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Impact of the suspension and restart of the Dutch breast cancer screening program on breast cancer incidence and stage during the COVID-19 pandemic

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ABSTRACT

The COVID-19 pandemic forced the Dutch national breast screening program to a halt in week 12, 2020. In week 26, the breast program was resumed at 40% capacity, which increased to 60% in week 34. We examined the impact of the suspension and restart of the screening program on the incidence of screen-detected and non-screen-detected breast cancer. We selected women aged 50–74, diagnosed during weeks 2–35 of 2018 (n = 7250), 2019 (n = 7302), or 2020 (n = 5306), from the Netherlands Cancer Registry. Weeks 2–35 were divided in seven periods, based on events occurring at the start of the COVID-19 pandemic. Incidence of screen-detected and non-screen-detected tumors was calculated overall and by age group, cT-stage, and cTNM-stage for each period in 2020, and compared to the incidence in the same period of 2018/2019 (averaged). The incidence of screen-detected tumors decreased during weeks 12–13, reached almost zero during weeks 14–25, and increased during weeks 26–35. Incidence of non-screen-detected tumors decreased to a lesser extent during weeks 12–16. The decrease in incidence was seen in all age groups and mainly occurred for cTis, cT1, DCIS, and stage I tumors. Due to the suspension of the breast cancer screening program, and the restart at reduced capacity, the incidence of screen-detected breast tumors decreased by 67% during weeks 9–35 2020, which equates to about 2000

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potentially delayed breast cancer diagnoses. Up to August 2020 there was no indication of a shift towards higher stage breast cancers after restart of the screening.

1. Introduction

The COVID-19 pandemic put an overwhelming burden on health care services trying to take care of all COVID-19 patients. In the Netherlands, the first COVID-19 cases were identified at the end of February 2020 (week 9), with the virus spreading gradually across the country in the months after (National Institute for Public Health and the Environment, 2020). From March 16, 2020 (week 12) the first social measures were introduced and health care services had to shift focus to patients with COVID-19, thereby generating pressure on all other health care domains.

In the Netherlands, the breast cancer screening program invites women aged 50–74 years for biennial screening mammography. However, to alleviate the burden on health care services, to reallocate personal protective equipment to health care staff tackling COVID-19, and to mitigate spread of COVID-19, the Dutch national breast cancer screening program was suspended from March 16, 2020 (week 12). Women who had received an abnormal screening result just before or during the suspension of the screening program were still able to attend the hospital for further diagnostic work-up. Combined with the decreased health care seeking behavior of women with complaints and the decreased number of referrals from general practitioners (GPs) (Filipe et al., 2020), this has led to a decrease in the number of breast cancer diagnoses (Dinmohamed et al., 2020b). Previous analyses, with data available until the end of April 2020 (week 17), showed that in particular the incidence of the lowest staged breast cancers had decreased (Eijkelboom et al., 2021).

Since early April 2020 (week 14), the demand for critical COVID-19 care steadily decreased. Subsequently, hospital capacity for the diagnostic work-up of suspected breast cancer cases gradually increased and protective equipment became available for all health care staff and the screening workforce. In week 26, pilots were started to test the reorganized screening logistics of planning. Furthermore, social distancing measures were taken within the screening units and additional information (text and instruction videos) was added to the website of the screening program. The pilots were followed by a national restart in week 28, with a limited capacity of 40% of the number of women routinely screened per day to be able to comply with social distancing measures within the screening unit. The screening program restarted where it left off, therefore the first women to be invited for a screening mammography were the women who were not able to attend in March due to the suspension of the program, without any additional criteria on underlying risks (like age).

From August 17, 2020 onwards (week 34), capacity could be increased to 60%. The restart of the screening program and the increased hospital capacity for non-COVID care led to an increase in breast cancer diagnoses (Dinmohamed et al., 2020a). However, the effect of the suspension of the screening program on the incidence of screen-detected breast tumors, as well as reluctance of women to visit their GP, lack of capacity at the GPs and limited referral to the hospital on the incidence of non-screen-detected breast tumors, is unknown. In addition, the impact of the restart on specific characteristics (e.g., age, and breast cancer stage) is unknown.

The aim of this study was to investigate the impact of the suspension and restart of the Dutch breast cancer screening program on the incidence of screen-detected and non-screen-detected breast tumors in women aged 50–74 by age group, clinical T-stage (cT), and clinical cancer stage (cTNM stage).

2. Methods

2.1. Patients

Women aged between 50 and 74 years old and diagnosed with either ductal carcinoma in situ (DCIS) or invasive breast cancer during weeks 2–35 of 2018, 2019 or 2020 were selected from the Netherlands Cancer Registry (NCR). Women with a first primary breast cancer as well as women with a previous breast cancer or synchronous breast cancer were included. The NCR is a nationwide population-based registry that includes all newly diagnosed malignancies since 1989 notified by the Nationwide Histopathology and Cytopathology Data network and Archive (PALGA). Subsequently, trained registration clerks report patient, tumor and treatment characteristics. In the present study, four patient and tumor characteristics were used, these characteristics are among the first to be reported: method of detection (screen-detected or non-screen-detected), age at diagnosis, clinical T-stage, and clinical tumor stage (cTNM-stage).

The present study used data from the NCR, of which data is publicly available in an anonymized database upon request and was thus exempt form ethical compliance. The Privacy Review Board of the NCR approved the present study. Data were made available until August 30, 2020 (week 35).

2.2. Definitions

Weeks 2–35 of 2018, 2019 and 2020 were divided into seven periods, based on events that took place in the first period of the COVID-19 pandemic in 2020: period A covers weeks 2–8 (i.e. before the COVID-19 pandemic); period B, weeks 9–11 (i.e. between the first confirmed COVID-19 patient and the first social lockdown); period C, weeks 12–13 (i.e. the social lockdown was introduced and the national screening program was suspended); period D, weeks 14–16 (i.e. referrals from the screening program ended); period E, weeks 17–25 (i.e. effect was seen of the national call by official authorities to visit the GP when experiencing symptoms); period F, weeks 26–29 (i.e. pilots were started to test the logistics of screening with COVID-19 safety measures in place and restart of the national screening program); period G, weeks 30–35 (i.e. screening has restarted at restricted capacity in most of the Netherlands) (Fig. 1). Averaged data for the corresponding periods in 2018 and 2019 were included as a reference.

