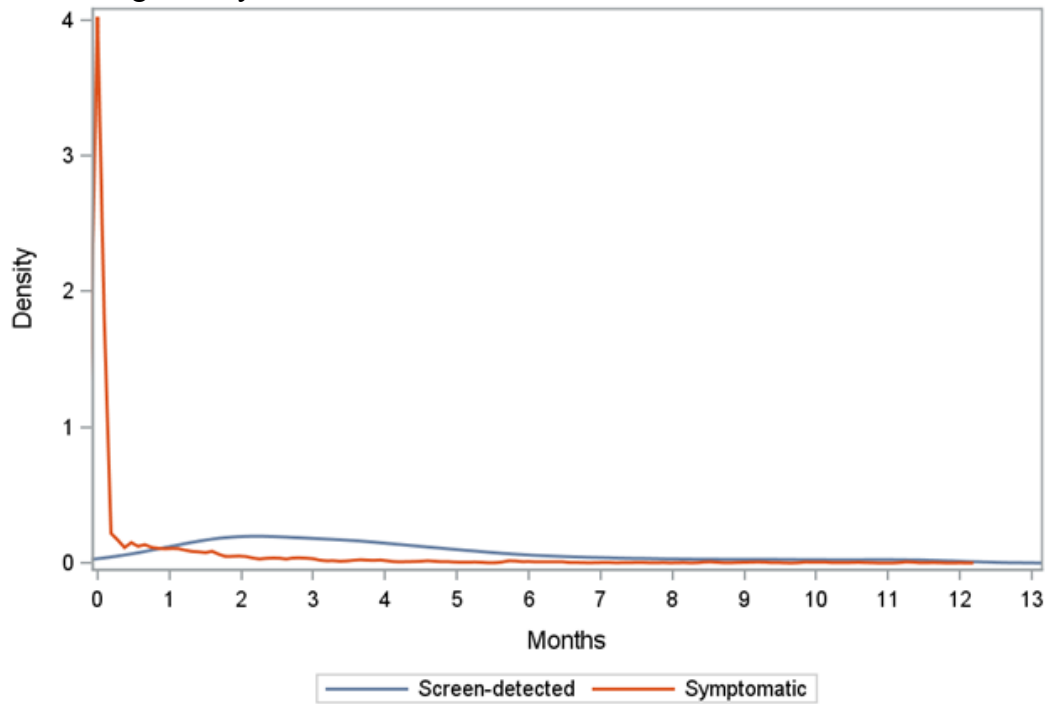


Supplementary Results

Supplementary Table 1: Number of case-control sets with different number of controls after removing women having had total hysterectomy

Number of controls	Number of case-control sets (%)
27	2 (0.1)
28	14 (0.3)
29	165 (3.9)
30	4073 (95.7)
Total	4254 (100.0)

Supplementary Figure 1: Distribution of months between the first abnormality in the past year and cervical cancer diagnosis by mode of detection recorded in the clinical chart



In this Audit, mode of detection (screen-detected or symptomatic) of all cervical cancer cases in 2002-2011 was retrieved from the clinical charts. To verify the time-frame of 6 months for removing Pap test that leads to cancer diagnosis (i.e. non-preventive test), this data was linked to the Swedish National Cervical Screening Registry (NKCx) to retrieve the last abnormal screening test in the past one year. We plotted the distribution of time (in months) between the first abnormality and cervical cancer diagnosis by mode of detection.

The result in the figure above clearly shows that the majority of cervical cancer cases had the initial abnormality within 6 months before cancer diagnosis, therefore when evaluating the screening tests leading to cancer prevention, all Pap tests within 6 months should be disregarded. The result further indicates that if the initial abnormality is within one month before cancer diagnosis, it is more likely to be a symptomatic cancer. The time-frames evaluated in this analysis can be used as a proxy in future studies which need to distinguish mode of detection of cervical cancer in absence of clinical data.

