%)

	Winter 2016	Winter 2017	Winter 2018	Winter 2019

Key: DPP4, dipeptidyl peptidase-4; SGLT2, sodium−glucose co-transporter 2; GLP-1 RA, glucagon-like peptide-1 receptor agonist; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; PCSK9, proprotein convertase subtilisin/kexin type 9

[a]$p < 0.05$ compared with the fall and winter of 2016; [b]$p < 0.05$ compared with the fall and winter of 2017; [c]$p < 0.05$ compared with the fall and winter of 2018

Table 2
Changes of metabolic syndrome components before (winter) and during (spring) the South Korea COVID-19 pandemic

Variables	Winter 2016	Spring 2017	2016-2017 changes	Winter 2017	Spring 2018	2017–2018 changes	Winter 2018	Spring 2019	2018–2019 changes	Winter 2019	Spring 2020	2019–2020 changes
Bwt, kg	66.91 ± 12.26	66.83 ± 12.21	-0.07 ± 5.12	67.47 ± 11.39	66.58 ± 12.16	-0.89 ± 5.94	67.22 ± 12.67	66.18 ± 11.69	-1.04 ± 7.75	65.76 ± 11.70	65.97 ± 12.02	0.21 ± 3.05[b,c]
BMI, kg/m^2	25.22 ± 3.25	25.2 ± 3.28	-0.02 ± 1.98	25.44 ± 2.96	25.1 ± 3.24	-0.34 ± 2.18	25.34 ± 3.57	24.95 ± 3.11	-0.39 ± 3.03	24.78 ± 3.06	24.87 ± 3.22	0.09 ± 1.16[b,c]
SBP, mm Hg	133.0 ± 14.7	132.3 ± 14.9	-0.7 ± 14.3	134.3 ± 14.1	131.5 ± 14.5	-2.8 ± 14.3	135.4 ± 15.1	133.9 ± 16.3	-1.4 ± 16.5	136.3 ± 15.6	138.9 ± 18.3	2.6 ± 18.2[a,b,c]
DBP, mm Hg	77.6 ± 10.6	76.5 ± 10.4	-1.2 ± 10.5	77.8 ± 9.8	75.2 ± 10.2	-2.6 ± 9.6	76.8 ± 11.0	75.0 ± 11.9	-1.7 ± 11.8	76.5 ± 11.8	76.1 ± 12.5	-0.4 ± 11.9[b,c]
FPG, mg/dL	140.1 ± 40.9	139.4 ± 38.9	-0.7 ± 36.8	143.3 ± 41.6	139.8 ± 39.5	-3.5 ± 37.4	141.6 ± 42.8	141.3 ± 41.9	-0.3 ± 41.6	138.8 ± 37.8	136.5 ± 40.3	-2.3 ± 36.2
HbA1c, %	7.16 ± 1.26	7.12 ± 1.22	-0.04 ± 0.82	7.17 ± 1.17	7.19 ± 1.24	0.03 ± 0.79	7.18 ± 1.18	7.23 ± 1.17	0.05 ± 0.78	7.12 ± 1.23	7.19 ± 1.25	0.07 ± 0.93[a]
TC, mg/dL	165.9 ± 36.2	164.8 ± 35.4	-1.1 ± 25.9	166.7 ± 37.6	166.5 ± 36.4	-0.2 ± 30.4	163.3 ± 35.4	162.1 ± 35.7	-1.2 ± 29.4	161.9 ± 37.8	166.1 ± 37.8	4.1 ± 33.2[a,b,c]
TG, mg/dL	148.2 ± 86.0	141.0 ± 94.9	-7.1 ± 80.8	147.6 ± 96.1	140.5 ± 90.4	-7.1 ± 76.3	139.0 ± 79.3	140.5 ± 91.9	1.5 ± 72.6	137.8 ± 91.9	142.6 ± 83.3	4.8 ± 69.4[a,b]
HDL-c, mg/dL	50.4 ± 10.7	50.1 ± 10.6	-0.3 ± 6.9	51.1 ± 11.4	49.7 ± 12.3	-1.4 ± 6.7	49.6 ± 11.7	50.8 ± 12.5	1.2 ± 7.4	52.2 ± 12.8	51.6 ± 13.0	-0.6 ± 7.9[b,c]
LDL-c, mg/dL	90.8 ± 26.0	89.7 ± 25.0	-1.1 ± 18.7	90.7 ± 27.0	98.1 ± 26.5	7.4 ± 21.6	96.9 ± 25.6	96.8 ± 26.2	-0.1 ± 20.9	96.1 ± 27.0	99.4 ± 27.5	3.4 ± 24.1[a,b,c]

Data presented as mean ± standard deviation, Key: Bwt, body weight; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol

[a]$p < 0.05$; compared with changes in 2016−2017; [b]$p < 0.05$ compared with changes in 2017−2018; [c]$p < 0.05$ compared with changes in 2018−2019.

Changes in cardiometabolic risk factors during the COVID-19 pandemic

The raw values of cardiometabolic risk components before and during social distancing are shown in Fig. 3. The body weight, BMI, SBP, and DBP values were higher in the spring of 2020 compared with the springs of other years. The increase in HbA1c levels was most prominent in the final seasons, from 7.27 ± 1.24% in the winter of 2019 to 7.33 ± 1.25% in the spring of 2020 (2019−2020 season) compared with other seasons. Differences in the levels of other factors—FPG, triglycerides, and HDL-c—were similar across all four years. The differences in cardiometabolic risk factors are shown in Table 2. The SBP and total cholesterol measures increased significantly during the COVID-19 pandemic when compared with the past three years. Increases in body weight and BMI were statistically significant in the 2019−2020 season when compared with those in the 2017−2018 and 2018−2019 seasons.

Risk of developing metabolic syndrome during the COVID-19 pandemic

During the COVID-19 pandemic, patients who worsened in terms of metabolic syndrome increased: 375 (25.3%) in 2019−2020 vs 309 (20.8%) in 2018−2019; RR 1.21, 95% CI 1.06−1.39) (Fig. 4a). Patients aged under 65 years developed metabolic syndrome (167 [22.1%] vs

144 [19.0%]; RR 1.24, 95% CI 1.02−1.52) and the HDL component (150 [19.8%] vs 129 (17.0%); RR 1.25, 95% CI 1.01−1.54) (Fig. 4b). Male patients were affected more severely with respect to metabolic syndrome components by the COVID-19 pandemic than were female patients (Fig. 4c). Male patients worsened for metabolic syndrome (198 [26.2%] vs 144 [19.0%]; RR 1.38, 95% CI 1.14−1.66), for the BP component (205 [27.1%] vs 166 [21.9%]; RR 1.23, 95% CI 1.03−1.48), for the HDL component (171 [22.6%] vs 135 [17.8%]; RR 1.27, 95% CI 1.04−1.55), and for the HbA1c component (189 [25.0%] vs 146 [19.3%]; RR 1.29, 95% CI 1.07−1.57).

Changes in coronary heart disease risk during the COVID-19 pandemic

The changes in 10-year CHD risk by FRS are shown in Fig. 5. The 10-year CHD risk increased in the 2019−2020 season but not in the other three seasons: $1.0 \pm 6.2\%$ in 2019−2020 vs − $0.7 \pm 6.0\%$ in 2018−2019, − $0.2 \pm 5.3\%$ in 2017−2018, and − $0.2 \pm 5.4\%$ in 2016−2017, all $p < 0.05$. During the COVID-19 pandemic, the number of patients with 10-year CHD risk from low to intermediate during the COVID-19 pandemic significantly increased when compared with the past three years (176 vs 141 vs 86 vs 113, all $p < 0.05$).

Discussion

Here, we found that cardiometabolic risk factors deteriorated significantly in subjects with metabolic impairment in South Korea during the COVID-19 pandemic. In this critical 2019−2020 season, the proportion of subjects with metabolic syndrome increased significantly by 21% compared with the 2018−2019 season. The 10-year CHD risk also increased by $1.0 \pm 6.2\%$ compared with the past three years. We also found that not only the body weight or BMI but also blood pressures, lipid profiles, and HbA1c changed in an unfavorable direction during the COVID-19 pandemic.

Social distancing policy, to tackle COVID-19, naturally reduces people's physical activities. In many countries, trips to all major destinations except to personal residences dropped significantly by 50−80% in early March when COVID-19 was declared a pandemic (https://kojects.com/2020/06/01/mobility-korea-covid-19/). A recent self-reporting survey showed that people spent more time at home and actually gained weight during the COVID-19 pandemic [27]. It was reported that acutely reduced physical activities during the COVID-19 pandemic might help increase insulin resistance and gain fat mass [28]. Various public health interventions including staying at home, refraining from nonessential social activities, and school closures limit access to healthy food options [29]. Moreover, people are consuming home-delivered foods frequently, which are more obesogenic than homemade food [30]. The COVID-19 pandemic is also influencing mental health [31]. Scared of getting an infection or dying, many people are psychologically distressed, which might lead to systemic inflammation [18]. Stress stimulates elevations in blood pressure and blood glucose levels by releasing cortisol through the hypothalamic−pituitary−adrenal axis [32].

We found that the 10-year CHD risk of patients has increased during the COVID-19 pandemic in South Korea. Notably, patients aged over 65 years increased their 10-year CHD risk score the most ($1.2 \pm 7.1\%$) and this—potentially—could contribute to a high mortality rate from COVID-19 in the elderly. Body weight, blood pressure, and lipid levels decreased in spring before the COVID-19 pandemic, similar to the results from previous studies [33−35] However, these cardiometabolic risk parameters increased significantly in the same period in the pandemic season. This opposite trend might reflect the impact of the pandemic on cardiometabolic risk parameters in most of our patients.

Several mechanisms have been suggested to explain the causality of the COVID-19 pandemic and the increased risk of metabolic disorders and CVDs. The sympathetic system is activated with increased levels of catecholamines after catastrophic events, which influences the heart and blood vessels negatively [36]. In metabolic dysregulated status, the renin−angiotensin system is activated inappropriately, which also leads to increased production of angiotensinogen (up to 30% of circulating angiotensinogen) and to elevated plasma renin activity, which in turn contributes to increasing blood pressure and deteriorating glucose metabolism [37, 38]. Although the effects of this pandemic may not be seen in the short term, its long-term impacts on cardiometabolic risk cannot be ignored given the stressful socioeconomic conditions [17].

