Survival of older women with cervical cancer: What is the impact of screening history?

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ASCCP Improving Lives Through the Prevention & Treatment of Anogenital & HPV-Related Diseases

ASCCP2018 Annual Meeting

Disclosures

- No financial relationships or conflict of interest to disclose

Introduction

- Ontario, Canada: almost 5 million women eligible for cervical cancer screening; universal health care
- Organized program with database containing screen data on 85% of women undergoing pap testing, letters of invitation, recall and results letter
- The Ontario cervical cancer screening program current guidelines recommends women between the ages of 21 – 69 to be screen every 3 years.
- Screening programs have helped reduce the incidence of invasive cervical cancer by detecting preinvasive disease
- Screening participation rates peak in 30-39 and 40-49 age groups at 65% and drop precipitously to 52.8% in the 60-69 age group.

Introduction

- Though cervical cancer screening is important for all age groups, the greatest benefit of screening is derived in older age groups

- Case Control Study published out of Ontario determined that the greatest protective effect of screening was a pap performed at 4-36 month interval in women 40-69 where as no benefit to screening at this interval in women under 40.
- OR of developing cervical cancer in 40-69 age group ranged from 0.52-0.82.

(Vicus, et al. Int J Gynecol Cancer 2015)

Introduction

- Survival Benefit due to screening in women diagnosed with cervical cancer
- Sweden: population based cohort study of 1230 women diagnosed with cervical cancer to determine cure rates and 5 year survival stratified by screening history and mode of detection.
- Cure rates in screen detected cancers was 92% and for symptomatic women as 66%. Difference in cure rate of 26%
- Benefit of screening also in symptomatic women who were screened according to recommendations with a 14% difference in cure rate.
- Conclusion: Screening associated with improved cure not due to lead time bias but due to down staging. (Andrae et al. BMJ 2012)
- Rustagi et al. (Am J of Epidem 2014) screening in 55-79 Women. OR of cervical cancer death associated with pap 5-7 years before diagnosed was 0.26. Screening women 55-79 would avert 630 deaths. better with HPV screening

Introduction

Hypothesis:

- Women over 50 with cervical cancer who do not adhere to screening guidelines have poorer survival outcomes compared to women of similar age who undergo screening cytology

Goals:

- Identify all women 50+ diagnosed with cervical cancer in Ontario between 2000-2012 and measure the association between screen history and survival

Retrospective cohort study:

Cohort: Women diagnosed with cervical cancer in Ontario between 2000 - 2012

Exclusion: women < 50 years old at diagnosis, previous hysterectomy, history of previous cervical cancer, no treatment after diagnosis, histologies other than adenocarcinoma and squamous carcinoma

Study Period: 2000-2012

Main effect variable: Previous patient screening history

- 6 months – 1 yr, 1 – 2 yrs, 2 – 3 yrs, 3 – 4 yrs, 4 – 5 yrs, more than 5 yrs/never

Primary Outcome: Overall survival

Methodology

Patient Characteristics

- Age
- Cancer stage*
- Histology
  - Adenocarcinoma
  - Squamous cell
- Neighborhood income quintile
- PEM status at diagnosis
  - Rostered
  - Not Rostered

*data only available after 2010

- Treatment after cancer diagnosis
  - Only surgery
  - Concurrent chemo-radiation
  - Only radiation
  - Only chemo
  - Surgery + chemo / radiation
- Time from index pap to cancer
- Pap cytology result
  - Normal
  - AGC/AIS
  - HSIL/ASC-H
  - LSIL/ASCUS
  - Squamous/Adenocarcinoma
  - Other
  - Unknown

Methodology: Administrative Databases

Cytobase:
- Provincial repository of all cervical cytology samples collected outside of hospitals.

Registered Persons Database(RPDB):
- Regularly updated record containing demographic information on residents of Ontario.

Ontario Health Insurance Program (OHIP):
- Provincially administered federally funded universal health system accessible to citizens, permanent residents and refugees.