Supplementary Table 2: SNOMED codes for cytological diagnoses in the study, defined by the Swedish Association for Clinical Cytology

Cytological diagnosis	SNOMED code
Normal cytology	M00110
Low-grade abnormalities	
Atypical squamous cells of undetermined significance	M69710
Mild squamous dysplasia	M74006
High-grade abnormalities	
Suspected high-grade squamous dysplasia	M69719
Moderate squamous dysplasia	M74007
Severe squamous dysplasia	M80702
Atypical glandular cells	M69720
Atypical cells of uncertain origin	M69700
Squamous cell cancer	M80703
Adenocarcinoma/Adenocarcinoma in situ	M81403
Malignancy of uncertain origin	M80009

Supplementary Table 3: Odds ratios of cervical cancer (all stages, aged 29+) by screening status in the past two screening rounds, by histopathological type, further adjusted for parity

Screening history ^a	All types			Squamous cell cancer			Adenocarcinoma		
	Crude OR	Adjusted for education	Adjusted further for parity ^b	Crude OR	Adjusted for education	Adjusted further for parity ^b	Crude OR	Adjusted for education	Adjusted further for parity ^b
Unscr. – Unscr.	4.03(3.69-4.40)	4.14(3.79-4.52)	4.53(4.13-4.96)	5.15(4.65-5.72)	5.28(4.75-5.87)	5.80(5.20-6.46)	1.61(1.30-1.98)	1.70(1.38-2.10)	1.80(1.44-2.25)
Scr. – Unscr.	2.41(2.18-2.65)	2.40(2.18-2.65)	2.45(2.22-2.71)	2.60(2.31-2.93)	2.60(2.31-2.93)	2.65(2.35-3.00)	1.94(1.60-2.35)	1.95(1.61-2.37)	2.07(1.70-2.52)
Unscr. – Scr.	1.62(1.46-1.81)	1.63(1.46-1.81)	1.57(1.40-1.76)	1.89(1.66-2.15)	1.89(1.66-2.16)	1.82(1.59-2.09)	1.10(0.87-1.39)	1.11(0.88-1.40)	1.06(0.84-1.36)
Scr. – Scr.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

Unscr. = Unscreened; Scr. = Screened

- a. Left-hand side of hyphen represents the previous screening round, and right-hand side represents the most recent screening round
- b. Restricted to women born in 1932 and onward, due to lack of complete in the Multi-Generation Register before 1932. There were 775 (18%) case subjects born before 1932 thus were not included in the sensitivity analysis. They were at age 70-98 at cancer diagnosis. Age-specific comparisons were presented in Supplementary Table 4.

Supplementary Table 4: Odds ratios of cervical cancer (all stages) by screening status in the past two screening rounds, by age and histopathological type, further adjusted for parity

Screening history ^a	All types			Squamous cell cancer			Adenocarcinoma		
	Crude OR	Adjusted for education	Adjusted further for parity	Crude OR	Adjusted for education	Adjusted further for parity	Crude OR	Adjusted for education	Adjusted further for parity
Age 26-28^b									
Unscreened	1.75(1.23-2.48)	2.04(1.43-2.91)	1.95(1.37-2.79)	2.00(1.32-3.04)	2.31(1.51-3.53)	2.29(1.49-3.50)	0.75(0.30-1.86)	0.87(0.35-2.16)	0.65(0.25-1.66)
Screened	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Age 29-39									
Unscr. – Unscr.	2.62(2.20-3.12)	2.92(2.44-3.49)	2.71(2.26-3.25)	3.35(2.72-4.12)	3.63(2.93-4.48)	3.39(2.74-4.21)	1.14(0.74-1.73)	1.39(0.90-2.13)	1.30(0.84-2.01)
Scr. – Unscr.	3.05(2.59-3.59)	3.05(2.59-3.59)	3.04(2.58-3.58)	3.37(2.76-4.12)	3.36(2.75-4.11)	3.36(2.75-4.11)	2.49(1.81-3.41)	2.55(1.86-3.49)	2.52(1.84-3.46)
Unscr. – Scr.	1.48(1.23-1.79)	1.49(1.23-1.80)	1.48(1.22-1.79)	1.79(1.43-2.24)	1.79(1.43-2.24)	1.78(1.42-2.23)	0.84(0.55-1.27)	0.86(0.56-1.31)	0.85(0.56-1.29)
Scr. – Scr.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Age 40-49									
Unscr. – Unscr.	5.02(4.22-5.98)	5.17(4.33-6.18)	5.25(4.39-6.29)	6.58(5.30-8.15)	6.69(5.38-8.33)	6.87(5.52-8.55)	2.39(1.63-3.49)	2.56(1.74-3.77)	2.48(1.68-3.68)
Scr. – Unscr.	2.72(2.24-3.31)	2.72(2.24-3.32)	2.72(2.24-3.32)	3.09(2.41-3.95)	3.09(2.41-3.96)	3.09(2.41-3.95)	2.48(1.74-3.54)	2.50(1.75-3.57)	2.50(1.75-3.56)
Unscr. – Scr.	1.72(1.38-2.13)	1.72(1.39-2.13)	1.73(1.39-2.14)	2.01(1.54-2.62)	2.01(1.54-2.62)	2.02(1.54-2.64)	1.26(0.83-1.91)	1.27(0.83-1.93)	1.25(0.82-1.91)
Scr. – Scr.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Age 50-65									
Unscr. – Unscr.	6.16(5.30-7.16)	6.21(5.34-7.24)	6.38(5.48-7.43)	7.65(6.42-9.11)	7.73(6.48-9.23)	7.99(6.68-9.54)	1.95(1.28-2.97)	2.01(1.32-3.06)	2.05(1.34-3.12)
Scr. – Unscr.	2.03(1.67-2.47)	2.03(1.67-2.46)	2.03(1.67-2.47)	2.17(1.72-2.74)	2.17(1.72-2.74)	2.17(1.72-2.74)	1.17(0.74-1.84)	1.17(0.74-1.85)	1.18(0.75-1.86)
Unscr. – Scr.	1.53(1.24-1.90)	1.54(1.24-1.91)	1.53(1.24-1.90)	1.68(1.30-2.16)	1.68(1.30-2.16)	1.67(1.30-2.16)	1.20(0.75-1.93)	1.22(0.76-1.96)	1.23(0.76-1.97)
Scr. – Scr.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