In this study, both males and patients under 65 years showed a significantly increased risk for metabolic syndrome during the COVID-19 pandemic. In general, middle-aged men are more involved in economic activity than women or elderly populations [39]. Based on this, current preventive measures might have a greater impact on physical activity in these subgroups. Such insufficient physical activity is likely to deteriorate cardiometabolic health eventually [40].

In this analysis, compared with other cardiometabolic parameters, there was no increase in the HbA1c levels during the COVID-19 pandemic. The results might be because of increased usage of potent novel antidiabetic agents such as SGLT2 inhibitors and GLP-1 RAs. Indeed, the

patients who started SGLT2 inhibitors after September 2019 showed reductions in HbA1c levels in the spring of 2020 (data not shown). Importantly, SGLT2 inhibitors should be avoided for severely ill patients because this agent can cause ketoacidosis and acute kidney injury [41]. The use of liraglutide also increased more than fivefold in the 2019–2020 season compared with previous seasons. Given that the beneficial roles of GLP-1 RAs for preventing cardiovascular and kidney diseases have been well established [42], these can be an ideal option for the treatment of patients with type 2 DM at such risk even during the COVID-19 pandemic [43].

During this pandemic, specific schemes are required to curtail a potential vicious cycle because patients with dysregulated metabolism have a worse prognosis when infected. Metabolic syndrome represents a state of chronic low-grade inflammation and the elevated release of cytokines in metabolic syndrome status is likely to provoke a "cytokine storm" in those individuals infected with SARS-CoV-2, which may lead to multiorgan failure [44, 45]. Considering the deterioration in cardiometabolic profiles during the COVID-19 pandemic, physicians should focus on patients with metabolic impairments to prevent future adverse cardiovascular events. Governments and medical institutions must promote physical activity, healthy eating, and mental health care during such pandemics. Social media or web-based programs can provide convenient tools to guide such patients to have healthy lifestyles. Active counseling to help people with metabolic dysregulation cope with barriers against healthier lifestyles would be helpful in this critical situation [46].

Our research had advantages in that we exclusively included regularly attending outpatients, who were followed up for four years to reduce bias. Because SNUBH is a tertiary hospital receiving patients from all over the country, our results might be representative of our population at large. Nonetheless, some limitations need to be mentioned. We did not investigate changes in physical activity or dietary habits. Moreover, it was not possible to observe the actual occurrence of CHD given the short observation period. Instead, we used the 10-year CHD risk estimated from the FRS, but this is a well-established tool that has been used widely for this purpose [23].

Conclusions

We found that the COVID-19 pandemic had a negative influence on cardiometabolic profiles in subjects with metabolic impairments. This might be because of decreased physical activity and unhealthy dietary patterns linked to preventive measures such as social distancing and lockdown [47]. According to the Community Mobility Reports released by Google (https://www.google.com/covid19/mobility/?hl = en-GB), the movement trends are decreasing in many countries during the COVID-19 pandemic. From this phenomenon, we can speculate that similar aggravation in cardiometabolic risks can be found in other countries struggling with the pandemic. At present, most patients who die from COVID-19 are in their 70 s or 80 s. Of note, it should be kept in mind that individuals with cardiometabolic risk factors are more vulnerable to SARS-CoV-2 infection and have a higher chance of morbidity and mortality compared with those without. This means that the COVID-19 pandemic will lead to more serious collateral health problems in not-very-old populations through increasing comorbidity and mortality induced by aggravations of cardiovascular and metabolic disorders. Encouraging home exercise and healthy homemade meals by public media to mitigate the impact on cardiometabolic risks is strongly recommended during this crisis.

Abbreviations

BMI: Body mass index; CDW: Clinical data warehouse; CHD: Coronary heart disease; CI: Confidence interval; COVID-19: Coronavirus disease 2019; CVD: Cardiovascular disease; DBP: Diastolic blood pressure; DM: Diabetes mellitus; FPG: Fasting plasma glucose; FRS: Framingham risk score; GLP-1 RAs: Glucagon-like peptide-1 receptor agonists; HbA1c: Glycated hemoglobin; HDL-c: High-density lipoprotein-cholesterol; ICD-10: International Classification of Diseases Tenth Edition; LDL-c: Low-density lipoprotein-cholesterol; RR: Relative risk; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SBP: Systolic blood pressure; SD: Standard deviation; SGLT2: Sodium–glucose co-transporter 2; SNUBH: Seoul National University Bundang Hospital; TG: Triglyceride

Declarations

Ethics approval and consent to participate

Approval for this study was provided by the independent Ethics Committee/Institutional Review Board of Seoul National University Bundang Hospital (SNUBH: B-2008/630-102). Need for consent was waived in this study.

Consent for publication

Not applicable.

Availability of data and materials

All datasets used and analyzed during this study are available from the corresponding author on reasonable request.

Competing interests

The authors of this manuscript have no conflicts of interest to declare.

Funding

None.

Authors' contributions

MS acquired and analyzed the data, and wrote the manuscript. BKK contributed to the study design and revised the manuscript for important intellectual content. SL directed the study design and wrote the manuscript. HIY, KHS, ESK, and HBK revised the manuscript for important intellectual content. All authors read and approved the final manuscript.
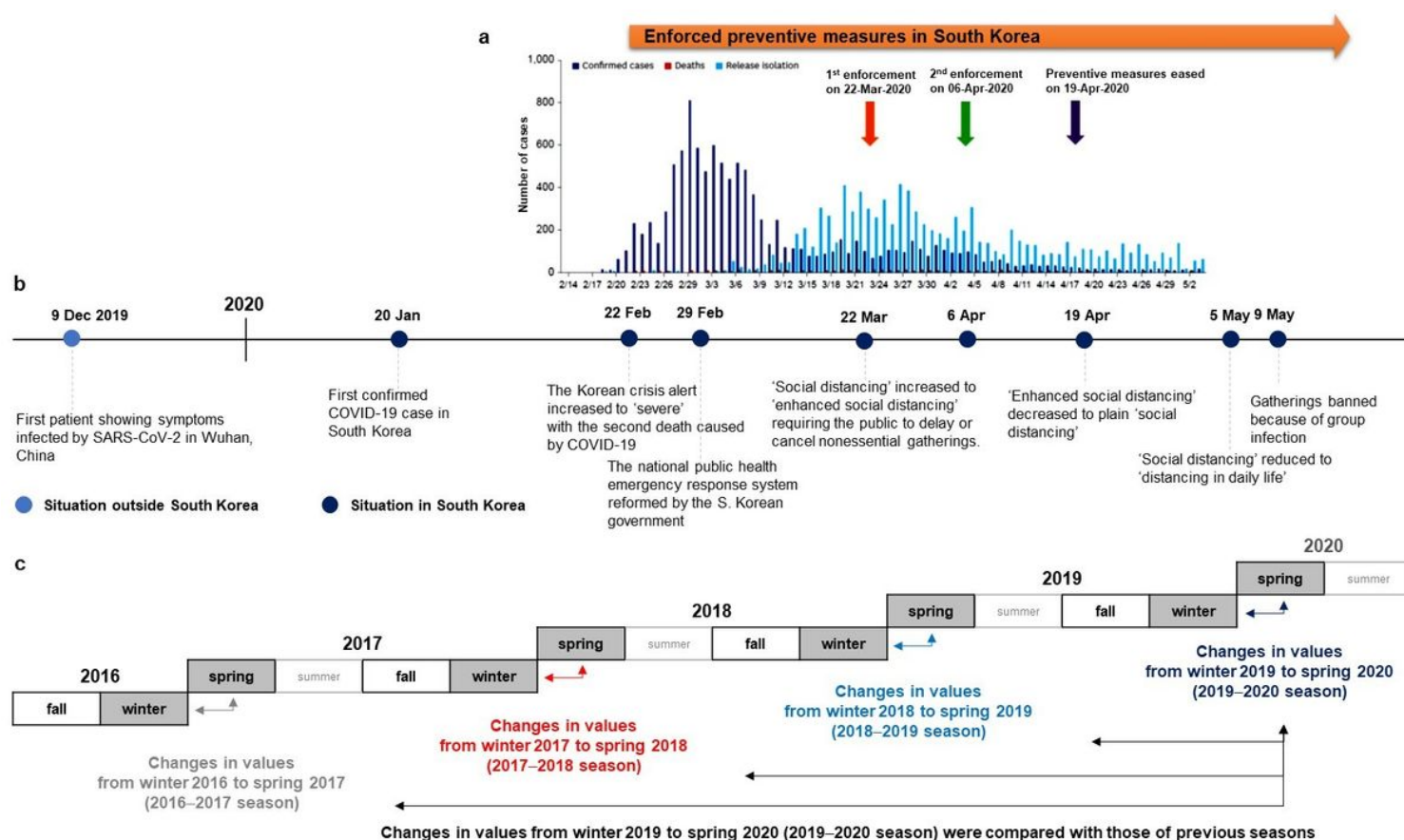
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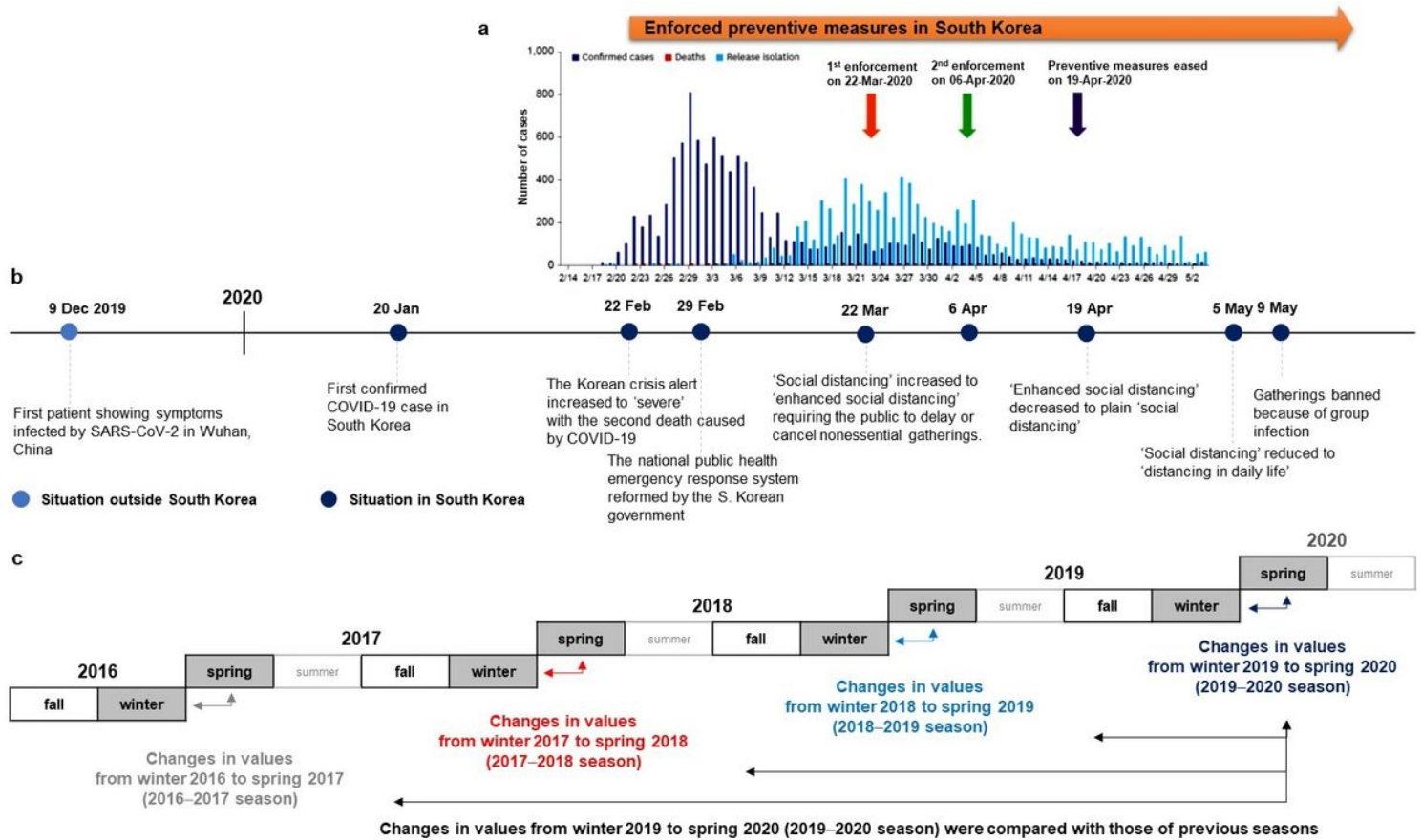
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Figures