Corporate physicians database (CPDB):
- Contains addresses, registration and program eligibility of healthcare providers
- Used to determine association of a patient with a primary care physician.

Ontario Cancer Registry (OCR):
- Contains 95% of all pathology reports related to cancer diagnoses in Ontario dating back to 1964.

Cancer Activity Level Reporting (ALR):
- Chemotherapy and radiation administration database

Postal Code Conversion File:
- Contains residence and demographic data at a postal code level
- Used to determine income quartiles

Methodology

Analysis

- Kaplan Meier survival (1-year, 2-year and 4-year survival)
  - Overall survival
  - Stratified by Screened/unscreened Pap
  - Stratified by treatment
  - Stratified by stage
  - Stratified by age
  - Stratified by histology
  - Stratified by Income quintiles
  - Stratified by time Pap to cancer

Models

- Univariate model for time to death after diagnosis
  - Age
  - Stage
  - Income quintiles
  - Screened/Unscreened
  - Treatment
  - PEM
- Multivariate model for time to death after diagnosis (entire cohort)
  - Age
  - Income quintiles
  - Screened/Unscreened
  - Treatment
  - PEM
- Subset analysis of time to death models for patients with known stage (Age, Income quintiles, Screened/Unscreened, PEM,Stage)

Demographic table

Characteristics of Women	Pap Performed	Pap not performed	Entire cohort
Total	566 (40%)	856 (60%)	1422
AGE	**N (%)**		
50 to 59	306 (54.1)	351 (41)	657 (46.2)
60 to 69	186 (32.9)	232 (27.1)	418 (29.4)
70+	74 (13.1)	273 (31.9)	347 (24.4)
Histology			
Adenocarcinoma	217 (38.3)	169 (19.7)	386 (27.1)
Squamous cell	349 (61.7)	687 (80.3)	1036 (72.9)
Cytology result			
AGC/AIS	11 (1.9)		11 (0.8)
HSIL/ASC-H	79 (14)		79 (5.6)
LSIL/ASCUS	50 (8.8)		50 (3.5)
Normal	328 (58)		328 (23.1)
Other	10 (1.8)		10 (0.7)
Squamous/Adenocarcinoma	4 (0.7)		4 (0.3)
Unknown	84 (14.8)		940 (66.1)