Tumors were grouped by their method of detection (screen-detected or non-screen-detected). Screen-detected tumors included cases diagnosed after being recalled for further diagnostic workup due to a positive screening result. Non-screen-detected tumors included all other tumors. Age at diagnosis was grouped into ages 50–54, 55–59, 60–64, 65–69, and 70–74 years. cT-stage (cTis, cT1, cT2, cT3, cT4) and cTNM-stage (DCIS and stage I, II, III, IV) were defined according to the TNM staging system (Brierley et al., 2017).

Fig. 1. Division of week 2–35 in seven periods and the corresponding weeks.

2.3. Statistical analysis

Descriptive statistics were used to compare the baseline characteristics of women diagnosed in weeks 2–35 of either 2018/2019 with those of women diagnosed in 2020, both overall and according to method of detection. Baseline characteristics were compared by using Chi-squared tests. A two-sided p-value <0.05 was considered statistically significant.

All incidences described below were calculated for 2018/2019 (averaged) and 2020, both overall and according to method of detection. First, the incidence of newly diagnosed tumors was calculated per week. Incidence was expressed per 100.000 women aged 50–74 living in the Netherlands, at the start of the year using data from Statistics Netherlands (CBS) (Statistics Netherlands (CBS), 2020). To calculate the percentage of potentially delayed breast cancer diagnoses, the difference in incidence between weeks 9–35 2020 and weeks 9–35 2018/2019 was expressed as percentage of the total incidence at weeks 9–35 2018/2019, overall and by cT-stage. Furthermore, to calculate the number of potentially delayed breast cancer diagnoses, breast cancer incidence in weeks 9–35 of 2020 was subtracted from the average incidence in weeks 9–35 of 2018/2019. This was then divided by 100.000 and multiplied by the number of women aged 50–74 years living in the Netherlands at the start of 2020. Both the percentage and number of potentially delayed breast cancer diagnoses were calculated overall and for screen- and non-screen-detected tumors separately. For representation in graphs, the average weekly incidence of newly diagnosed tumors was calculated over two weeks by age group, cT-stage, and cTNM-stage. Average weekly incidence was calculated over the last three weeks of a period if the period consisted of an odd number of weeks, so the combined weeks aligned the periods. For the incidence per age group, incidence was expressed per 100.000 women of that given age group living in the Netherlands at the start of the year. Furthermore, average weekly incidence in period A–G was calculated. Finally, incidence in period A–G 2020 was calculated by age group, cT-stage, and cTNM-stage and compared with the incidence in the same period of 2018/2019, using STATA's iri command with a midp-calculation (StataCorp LLC, 2020). A p-value of <0.05 was considered statistically significant.

3. Results

A total of 7250 women were diagnosed in weeks 2–35 2018, 7302 women were diagnosed in weeks 2–35 2019, and 5306 women were diagnosed in weeks 2–35 2020. Compared with the same period in 2018/2019, tumors diagnosed in period D–G 2020 were more often non-screen-detected (46.2% vs. 91.6%, 50.1% vs. 95.1%, 47.7% vs. 89.6%, and 45.6% vs. 59.0%, respectively, p-value<0.01 for all periods) (Table 1). Incidence of screen-detected tumors and non-screen-detected tumors increased to the same extent at each age group, cT-stage, and cTNM-stage after the restart of the screening program and the national call to visit the GP when experiencing symptoms (Tables 2–3).

3.1. Incidence all tumors

During period A and B of 2020 an average of 8.3 and 7.6 breast tumors were diagnosed per week, per 100.000 women aged 50–74. Incidence decreased to a weekly average of 5.0 in period C, and further decreased to 2.1 in period D. During period E, incidence started to increase to a weekly average of 3.7. In period F, an average of 4.6 tumors were diagnosed per week, and in period G incidence increased to 6.3 (Fig. 2A). Compared to weeks 9–35 2018/2019, 37% fewer breast tumors were diagnosed in weeks 9–35 2020 (of which 8% was expected to be cTis, 22% cT1, 5% cT2, 1% cT3, 0% cT4, 2% cTx), which equates to approximately 2200 fewer breast tumors. Compared with the same period in 2018/2019, incidence decreased significantly in all age groups in period C–F, 2020 (Supplementary Fig. 1A–E). In period C, incidence of cT1-2 and stage I–II tumors decreased significantly, while in period D and E the incidence of all tumors, except cT4 and stage IV, decreased significantly. Incidence of cTis, cT1, DCIS, and stage I tumors remained significantly lower in period F and G (Fig. 3A–B and 4A–B).

3.2. Incidence of screen-detected tumors

During period A and B of 2020 an average of 4.3 and 4.2 screen-detected tumors were diagnosed per week, per 100.000 women aged 50–74, respectively. In period C, incidence decreased to a weekly average of 3.1, and incidence was almost zero during period D and E. In period F, average weekly incidence increased to 0.4, and further increased to 2.6 in period G (Fig. 2B). Compared to weeks 9–35 2018/2019, 67% fewer screen-detected breast tumors were diagnosed in weeks 9–35 2020 (of which 14% was expected to be cTis, 40% cT1, 10% cT2, 1% cT3, 0% cT4, 1% cTx), which equals approximately 2000 fewer screen-detected breast tumors. Compared with the same period in 2018/2019, incidence of screen-detected tumors decreased significantly in all age groups in period D–G, 2020 (Supplementary Fig. 2A–E). In period B, incidence of cT_3 tumors fell significantly, while in period C the incidence of cT1 and stage I–II tumors fell significantly. The incidence of all tumors, decreased significantly in period D, except the incidence of cT4 and stage IV tumors, as this was already close to zero in 2018/2019. In period E, incidence of all tumors, except cT4, remained significantly lower. The incidence of cTis, cT1-3, DCIS, and stage I–II tumors remained significantly lower in period F, just as the incidence of cTis, cT1-2, DCIS, and stage I–II, tumors in period G (Figs. 3C–D and 4C–D).