Figure 1

Timeline of the South Korea COVID-19 outbreak and our research design reflecting it. a The effect of strengthening social distancing (from Korea Centers for Disease Control and Prevention, as of May 6, 2020). b The timeline of the COVID-19 pandemic in South Korea, c The research design to analyze the impact of preventive measures.

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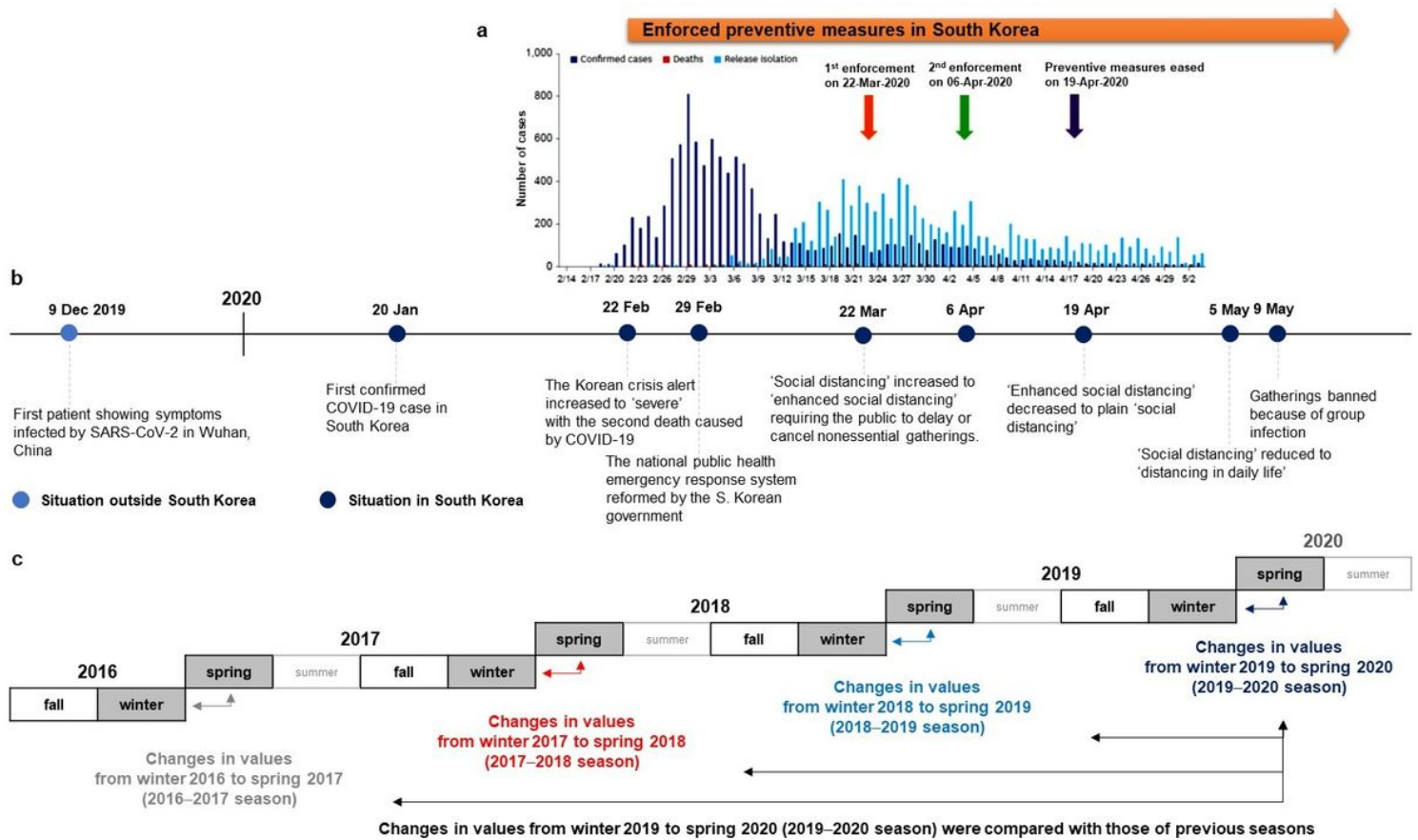
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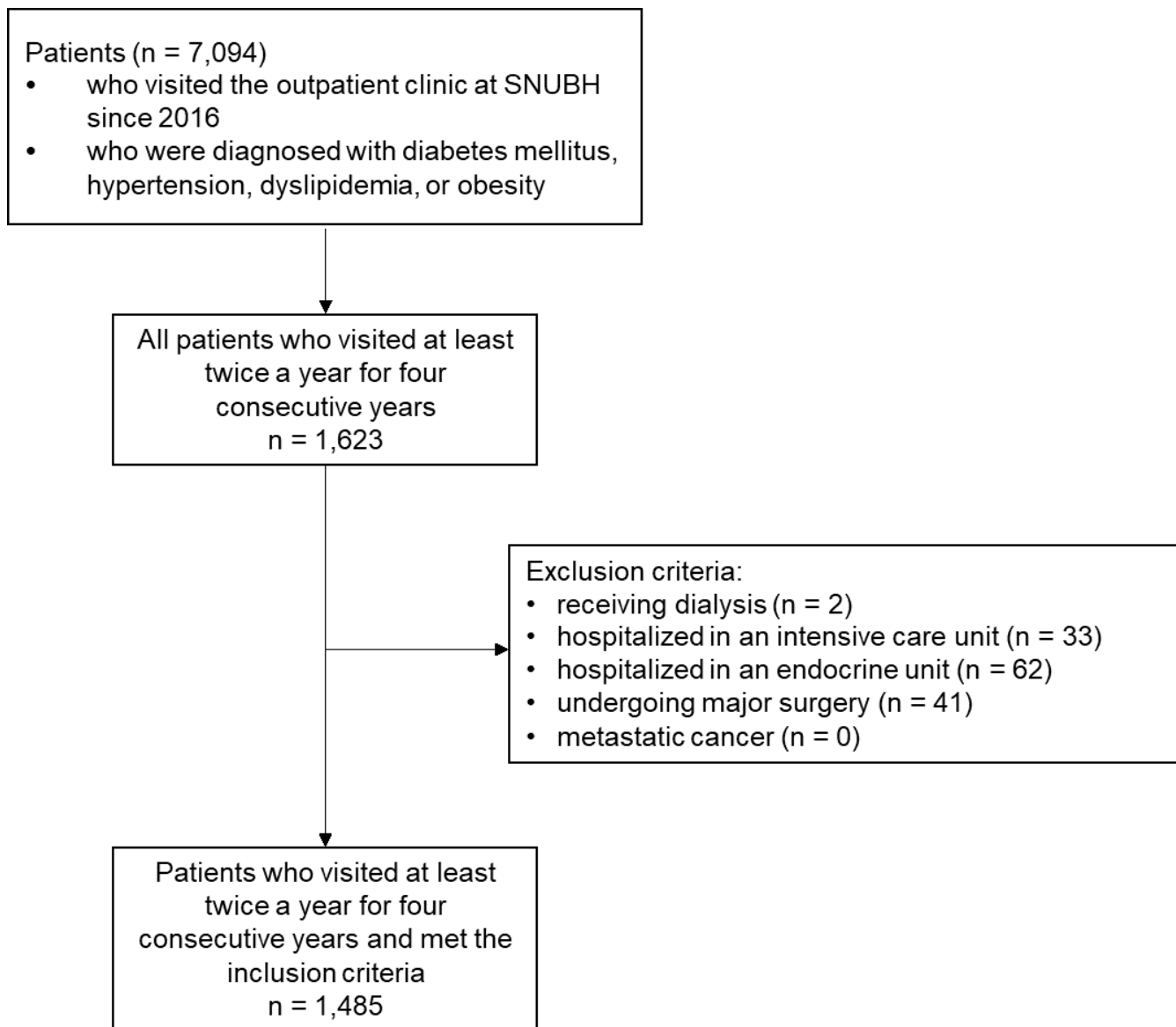
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Patients (n = 7,094)