Unscr. = Unscreened; Scr. = Screened

- a. Left hand side of hyphen represents the previous screening round, and right-hand side represents the most recent screening round
- b. Only one screening round was assessed due to age

Supplementary Table 5: Odds ratios of cervical cancer in relation to screening status in the past two screening rounds, defining screening intervals as 3/5 years and 3.5/5.5 years

Screening history ^a	Interval 3 and 5 years				Interval 3.5 and 5.5 years			
	No. of case sub.	No. of control sub.	OR	OR adjusted ^b	No. of case sub.	No. of control sub.	OR	OR adjusted ^b
Unscr. – Unscr.	1711	29670	4.03(3.69-4.40)	4.14(3.79-4.52)	1640	28485	3.87(3.55-4.21)	4.00(3.67-4.37)
Scr. – Unscr.	783	17716	2.41(2.18-2.65)	2.40(2.18-2.65)	663	14682	2.34(2.12-2.58)	2.34(2.12-2.58)
Unscr. – Scr.	502	16401	1.62(1.46-1.81)	1.63(1.46-1.81)	458	13712	1.67(1.50-1.86)	1.68(1.50-1.87)
Scr. – Scr.	1045	51829	Ref.	Ref.	1280	58737	Ref.	Ref.

Unscr. = Unscreened; Scr. = Screened

- a. Left hand side of hyphen represents the previous screening round, and right-hand side represents the most recent screening round
- b. Only one screening round was assessed due to age

Supplementary Table 6: Odds ratios of cervical cancer (all stages) among women having abnormalities compared to women unscreened in the past two screening rounds, by histological type

Screening history ^a	Squamous cell cancer				Adenocarcinoma			
	No. of case sub.	No. of control sub.	OR	OR adjusted ^a	No. of case sub.	No. of control sub.	OR	OR adjusted ^a
Unscr. – Unscr.	1368	22099	Ref.	Ref.	207	5103	Ref.	Ref.
Abn. – Nor.	52	1139	0.5 (0.4-0.7)	0.5 (0.4-0.7)	27	354	1.8 (1.1-2.7)	1.6 (1.1-2.5)
Abn. – Unscr.	62	206	3.7 (2.7-4.9)	3.5 (2.6-4.7)	17	57	6.6 (3.7-11.7)	6.2 (3.5-11.1)
Nor./Unscr. – Abn.	272	1199	2.5 (2.2-3.0)	2.5 (2.1-2.9)	74	317	5.2 (3.8-7.1)	4.9 (3.6-6.7)
Abn. – Abn.	45	226	2.3 (1.6-3.1)	2.2 (1.6-3.1)	23	68	7.7 (4.6-12.7)	7.2 (4.4-12.0)

Nor. = normal; Abn. = abnormal; Unscr. = unscreened.