3.3. Incidence of non-screen-detected tumors

During period A of 2020, an average of 4.0 non-screen-detected tumors were diagnosed per week, per 100.000 women aged 50–74. Incidence decreased slightly to a weekly average of 3.4 in period B, and further decreased to a weekly average of 1.9 in period C and D. During period E, incidence increased to a weekly average of 3.6. In period F and G an average of 4.2 and 3.8 tumors were diagnosed per week, respectively (Fig. 2B). Compared to weeks 9–35 2018/2019, 7% fewer non-screen-detected breast tumors were diagnosed in weeks 9–35 2020 (of which 2% was expected to be cTis, 3% cT1, 1% cT2, 0% cT3, 1% cT4, 0% cTx), which equates to approximately 200 fewer non-screen-detected breast tumors. Compared to the same periods in 2018/2019, the incidence of non-screen-detected tumors decreased significantly in all age groups in period C and/or D, 2020 (Supplementary Fig. 3A–E). Incidence of cT1-2 and stage I–II tumors fell significantly in period C of 2020, just as the incidence of all tumors, except cT4 and stage IV, in period D. In period G, incidence of stage I tumors increased significantly (Figs. 3E–F and 4E–F).

4. Discussion

The incidence of breast cancer diagnoses decreased substantially due to the lockdown and the suspension of the screening program at week 12, 2020 in relation to the COVID-19 pandemic. The suspension of the breast cancer screening program resulted in a strong decrease of screen-detected breast cancer. As expected, the incidence of the lowest stages decreased to the largest extent. These small tumors are known to be mainly detected through the screening program (de Munck et al., 2018). However, while the incidence of screen-detected tumors decreased, data up to August 2020 (week 35) showed no shift towards a higher tumor stage at diagnosis after the restart of the screening program. This reflects the approach of the screening program to first invite women who were not able to attend due to the suspension of the program, without any additional criteria on age or other underlying risks. Finally, incidence decreased to the same extent in each age group, indicating that no age group was more or less likely to visit the GP or screening units.

The pilots in the screening program started at week 26, to test compliance with social distancing measures and to find a COVID-19

Table 1
Baseline characteristics of breast tumors in women 50–74 years old, by diagnosis period.

		Period A (weeks 2–8)			Period B (weeks 9–11)			Period C (weeks 12–13)			Period D (weeks 14–16)			Period E (weeks 17–25)			Period F (weeks 26–29)			Period G (weeks 30–35)		
		2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P
Patients		1528	1625		648	643		457	285		661	179		1860	965		879	528		1244	1081	
Method of detection (N, %)	Screen-detected	807 (52.8)	843 (51.9)	0.57	352 (54.2)	353 (54.9)	0.76	257 (56.2)	174 (61.1)	0.12	356 (53.8)	11 (6.2)	<0.01	928 (49.9)	23 (2.4)	<0.01	460 (52.3)	43 (8.1)	<0.01	677 (54.4)	430 (39.8)	<0.01
	Non-screen-detected	721 (47.2)	780 (48.0)		297 (45.8)	289 (45.0)		200 (43.8)	109 (38.3)		306 (46.2)	164 (91.6)		933 (50.1)	918 (95.1)		419 (47.7)	473 (89.6)		567 (45.6)	638 (59.0)	
	Unknown	0 (0.0)	2 (0.1)		0 (0.0)	1 (0.2)		0 (0.0)	2 (1.1)		0 (0.0)	4 (2.2)		0 (0.0)	24 (2.5)		0 (0.0)	12 (2.3)		0 (0.0)	13 (1.2)	
Age (N, %)	50–54	302 (19.8)	297 (18.3)	0.18	130 (20.0)	126 (19.6)	0.60	90 (19.7)	64 (22.5)	0.72	140 (21.2)	37 (20.7)	0.10	372 (20.0)	223 (23.1)	0.01	168 (19.1)	102 (19.3)	0.72	263 (21.2)	208 (19.2)	0.04
	55–59	283 (18.5)	296 (18.2)		115 (17.8)	99 (15.4)		77 (16.8)	48 (16.8)		123 (18.5)	47 (26.3)		325 (17.5)	188 (19.5)		145 (16.4)	100 (18.9)		222 (17.8)	219 (20.3)	
	60–64	287 (18.8)	278 (17.1)		125 (19.3)	140 (21.8)		88 (19.3)	57 (20.0)		139 (21.0)	27 (15.1)		356 (19.1)	194 (20.1)		173 (19.6)	97 (18.4)		224 (18.0)	209 (19.3)	
	65–69	312 (20.4)	346 (21.3)		135 (20.8)	134 (20.8)		103 (22.5)	54 (19.0)		125 (18.8)	34 (19.0)		380 (20.4)	158 (16.4)		201 (22.9)	115 (21.8)		273 (22.0)	199 (18.4)	
	70–74	344 (22.5)	408 (25.1)		144 (22.2)	144 (22.4)		100 (21.8)	62 (21.8)		136 (20.5)	34 (19.0)		429 (23.0)	202 (20.9)		194 (22.0)	114 (21.6)		262 (21.1)	246 (22.8)	
cT-stage (N, %)	cT0	12 (0.8)	15 (0.9)	0.70	7 (1.0)	6 (0.9)	0.92	2 (0.4)	2 (0.7)	0.22	5 (0.8)	0 (0.0)	<0.01	8 (0.4)	14 (1.5)	<0.01	5 (0.6)	3 (0.6)	<0.01	6 (0.5)	8 (0.7)	0.01
	cTis	248 (16.2)	288 (17.7)		103 (15.8)	103 (16.0)		71 (15.4)	57 (20.0)		109 (16.4)	19 (10.6)		289 (15.5)	85 (8.8)		144 (16.4)	40 (7.6)		204 (16.4)	144 (13.3)	
	cT1	785 (51.4)	806 (49.6)		345 (53.2)	337 (52.4)		245 (53.7)	134 (47.0)		337 (50.9)	67 (37.4)		940 (50.5)	412 (42.7)		468 (53.2)	248 (47.0)		643 (51.7)	532 (49.2)	
	cT2	359 (23.5)	395 (24.3)		134 (20.6)	138 (21.5)		106 (23.1)	69 (24.2)		150 (22.6)	67 (37.4)		443 (23.8)	320 (33.2)		190 (21.6)	168 (31.8)		294 (23.6)	287 (26.6)	
	cT3	61 (4.0)	63 (3.9)		35 (5.3)	30 (4.7)		20 (4.4)	14 (4.9)		35 (5.2)	12 (6.7)		96 (5.1)	70 (7.3)		34 (3.8)	42 (8.0)		47 (3.7)	61 (5.6)	
	cT4	45 (3.0)	43 (2.7)		16 (2.4)	20 (3.1)		7 (1.5)	8 (2.8)		16 (2.3)	10 (5.6)		57 (3.0)	52 (5.4)		28 (3.1)	21 (4.0)		33 (2.7)	30 (2.8)	
	Unknown	20 (1.3)	15 (0.9)		11 (1.7)	9 (1.4)		7 (1.4)	1 (0.4)		12 (1.7)	4 (2.2)		29 (1.5)	12 (1.2)		12 (1.4)	6 (1.1)		18 (1.4)	19 (1.8)	
cTNM-stage (N, %)	DCIS	254 (16.6)	299 (18.4)	0.63	107 (16.4)	106 (16.5)	0.97	72 (15.8)	57 (20.0)	0.09	112 (16.9)	19 (10.6)	<0.01	297 (16.0)	91 (9.4)	<0.01	150 (17.0)	44 (8.3)	<0.01	208 (16.7)	148 (13.7)	0.03
	Stage I	737 (48.2)	756 (46.5)		322 (49.7)	313 (48.7)		225 (49.3)	123 (43.2)		314 (47.5)	60 (33.5)		883 (47.5)	372 (38.6)		436 (49.6)	221 (41.9)		597 (48.0)	498 (46.1)	
	Stage II	386 (25.3)	415 (25.5)		160 (24.6)	159 (24.7)		122 (26.6)	74 (26.0)		173 (26.1)	74 (41.3)		493 (26.5)	351 (36.4)		208 (23.7)	182 (34.5)		321 (25.8)	312 (28.9)	
	Stage III	70 (4.6)	73 (4.5)		26 (3.9)	29 (4.5)		20 (4.4)	15 (5.3)		31 (4.6)	11 (6.2)		91 (4.9)	64 (6.6)		39 (4.4)	46 (8.7)		50 (4.0)	51 (4.7)	
	Stage IV	65 (4.3)	69 (4.3)		27 (4.1)	28 (4.4)		13 (2.9)	15 (5.3)		25 (3.8)	15 (8.4)		80 (4.3)	77 (8.0)		38 (4.3)	33 (6.3)		58 (4.6)	64 (5.9)	
	Unknown	17 (1.1)	13 (0.8)		8 (1.2)	8 (1.2)		5 (1.1)	1 (0.4)		7 (1.1)	0 (0.0)		17 (0.9)	10 (1.0)		10 (1.1)	2 (0.4)		11 (0.9)	8 (0.7)	