•    who visited the outpatient clinic at SNUBH
     since 2016
•    who were diagnosed with diabetes mellitus,
     hypertension, dyslipidemia, or obesity
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All patients who visited at least
       twice a year for four
        consecutive years
           n = 1,623
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Exclusion criteria:
•   receiving dialysis (n = 2)
•   hospitalized in an intensive care unit (n = 33)
•   hospitalized in an endocrine unit (n = 62)
•   undergoing major surgery (n = 41)
•   metastatic cancer (n = 0)
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Patients who visited at least
     twice a year for four
consecutive years and met the
       inclusion criteria
          n = 1,485
```

Figure 2

Flow chart of study population selection

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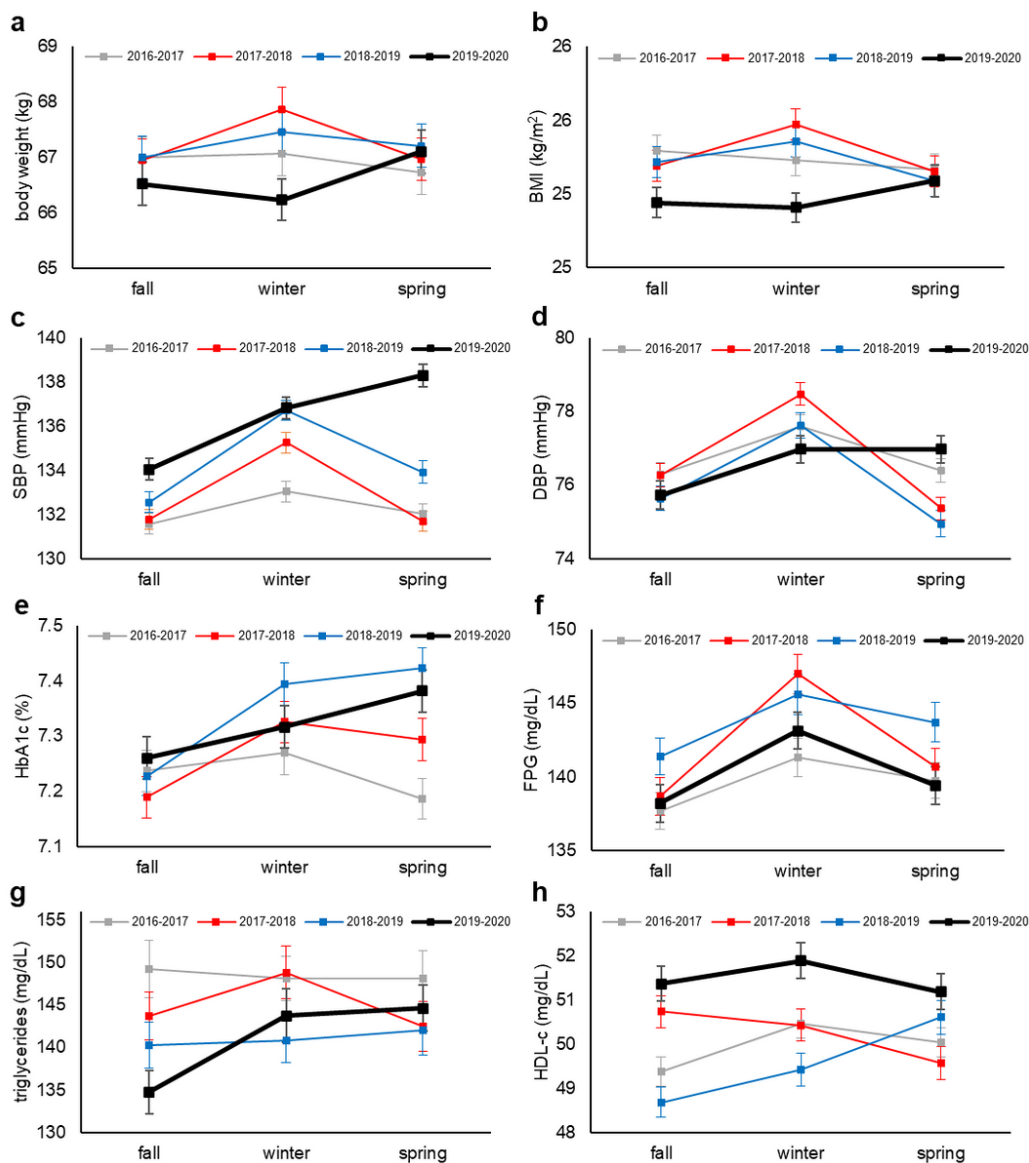n = 1,485

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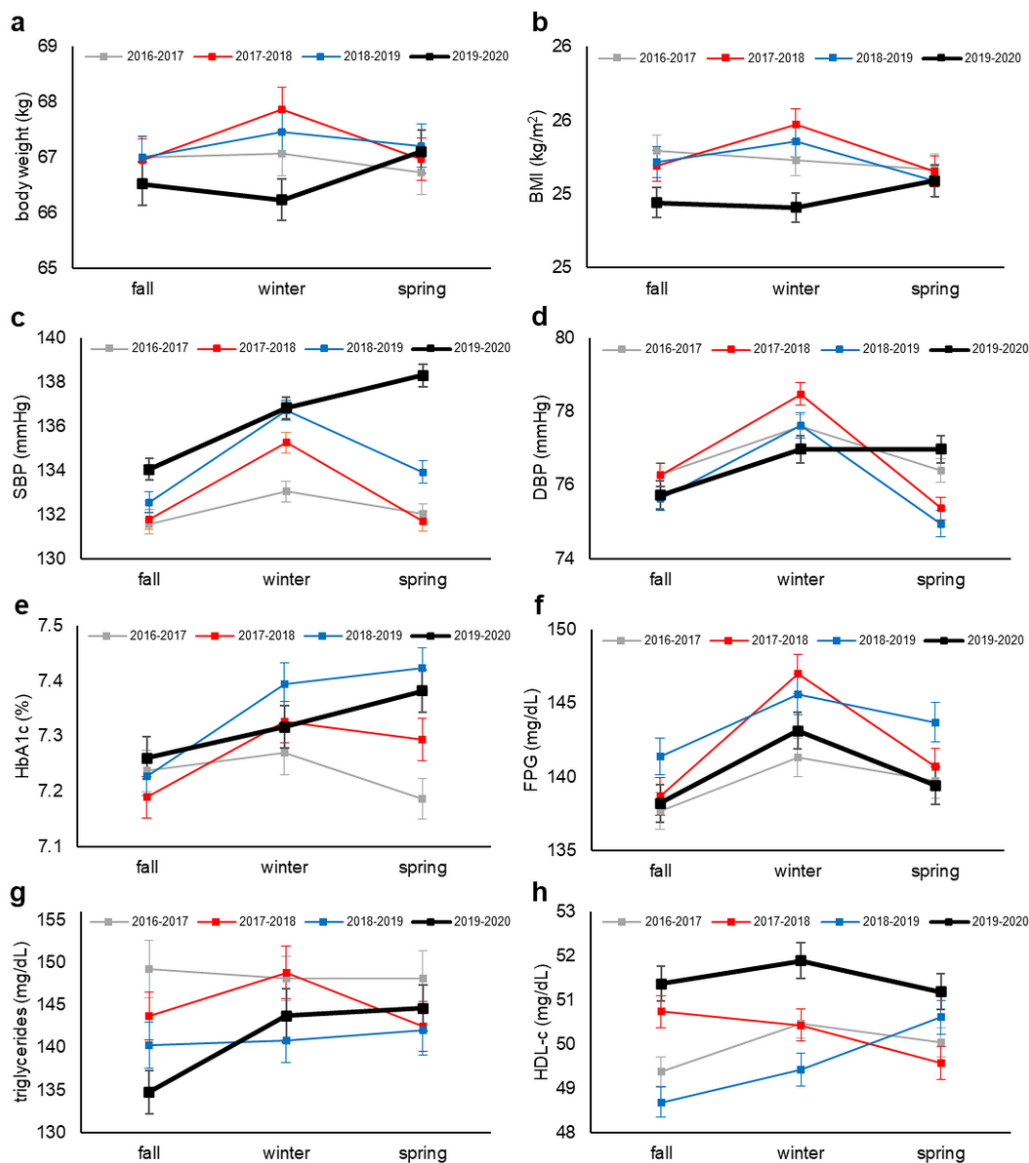Flow chart of study population selection

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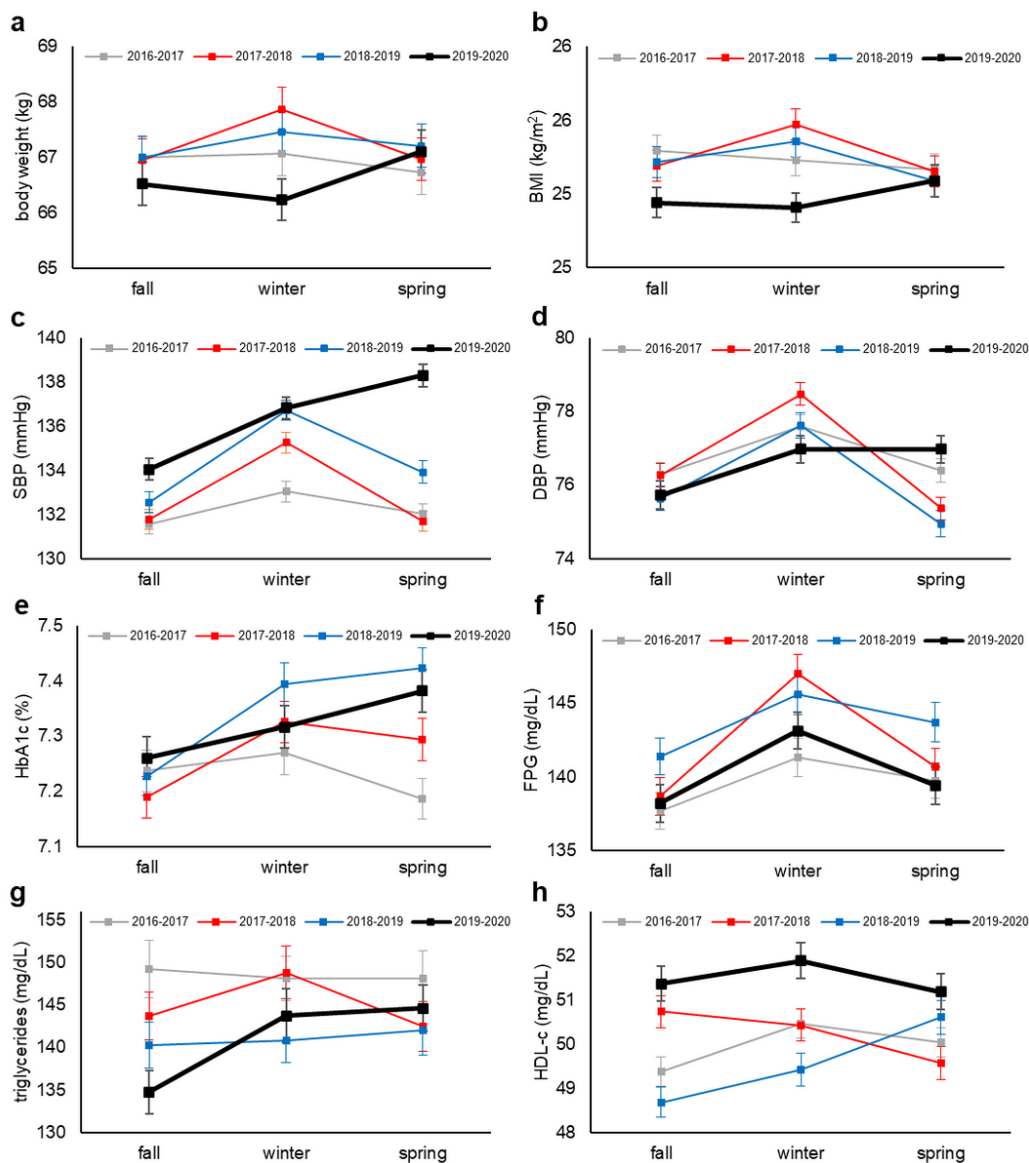
Figure 3