- a. Left-hand side of hyphen represents the previous screening round, and right-hand side represents the most recent screening round
- b. Adjusted for education and age group

Supplementary Table 7: Odds ratios of cervical cancer (all types) in relation to screening status in the past two screening rounds, by age and stage of cancer cases

Screening status ^a	Stage IA (microinvasive)				Stage IB+ (frankly invasive)				Stage II+ (advanced)			
	No. of case sub.	No. of control sub.	OR	OR adjusted ^b	No. of case sub.	No. of control sub.	OR	OR adjusted ^b	No. of case sub.	No. of control sub.	OR	OR adjusted ^b
Age 26-28^c												
Unscreened	35	683	2.32(1.37-3.94)	2.82(1.65-4.80)	33	821	1.38(0.86-2.22)	1.57(0.97-2.53)	6	206	0.81(0.30-2.20)	1.09(0.40-2.97)
Screened	24	1087	Ref.	Ref.	38	1309	Ref.	Ref.	12	334	Ref.	Ref.
Age 29-39												
Unscr. – Unscr.	71	1639	2.14(1.58-2.89)	2.47(1.82-3.35)	152	2559	2.93(2.36-3.64)	3.19(2.56-3.98)	46	587	5.32(3.35-8.43)	5.52(3.45-8.85)
Scr. – Unscr.	128	1803	3.48(2.69-4.50)	3.51(2.71-4.53)	165	2924	2.78(2.25-3.44)	2.76(2.23-3.41)	33	596	3.74(2.28-6.12)	3.70(2.26-6.07)
Unscr. – Scr.	64	2222	1.41(1.04-1.92)	1.44(1.06-1.96)	108	3496	1.53(1.20-1.94)	1.52(1.20-1.93)	27	788	2.34(1.39-3.94)	2.32(1.38-3.91)
Scr. – Scr.	117	5704	Ref.	Ref.	194	9540	Ref.	Ref.	32	2163	Ref.	Ref.
Age 40-49												
Unscr. – Unscr.	52	724	3.83(2.64-5.56)	3.62(2.46-5.32)	219	2185	5.42(4.44-6.62)	5.71(4.67-6.99)	112	695	10.5(7.51-14.7)	10.8(7.69-15.2)
Scr. – Unscr.	50	861	3.12(2.14-4.54)	3.12(2.14-4.55)	123	2588	2.58(2.05-3.26)	2.59(2.06-3.26)	19	844	1.45(0.86-2.47)	1.45(0.86-2.47)
Unscr. – Scr.	41	1048	2.09(1.41-3.11)	2.08(1.40-3.09)	87	2998	1.58(1.22-2.04)	1.59(1.23-2.05)	22	1010	1.43(0.86-2.36)	1.41(0.86-2.34)
Scr. – Scr.	66	3498	Ref.	Ref.	192	10412	Ref.	Ref.	54	3493	Ref.	Ref.
Age 50-65												
Unscr. – Unscr.	24	375	2.55(1.56-4.16)	2.45(1.48-4.04)	361	2776	6.82(5.81-8.01)	6.91(5.88-8.13)	271	1522	14.5(11.4-18.4)	14.6(11.4-18.5)
Scr. – Unscr.	25	475	2.14(1.30-3.50)	2.11(1.29-3.45)	137	3658	2.02(1.64-2.50)	2.02(1.63-2.49)	59	1973	2.57(1.84-3.58)	2.54(1.82-3.55)
Unscr. – Scr.	22	492	1.75(1.05-2.90)	1.73(1.04-2.88)	92	3144	1.49(1.17-1.89)	1.49(1.17-1.89)	38	1658	1.84(1.26-2.69)	1.83(1.25-2.68)
Scr. – Scr.	57	2232	Ref.	Ref.	302	15243	Ref.	Ref.	101	7926	Ref.	Ref.
Age 66+^d												
Unscr. – Unscr.	18	542	0.97(0.39-2.40)	1.02(0.40-2.55)	814	18870	2.50(2.01-3.11)	2.46(1.98-3.07)	637	14662	3.06(2.33-4.02)	2.97(2.26-3.91)
Scr. – Unscr.	10	269	1.08(0.43-2.71)	1.12(0.44-2.82)	145	5138	1.27(0.99-1.64)	1.26(0.98-1.62)	102	3646	1.50(1.09-2.05)	1.47(1.07-2.01)
Unscr. – Scr.	6	112	1.57(0.52-4.71)	1.59(0.53-4.77)	82	2889	1.50(1.12-2.02)	1.50(1.11-2.02)	61	2176	1.78(1.24-2.55)	1.77(1.23-2.53)
Scr. – Scr.	9	261	Ref.	Ref.	108	4939	Ref.	Ref.	66	3579	Ref.	Ref.

Unscr. = Unscreened; Scr. = Screened

- Left hand side of hyphen represents the previous screening round, and right-hand side represents the most recent screening round
- Adjusted for education and age group
- This age group only experienced one screening round prior to cancer diagnosis
- Screening status for this age group refers to screening at ages 56-65