Abbreviations: DCIS: Ductal carcinoma in situ.
The average was taken over 2018 and 2019.
The p-value was calculated on known values only, using the chi-square test to compare patients diagnosed in period A–G 2020 with patients diagnosed in the same period of 2018/2019.

Table 2
Baseline characteristics of screen-detected breast tumors in women 50–74 years old, by diagnosis period.

		Period A (weeks 2–8)			Period B (weeks 9–11)			Period C (weeks 12–13)			Period D (weeks 14–16)			Period E (weeks 17–25)			Period F (weeks 26–29)			Period G (weeks 30–35)		
		2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P
Patients		807	843		352	353		257	174		356	11		928	23		460	43		677	430	
Age (N, %)	50–54	164 (20.3)	149 (17.7)	0.42	60 (17.1)	64 (18.1)	0.68	50 (19.5)	36 (20.7)	0.96	80 (22.5)	3 (27.3)	0.90	175 (18.9)	3 (13.0)	0.07	76 (16.5)	9 (20.9)	0.20	134 (19.7)	67 (15.6)	0.06
	55–59	130 (16.1)	142 (16.8)		59 (16.8)	50 (14.2)		46 (17.7)	31 (17.8)		61 (17.0)	2 (18.2)		157 (16.9)	5 (21.7)		69 (15.0)	7 (16.3)		117 (17.2)	90 (20.9)	
	60–64	150 (18.5)	145 (17.2)		71 (20.2)	81 (23.0)		51 (19.7)	33 (19.0)		73 (20.4)	1 (9.1)		175 (18.8)	2 (8.7)		93 (20.2)	3 (7.0)		122 (18.0)	84 (19.5)	
	65–69	177 (21.9)	200 (23.7)		77 (21.8)	71 (20.1)		58 (22.4)	35 (20.1)		71 (19.8)	2 (18.2)		195 (21.0)	2 (8.7)		117 (25.4)	10 (23.3)		159 (23.4)	84 (19.5)	
	70–74	187 (23.2)	207 (24.6)		85 (24.2)	87 (24.7)		53 (20.7)	39 (22.4)		72 (20.3)	3 (27.3)		227 (24.4)	11 (47.8)		105 (22.8)	14 (32.6)		147 (21.7)	105 (24.4)	
cT-stage (N, %)	T0	0 (0.0)	2 (0.2)	0.30	2 (0.4)	0 (0.0)	0.08	0 (0.0)	1 (0.6)	0.03	0 (0.0)	0 (0.0)	0.84	2 (0.2)	0 (0.0)	0.98	0 (0.0)	0 (0.0)	0.94	0 (0.0)	0 (0.0)	0.31
	Tis	185 (22.9)	216 (25.6)		77 (21.9)	69 (19.6)		53 (20.5)	48 (27.6)		81 (22.8)	4 (36.4)		200 (21.6)	5 (21.7)		102 (22.2)	9 (20.9)		148 (21.9)	96 (22.3)	
	T1	482 (59.7)	485 (57.5)		218 (61.9)	225 (63.7)		157 (61.0)	94 (54.0)		206 (57.8)	6 (54.6)		544 (58.7)	13 (56.5)		282 (61.2)	27 (62.8)		414 (61.1)	252 (58.6)	
	T2	117 (14.4)	120 (14.2)		42 (11.8)	51 (14.5)		41 (15.8)	26 (14.9)		56 (15.6)	1 (9.1)		147 (15.9)	4 (17.4)		64 (13.8)	6 (14.0)		100 (14.8)	68 (15.8)	
	T3	14 (1.7)	16 (1.9)		9 (2.6)	2 (0.6)		4 (1.6)	3 (1.7)		8 (2.3)	0 (0.0)		20 (2.1)	1 (4.4)		7 (1.5)	0 (0.0)		9 (1.3)	11 (2.6)	
	T4	1 (0.1)	1 (0.1)		1 (0.1)	2 (0.6)		0 (0.0)	2 (1.2)		1 (0.1)	0 (0.0)		4 (0.4)	0 (0.0)		1 (0.2)	0 (0.0)		0 (0.0)	0 (0.0)	
	Unknown	10 (1.2)	3 (0.4)		5 (1.3)	4 (1.1)		3 (1.2)	0 (0.0)		5 (1.4)	0 (0.0)		12 (1.3)	0 (0.0)		5 (1.1)	1 (2.3)		7 (1.0)	3 (0.7)	
cTNM-stage (N, %)	DCIS	185 (22.9)	215 (25.5)	0.40	79 (22.3)	69 (19.6)	0.51	53 (20.7)	48 (27.6)	0.17	83 (23.2)	4 (36.4)	0.83	203 (21.8)	5 (21.7)	0.97	102 (22.2)	9 (20.9)	0.86	148 (21.8)	96 (22.3)	0.98
	Stage I	467 (57.8)	459 (54.5)		208 (59.0)	212 (60.1)		146 (56.9)	90 (51.7)		199 (55.8)	6 (54.6)		526 (56.7)	13 (56.5)		274 (59.5)	25 (58.1)		393 (58.1)	244 (56.7)	
	Stage II	133 (16.4)	146 (17.3)		58 (16.4)	63 (17.9)		51 (19.9)	31 (17.8)		66 (18.4)	1 (9.1)		172 (18.5)	5 (21.7)		73 (15.8)	7 (16.3)		121 (17.8)	81 (18.8)	
	Stage III	10 (1.2)	14 (1.7)		4 (1.0)	2 (0.6)		4 (1.4)	2 (1.2)		6 (1.6)	0 (0.0)		14 (1.5)	0 (0.0)		4 (0.9)	1 (2.3)		6 (0.9)	4 (0.9)	
	Stage IV	5 (0.6)	6 (0.7)		1 (0.3)	3 (0.9)		1 (0.2)	2 (1.2)		1 (0.3)	0 (0.0)		5 (0.5)	0 (0.0)		4 (0.8)	0 (0.0)		4 (0.6)	2 (0.5)	
	Unknown	9 (1.1)	3 (0.4)		4 (1.0)	4 (1.1)		3 (1.0)	1 (0.6)		3 (0.7)	0 (0.0)		10 (1.0)	0 (0.0)		5 (1.0)	1 (2.3)		6 (0.9)	3 (0.7)	