The changes in metabolic syndrome components before (i.e., fall and winter, 2019) and during (i.e., spring, 2020) the COVID-19 pandemic in South Korea: a body weight, b BMI, c SBP, d DBP, e HbA1c, f FPG, g triglycerides, h HDL-c. Key: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; HbA1c, glycated hemoglobin; FPG, fasting plasma glucose; HDL-c, high-density lipoprotein-cholesterol.

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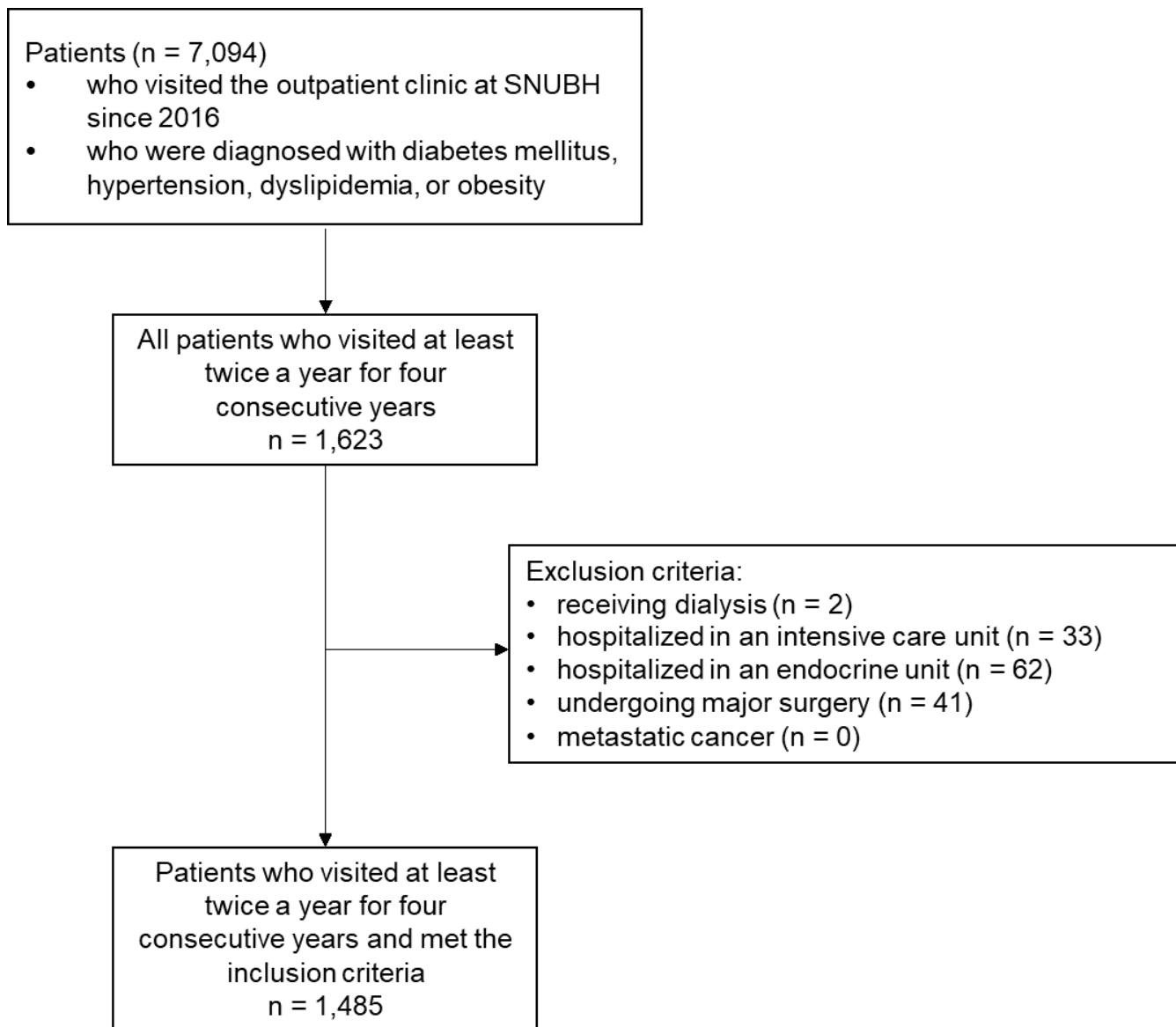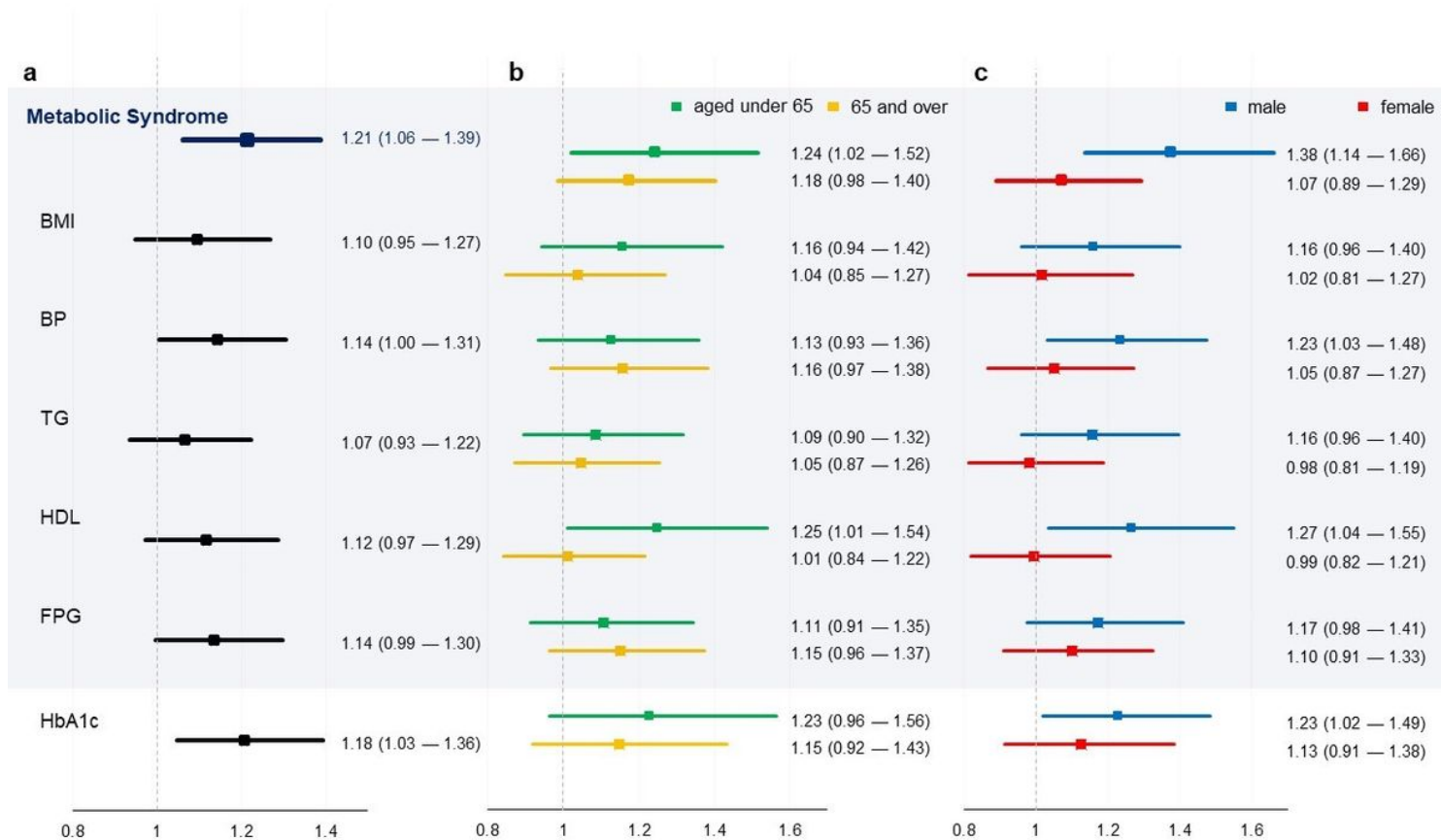
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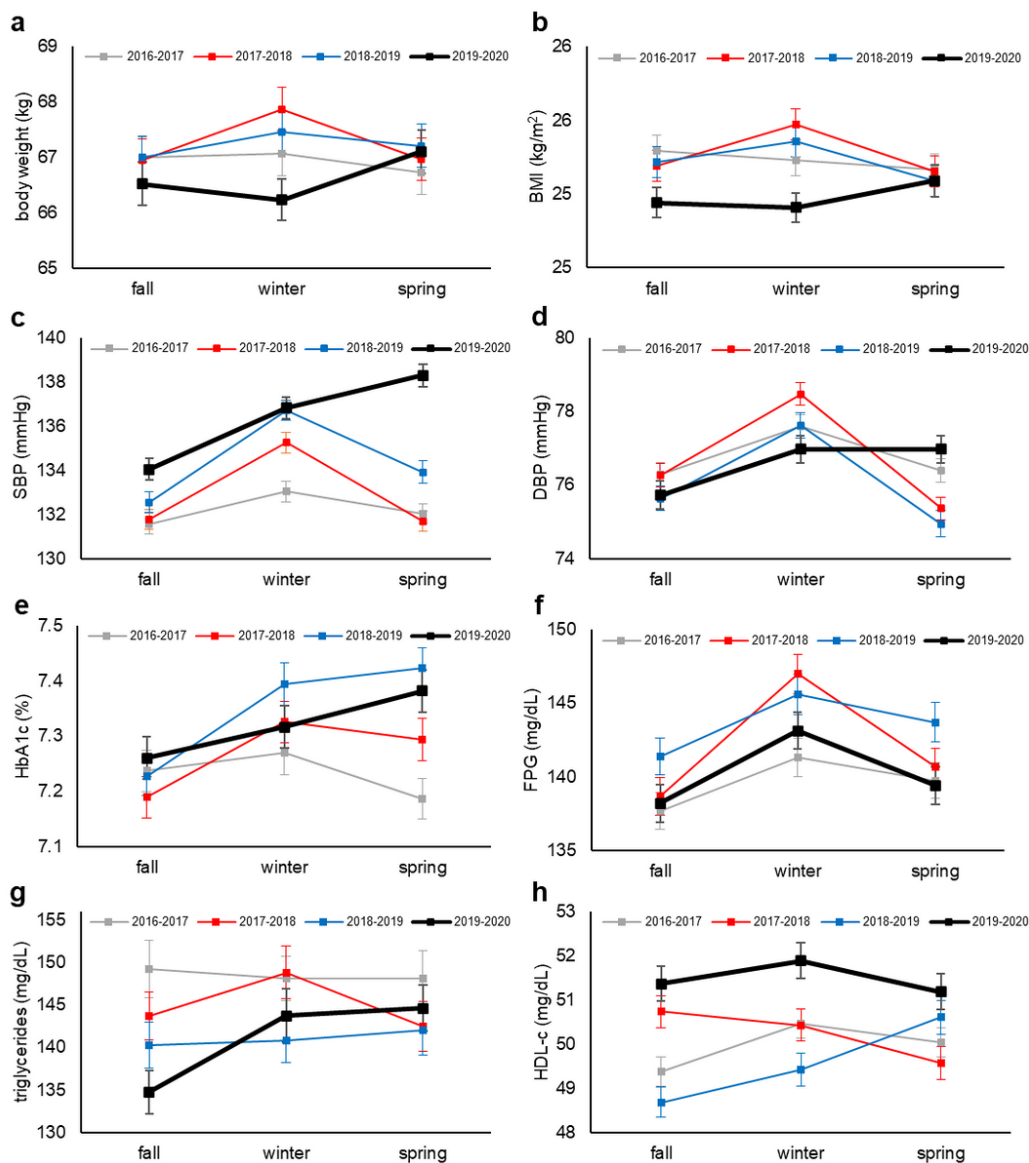**Figure 3**