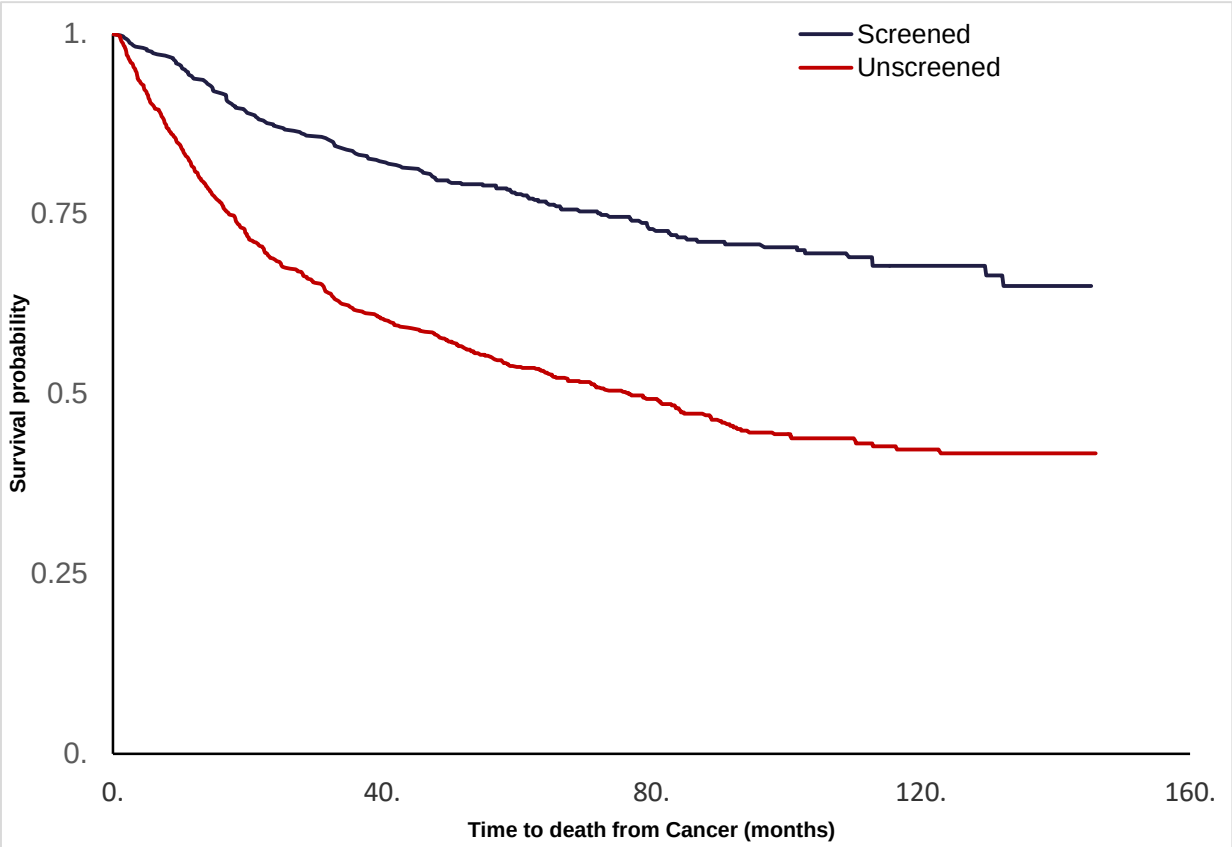
Demographic table

Characteristics of Women	Pap Performed	Pap not performed	Entire cohort
STAGE OF CANCER			
IA	59 (10.4)	50 (5.8)	109 (7.7)
IB	82 (14.5)	62 (7.2)	144 (10.1)
II	47 (8.3)	78 (9.1)	125 (8.8)
III	32 (5.7)	84 (9.8)	116 (8.2)
IV	23 (4.1)	60 (7)	83 (5.8)
Unknown	323 (57.1)	522 (61)	845 (59.4)
Treatment			
Only surgery	295 (52.1)	191 (22.3)	486 (34.2)
Concurrent chemoradiation	178 (31.4)	392 (45.8)	570 (40.1)
Only radiation	57 (10.1)	233 (27.2)	290 (20.4)
Only chemo	5 (0.9)	19 (2.2)	24 (1.7)
Surgery + chemo /rad	31 (5.5)	21 (2.5)	52 (3.7)

Demographic table

Characteristics of Women	Pap Performed	Pap not performed	Entire cohort
Time Pap to Cancer			
6-12 mo	168 (29.7)	(0)	168 (11.8)
13-24 mo	175 (30.9)	(0)	175 (12.3)
25-36 mo	104 (18.4)	(0)	104 (7.3)
37-48 mo	66 (11.7)	(0)	66 (4.6)
49-60 mo	53 (9.4)	(0)	53 (3.7)
No pap	(0)	856 (100)	856 (60.2)
Income quintiles			
Q1	103 (18.2)	211 (24.6)	314 (22.1)
Q2	101 (17.8)	165 (19.3)	266 (18.7)
Q3	97 (17.1)	124 (14.5)	221 (15.5)
Q4	109 (19.3)	128 (15)	237 (16.7)
Q5	93 (16.4)	109 (12.7)	202 (14.2)
RURAL or Unknown	63 (11.1)	119 (13.9)	182 (12.8)
PEM			
0	164 (29)	382 (44.6)	546 (38.4)
1	402 (71)	474 (55.4)	876 (61.6)