Abbreviations: DCIS: Ductal carcinoma in situ.
The average was taken over 2018 and 2019.
The p-value was calculated on known values only, using the chi-square test to compare patients diagnosed in period A–G 2020 with patients diagnosed in the same period of 2018/2019.

Table 3
Baseline characteristics of non-screen-detected breast tumors in women 50–74 years old, by diagnosis period.

		Period A (weeks 2–8)			Period B (weeks 9–11)			Period C (weeks 12–13)			Period D (weeks 14–16)			Period E (weeks 17–25)			Period F (weeks 26–29)			Period G (weeks 30–35)		
		2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P	2018/2019	2020	P
Patients		721	780		297	289		200	109		306	164		933	918		419	473		567	638	
Age (N, %)	50–54	139 (19.2)	148 (19.0)	0.25	70 (23.4)	61 (21.1)	0.76	40 (20.0)	27 (24.8)	0.62	60 (19.5)	34 (20.7)	0.23	197 (21.1)	215 (23.4)	0.26	92 (21.8)	90 (19.0)	0.74	130 (22.9)	138 (21.6)	0.63
	55–59	153 (21.2)	153 (19.6)		56 (18.9)	49 (17.0)		31 (15.5)	16 (14.7)		62 (20.3)	44 (6.8)		168 (18.0)	176 (19.2)		76 (18.0)	92 (19.5)		105 (18.5)	125 (19.6)	
	60–64	138 (19.1)	132 (16.9)		54 (18.2)	59 (20.4)		38 (18.8)	24 (22.0)		67 (21.8)	26 (15.9)		182 (19.5)	183 (19.9)		80 (19.0)	94 (19.9)		103 (18.1)	122 (19.1)	
	65–69	135 (18.7)	146 (18.7)		58 (19.6)	63 (21.8)		45 (22.5)	19 (17.4)		54 (17.7)	31 (18.9)		185 (19.8)	155 (16.9)		84 (20.1)	101 (21.4)		115 (20.2)	113 (17.7)	
	70–74	157 (21.8)	201 (25.8)		59 (19.9)	57 (19.7)		47 (23.3)	23 (21.1)		64 (20.8)	29 (17.7)		202 (21.7)	189 (20.6)		89 (21.1)	96 (20.3)		115 (20.3)	140 (21.9)	
cT-stage (N, %)	cT0	12 (1.7)	13 (1.7)	0.93	5 (1.7)	6 (2.1)	0.62	2 (1.0)	1 (0.9)	0.68	5 (1.6)	0 (0.0)	0.25	7 (0.7)	14 (1.5)	0.36	5 (1.2)	3 (0.6)	0.07	6 (1.1)	8 (1.3)	0.30
	cTis	63 (8.7)	72 (9.2)		26 (8.6)	34 (11.8)		18 (9.0)	9 (8.3)		28 (9.0)	15 (9.2)		89 (9.5)	80 (8.7)		42 (10.0)	31 (6.6)		56 (9.9)	48 (7.5)	
	cT1	304 (42.1)	320 (41.0)		127 (42.8)	112 (38.8)		89 (44.3)	40 (36.7)		131 (42.9)	61 (37.2)		396 (42.5)	396 (43.1)		186 (44.4)	219 (46.3)		229 (40.4)	277 (43.4)	
	cT2	242 (33.6)	274 (35.1)		92 (31.0)	87 (30.1)		65 (32.5)	42 (38.5)		94 (30.8)	62 (38.4)		296 (31.7)	299 (32.6)		126 (30.1)	153 (32.4)		194 (34.3)	214 (33.5)	
	cT3	47 (6.5)	47 (6.0)		26 (8.6)	28 (9.7)		16 (8.0)	10 (9.2)		27 (8.7)	12 (7.3)		76 (8.2)	67 (7.3)		27 (6.3)	41 (8.7)		38 (6.6)	48 (7.5)	
	cT4	44 (6.1)	42 (5.4)		15 (5.1)	17 (5.9)		7 (3.5)	6 (5.5)		15 (4.9)	10 (6.1)		53 (5.7)	51 (5.6)		27 (6.3)	21 (4.4)		33 (5.8)	27 (4.2)	
	Unknown	10 (1.4)	12 (1.5)		7 (2.2)	5 (1.7)		4 (1.8)	1 (0.9)		7 (2.1)	3 (1.8)		17 (1.8)	11 (1.2)		7 (1.7)	5 (1.1)		11 (1.9)	16 (2.5)	
cTNM-stage (N, %)	DCIS	69 (9.6)	84 (10.8)	0.87	28 (9.4)	37 (12.8)	0.44	19 (9.5)	9 (8.3)	0.15	30 (9.7)	15 (9.2)	0.42	95 (10.1)	86 (9.4)	0.53	48 (11.3)	35 (7.4)	0.14	61 (10.7)	52 (8.2)	0.34
	Stage I	270 (37.5)	296 (38.0)		115 (38.6)	101 (35.0)		79 (39.5)	33 (30.3)		116 (37.8)	54 (32.9)		357 (38.3)	358 (39.0)		163 (38.8)	196 (41.4)		204 (35.9)	251 (39.3)	
	Stage II	254 (35.2)	268 (34.4)		102 (34.4)	96 (33.2)		71 (35.3)	42 (38.5)		107 (35.0)	70 (42.7)		321 (34.4)	328 (35.7)		136 (32.3)	166 (35.1)		200 (35.3)	226 (35.4)	
	Stage III	60 (8.3)	59 (7.6)		22 (7.4)	27 (9.3)		17 (8.3)	12 (11.0)		25 (8.2)	10 (6.1)		77 (8.3)	60 (6.5)		35 (8.2)	43 (9.1)		44 (7.8)	43 (6.7)	
	Stage IV	61 (8.4)	63 (8.1)		26 (8.6)	24 (8.3)		13 (6.3)	13 (11.9)		24 (7.9)	15 (9.2)		76 (8.1)	77 (8.4)		34 (8.1)	32 (6.8)		54 (9.4)	61 (9.6)	
	Unknown	8 (1.1)	10 (1.3)		5 (1.5)	4 (1.4)		3 (1.3)	0 (0.0)		5 (1.5)	0 (0.0)		8 (0.8)	9 (1.0)		5 (1.2)	1 (0.2)		5 (0.9)	5 (0.8)	