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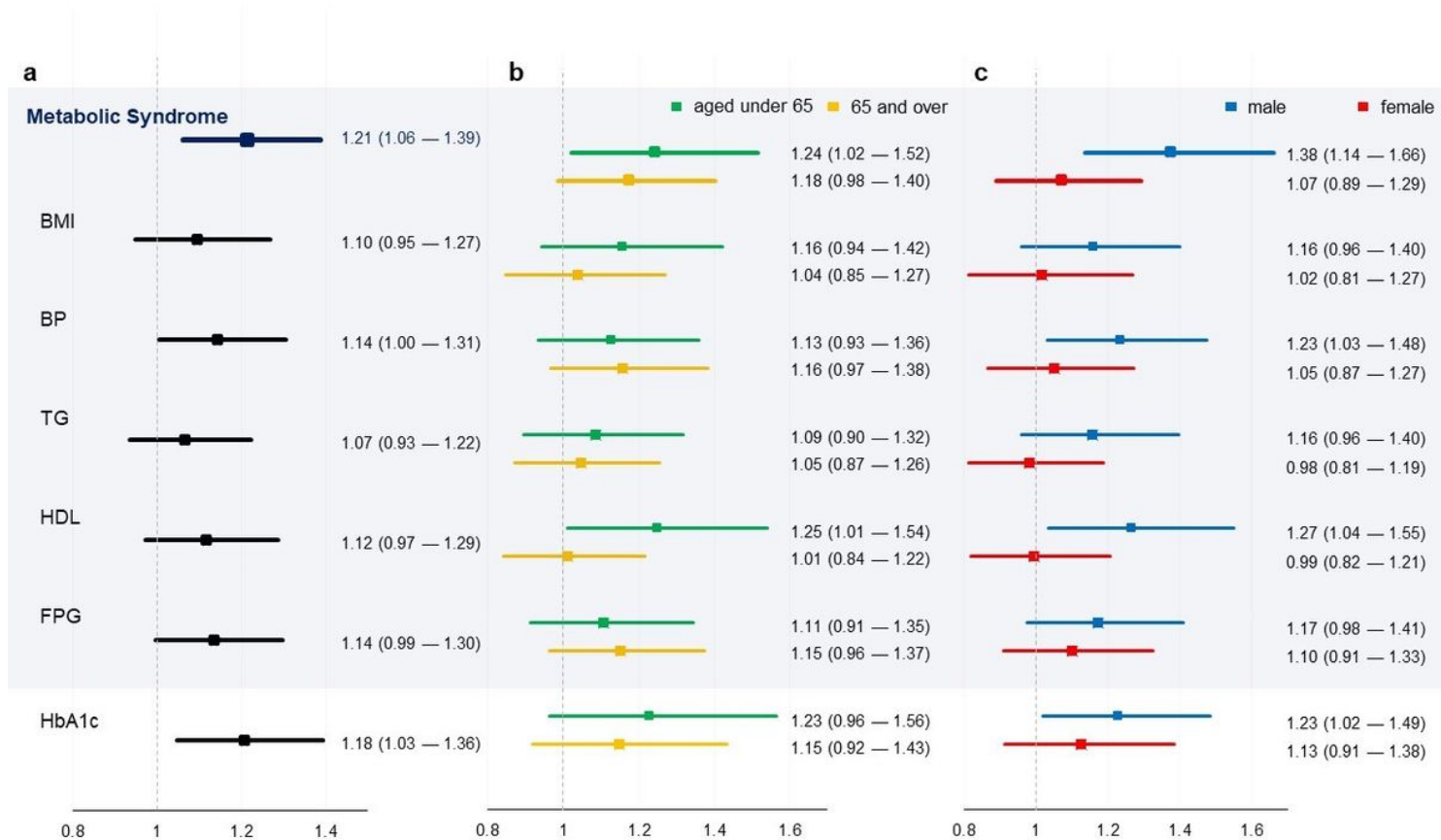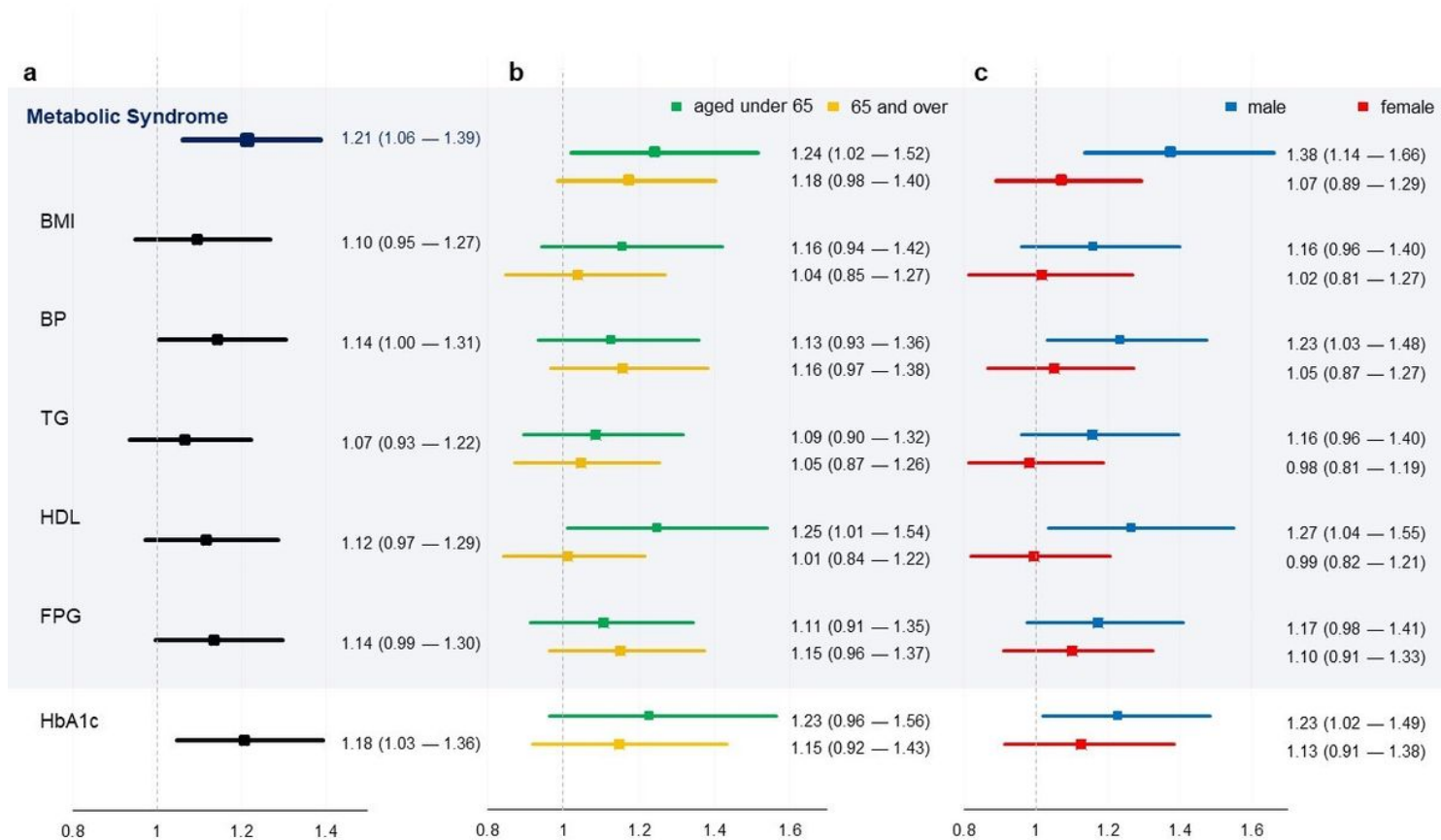
Figure 4

Relative risk of the patients who have worsened in metabolic syndrome components in the 2019–2020 season (COVID-19 pandemic period) when compared with that in the 2018–2019 season: a all patients, b age groups divided at 65 years, c sex. Key: BMI, body mass index; BP, blood pressure; TG, triglyceride; HDL-c, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin.
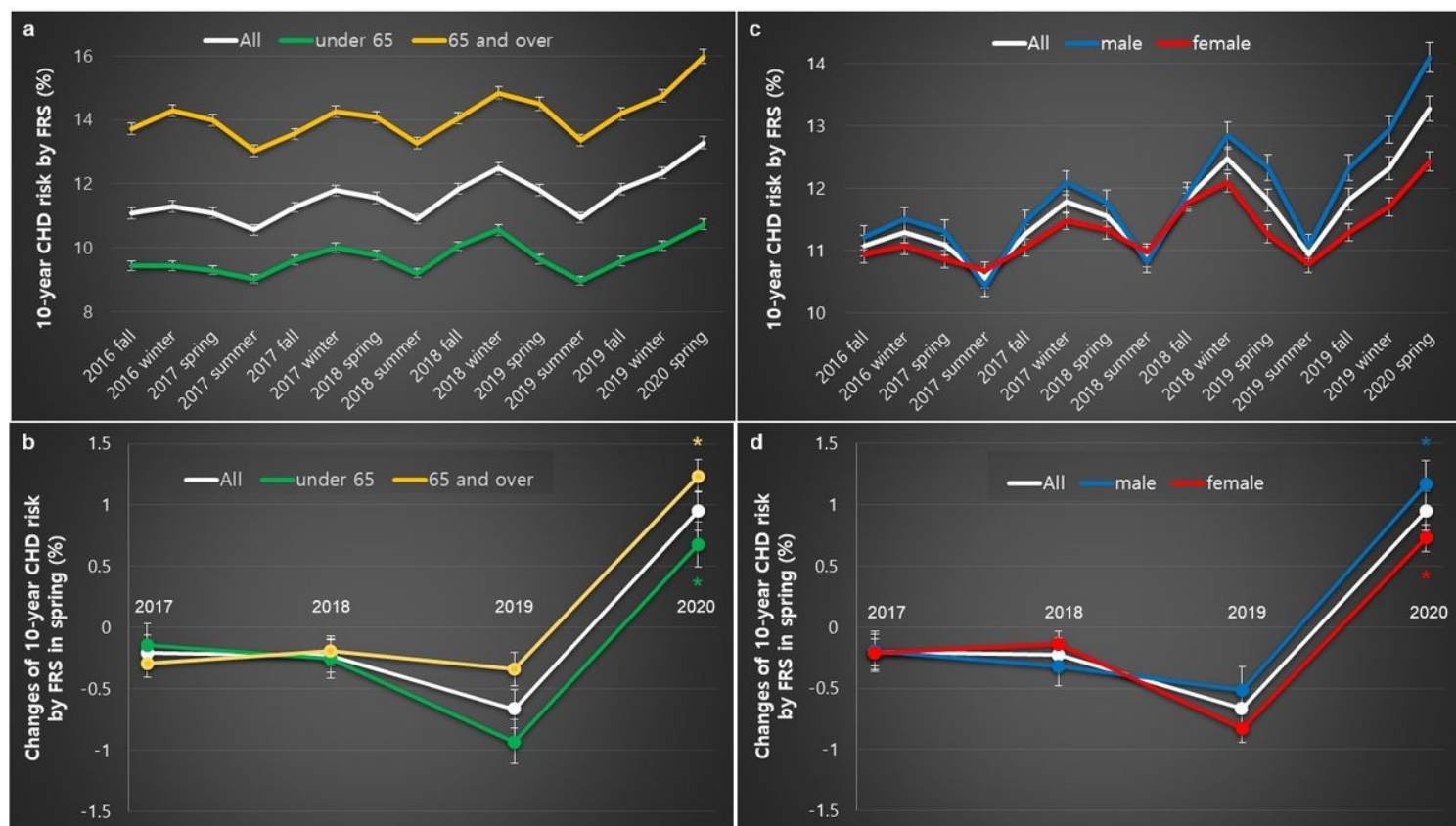