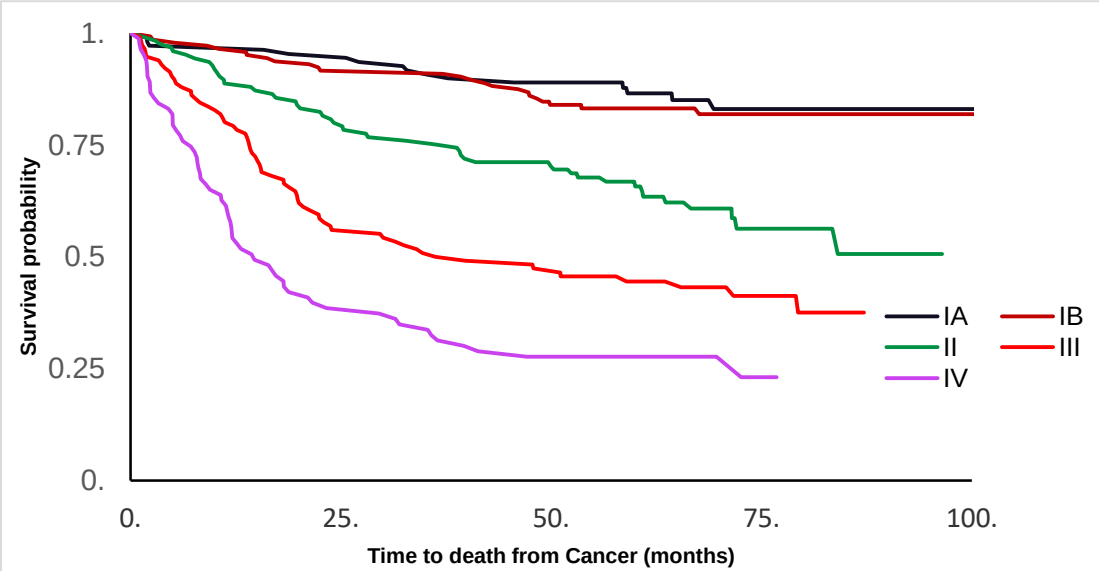
Results: Survival Analysis

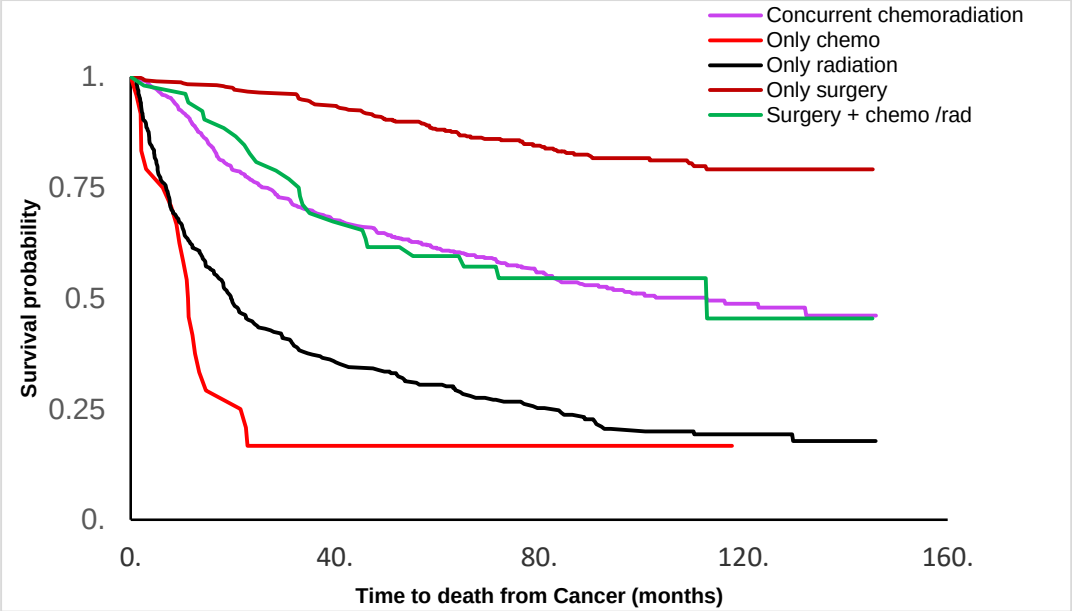


4 Year Overall Survival
Screened……79.9%
Unscreened…..58.2%
p<0.01

Figure 1. Overall Survival, full cohort.