Abbreviations: DCIS: Ductal carcinoma in situ.
The average was taken over 2018 and 2019.
The p-value was calculated on known values only, using the chi-square test to compare patients diagnosed in period A–G 2020 with patients diagnosed in the same period of 2018/2019.

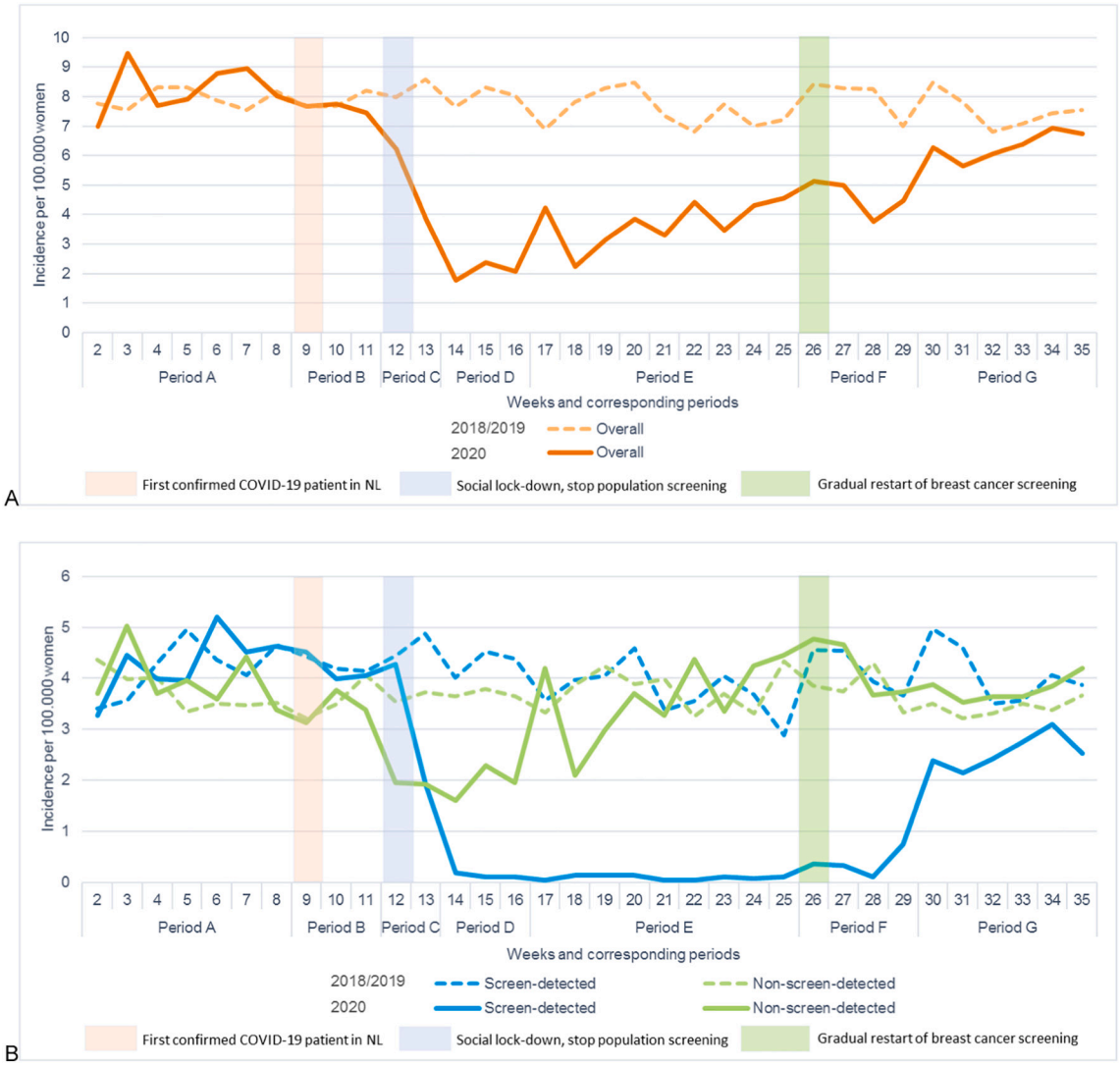

Fig. 2. Average weekly incidence, overall (A) and for screen-detected and non-screen-detected tumors (B) separately, per 100.000 women aged 50–74 years living in the Netherlands at the start of the year.
The following weeks in 2018 had 4 workings days instead of 5: week 14, 17, 19, and 21.
The following weeks in 2019 had 4 working days instead of 5: week 17, 22, and 24.
The following weeks in 2020 had 4 working days instead of 5: week 16, 18, 19, 21, and 23.

proof method to perform a screening mammography. This resulted in a slow increase in the incidence of screen-detected tumors. From week 28 onwards screening has restarted at limited capacity of 40%, resulting in a steep increase in the incidence of screen-detected tumors. In period G (weeks 30–35) the incidence per cT-stage and cTNM-stage of early stage screen-detected tumors returned to around 60% of the average incidence of screen-detected tumors in the reference period, which is in accordance with the increase in screening capacity to 60% as of August 17th (week 34).