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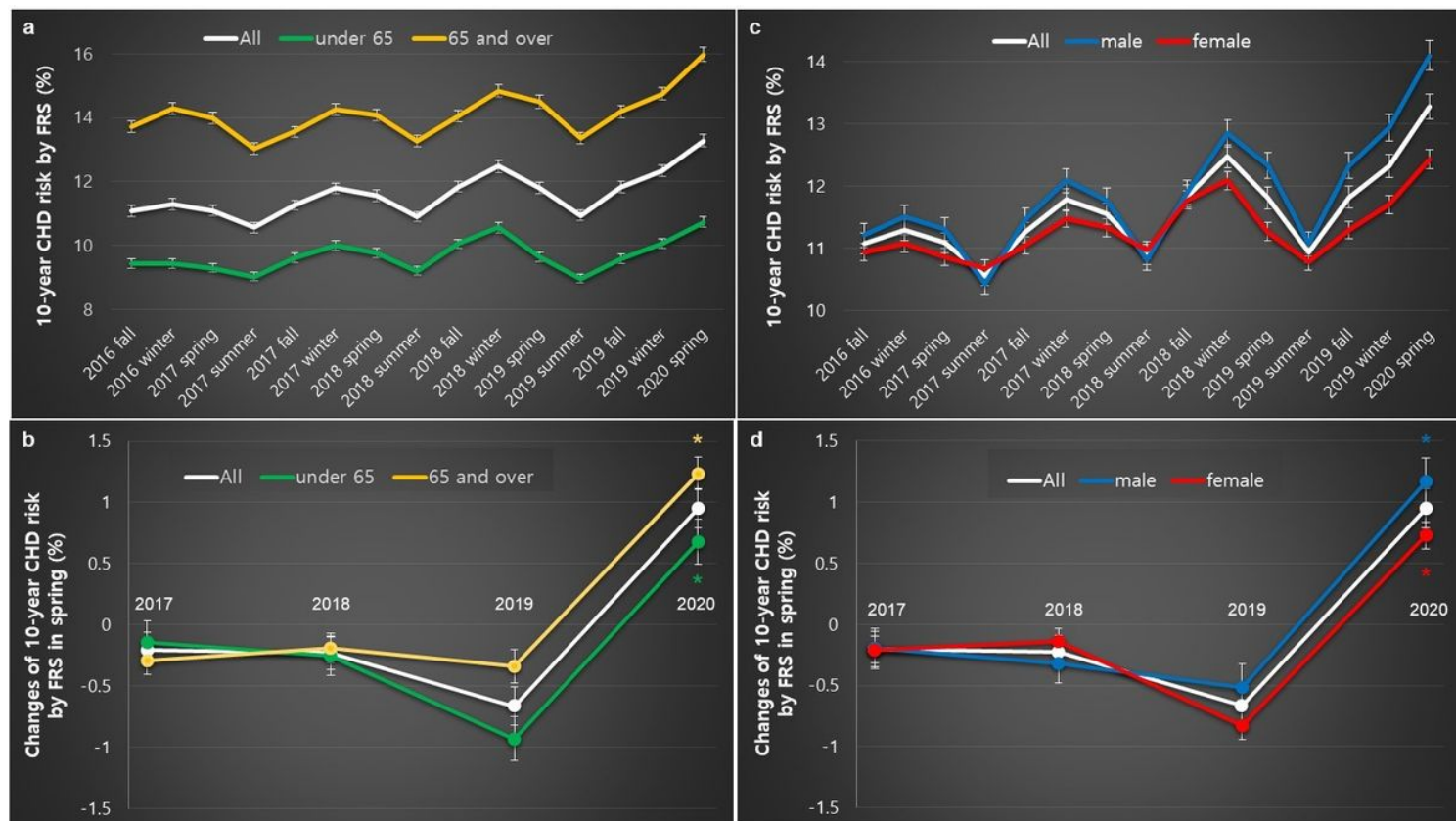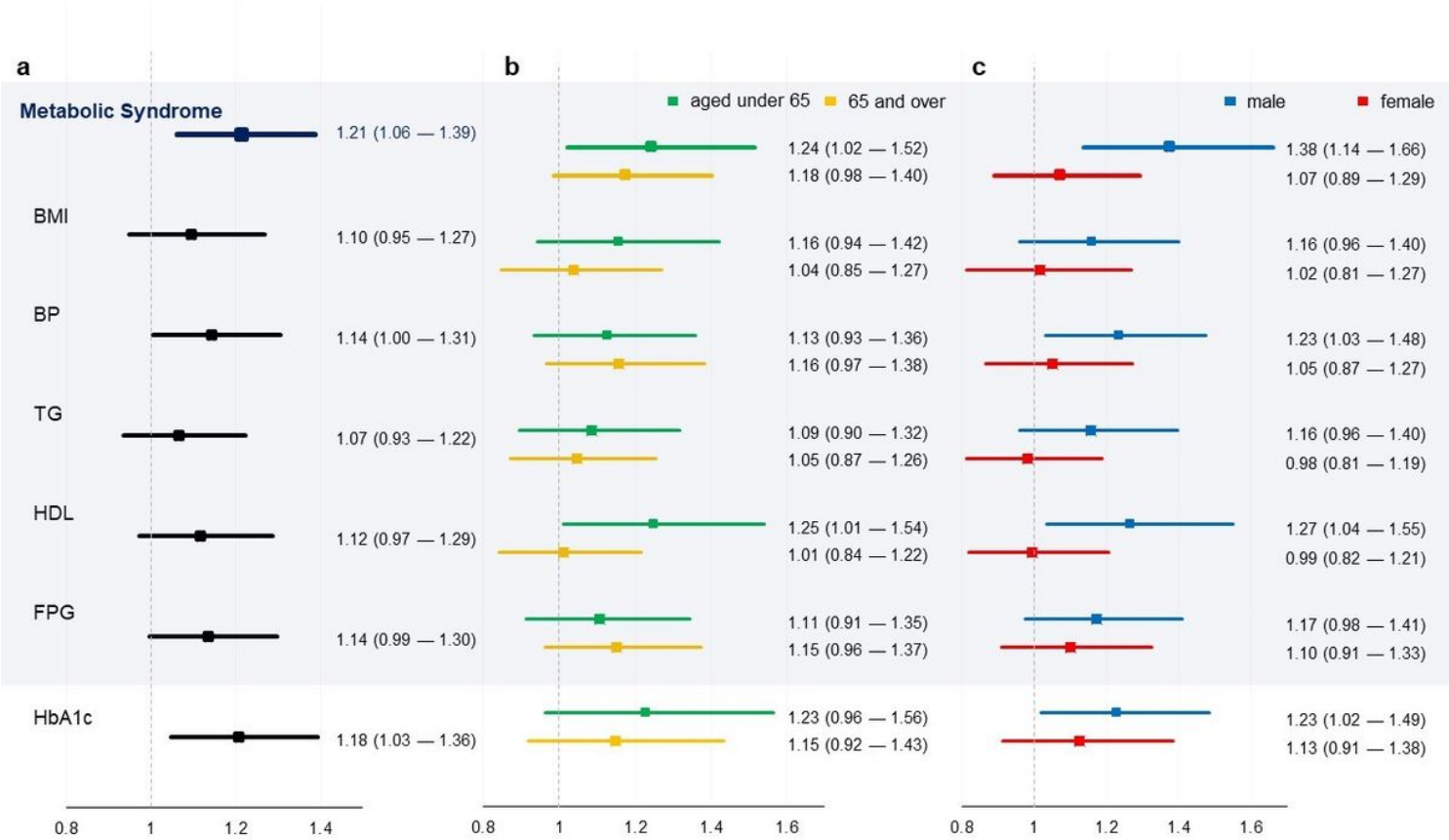
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The 10-year CHD risk by FRS: a, c 10-year CHD risk by FRS for four years, b, d Changes in 10-year CHD risk by FRS before (winter 2019) and during (spring 2020) the COVID-19 pandemic in South Korea. Key: CHD, co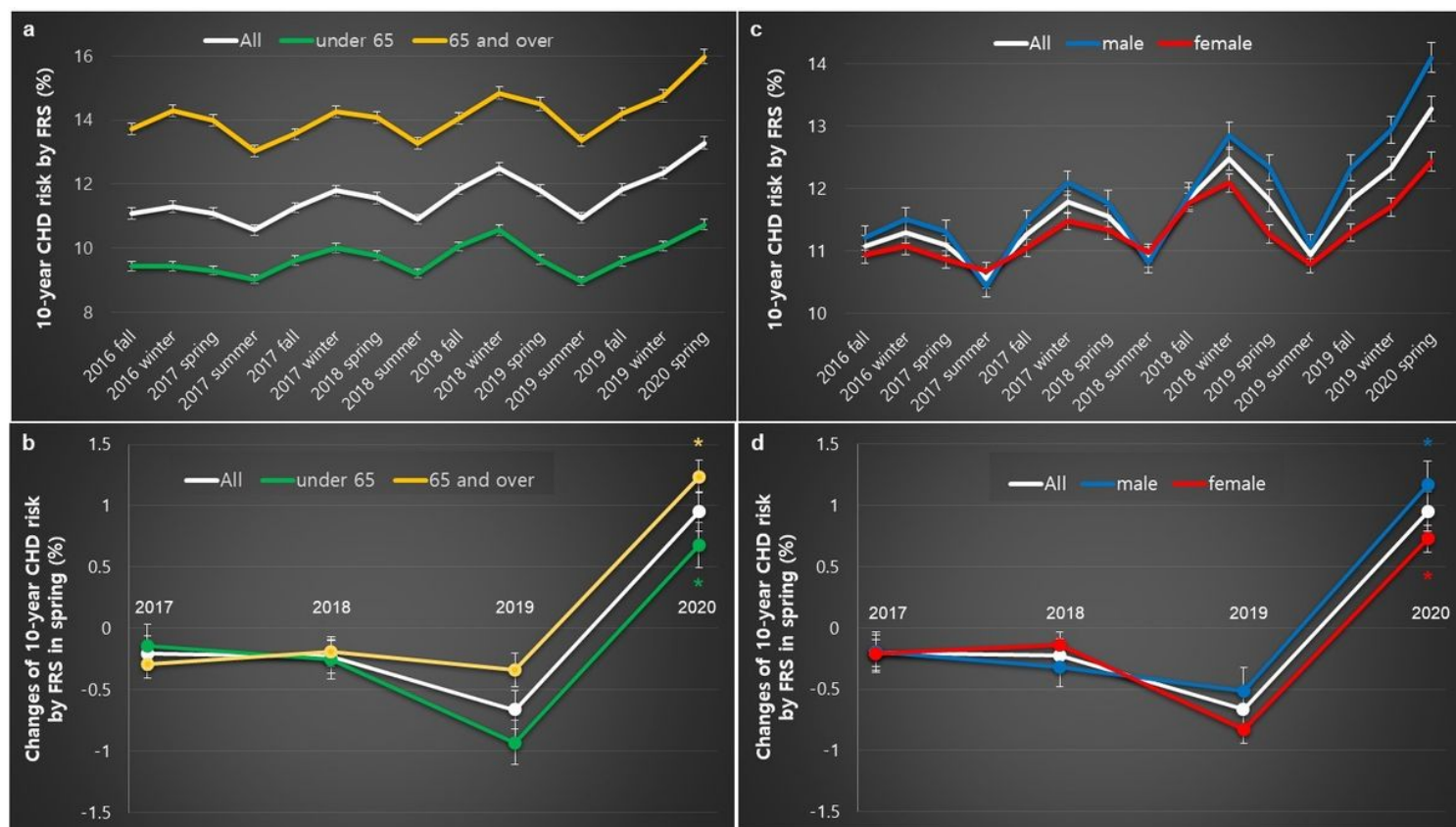ronary heart disease; FRS, Framingham risk score. * refers p < 0.05 of changes in 2019−2020 compared with changes in 2018−2019
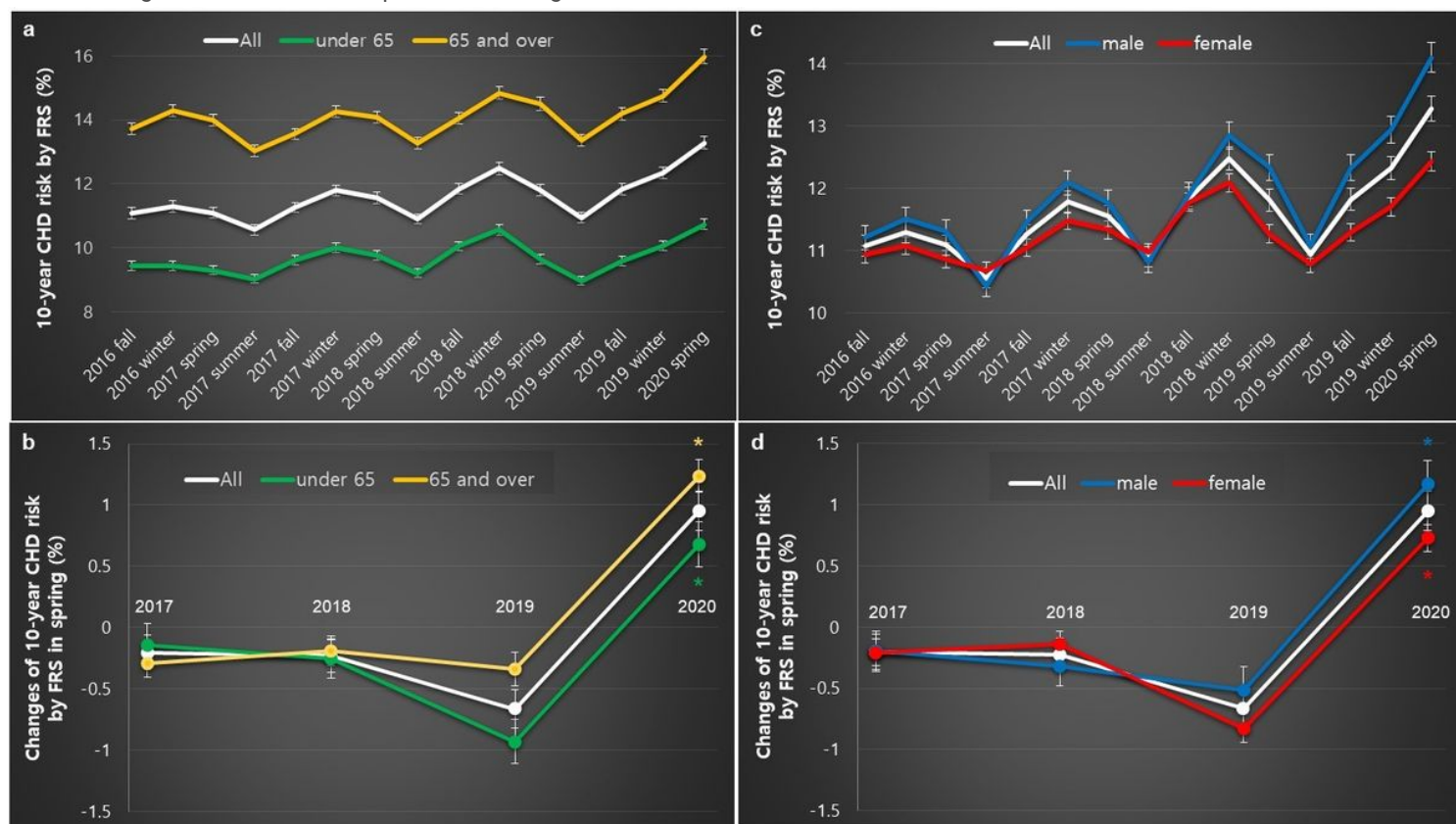

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