The incidence of the non-screen-detected tumors was less affected by the pandemic. Although the incidence of non-screen-detected tumors decreased earlier in time due to increased reluctance of women to visit their GP, lack of capacity at GPs and limited referral to the hospital, the decrease was less pronounced. The incidence of non-screen-detected tumors started to increase in week 17, which might be due to the national call, starting in week 14, to visit a GP when experiencing symptoms. From week 21 onwards, the incidence of non-screen-detected cT1-2 and stage I–II tumors was higher than the incidence in 2018/2019, indicating a catching-up process. This shows the influence and importance of maintaining the health seeking behavior of women in case of complaints. Moreover, it suggests that the diagnostic routing in the hospital may not have been affected by the COVID-19 pandemic. It is unknown how many women with non-screen-detected cancer would have attended the screening program and had their cancer detected through screening if the program was not suspended.

The overall incidence of cT3 and stage III tumors only slightly decreased during the beginning of the social lockdown, but returned quickly to the expected level. The incidence of cT4 and stage IV tumors did not decrease during weeks 2–35, 2020. As those higher stage tumors are in general mainly non-screen-detected tumors, the incidence was not expected to decrease due to the suspension of the screening program. Fortunately, the increased reluctance of women to visit their GP during the COVID-19 pandemic did not influence the incidence of higher stage tumors either.

This study benefited from using data from the NCR for all women diagnosed with breast cancer in the Netherlands, thereby accurately reflecting daily practice. Furthermore, data on incidence and stage were already available up to August 2020 (week 35). However, the study has some limitations. First, the COVID-19 pandemic is still ongoing. Therefore, the overall impact of the COVID-19 pandemic and delayed

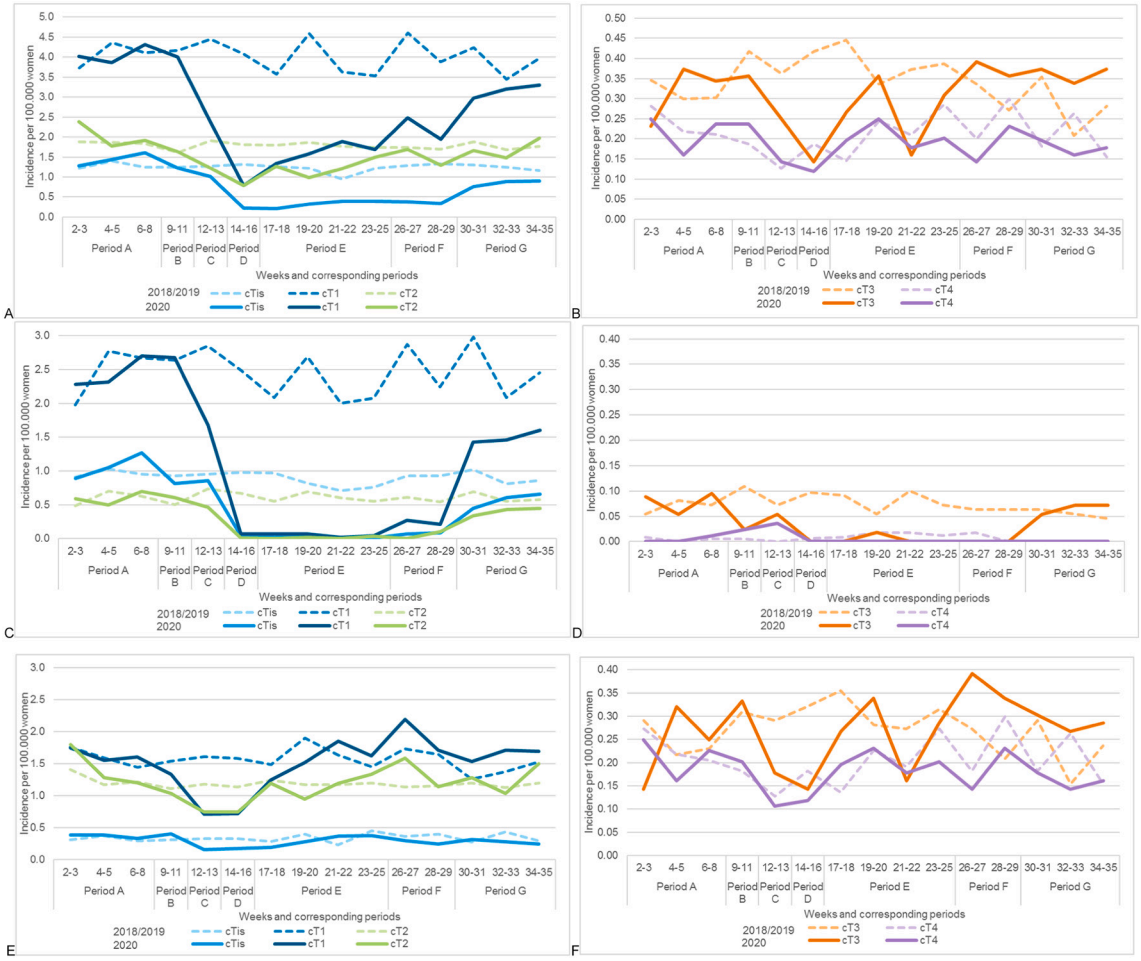

Fig. 3. Average weekly incidence over two or three weeks, overall (A,B) and for screen-detected (C,D) and non-screen-detected tumors (E,F) separately, per 100.000 women aged 50–74 years, stratified by cT-stage.

diagnoses on a possible stage shift towards higher stage tumors at time of diagnosis could not be studied yet. Second, the logistics of inviting women was slightly altered upon restart of the screening and data on actual attendance is not yet available. Specific data on altered logistics and actual attendance rate might have provided additional insight in the number of potential missed screen-detected breast cancer diagnoses. Third, the number of screen-detected second primary tumors was too low (97 in 2018, 106 in 2019 and 61 in 2020) to perform stratified analyses by first or second primary tumor.

4.1. Future expectations

From week 40 onwards, screening capacity has increased to 80%. However, as long as the screening capacity is below 100%, it is impossible to catch-up the delay and the backlog in breast cancer diagnosis will maintain. Furthermore, data on specific women who were not able to attend the screening program due to the COVID-19 pandemic is not yet available. In future studies specific time intervals between screening rounds and data on interval tumors will become available. When possible in a pandemic, it is important to maintain an operational national screening program to prevent a major backlog in early stage breast cancer diagnosis. Furthermore, the backlog in the screening program should be caught-up as soon as possible, to prevent a possible increase in delay in diagnosis, which might result in higher stage tumors, demanding more invasive treatment strategies and possible negatively effecting quality of life and prognosis. However, it should be taken into account that increasing the screening capacity demands for sufficient capacity in the hospitals to offer additional diagnosis and treatment. Finally, a delay in diagnosis automatically leads to a delay in treatment. Previous studies showed a negative association between delay in treatment and survival in patients with a higher stage tumor, a tumor larger than 40 mm, a triple negative breast tumor, or a metastatic tumor (Eriksson et al., 2018; Jung et al., 2011; Li et al., 2019; McLaughlin et al., 2012). This indicates that a delay in treatment is especially harmful for patients with a more aggressive tumor. However, our study showed that the diagnosis of mainly early stage tumors has been delayed. Future research is needed to analyze how this delay in breast cancer diagnosis has an impact on survival.

5. Conclusion

Suspension of the breast cancer screening program due to the COVID-19 pandemic reduced the incidence of breast cancer diagnoses. After screening was restarted, the incidence did not raise above the incidences observed in 2018/2019. The changes in the breast cancer screening process led to about 2000 delayed screen-detected breast cancers so far, predominantly in the lowest stages of the disease. Even though this significant delay, no shift towards a higher stage breast cancer was observed up to August 2020 (week 35). The incidence of the non-screen-detected tumors was less influenced by the pandemic.

Data sharing

All data collected for the study will be made available via the NCR

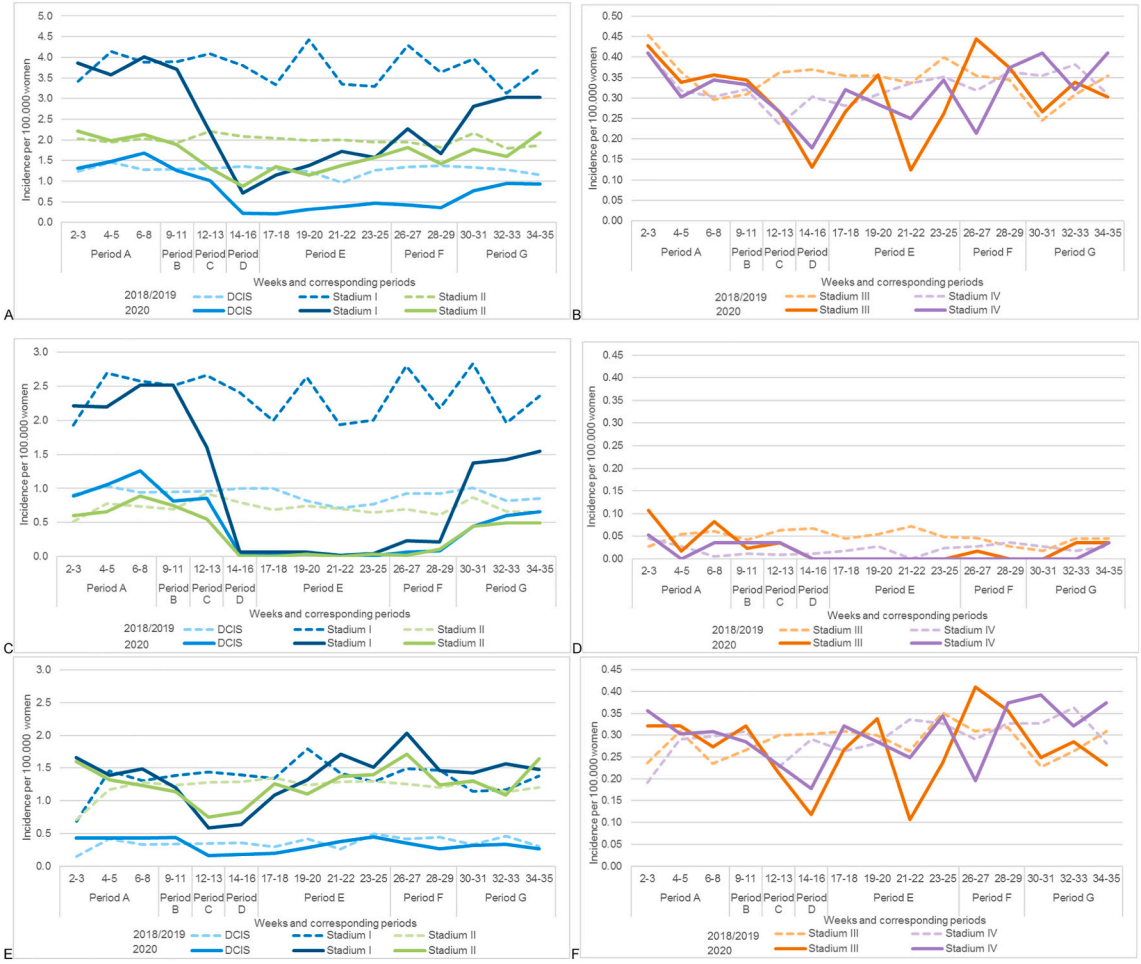

Fig. 4. Average weekly incidence over two or three weeks, overall (A,B) and for screen-detected (C,D) and non-screen-detected tumors (E,F) separately, per 100.000 women aged 50–74 years, stratified by cTNM-stage.

upon request and after approval of a proposal from the date of publication. The plan for the statistical analysis will be made available by the corresponding author upon request.

Prior presentation

Presented in part as an oral presentation at the AACR virtual meeting: COVID-19 and cancer, on February 3rd 2021.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2021.106602.

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