Results: Survival Analysis





4 Year Overall Survival

Stage IA……..89.0%
Stage IB……..86.1%
Stage II……71.2%
Stage III……..47.4%
Stage IV……..27.7%

p<0.01

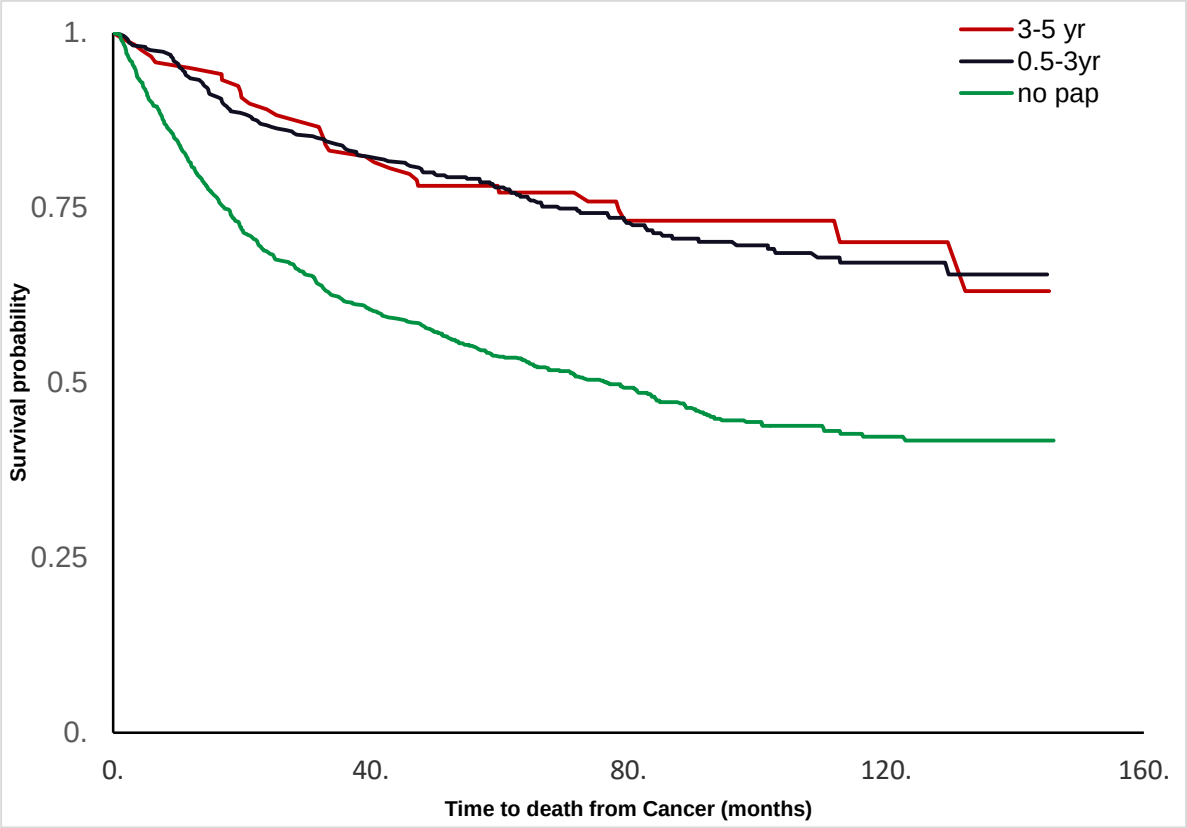
4 Year Overall Survival

Surgery……..91.2%
Chemo-Rad……..65.4%
Surgery+Chemo/
Rads……61.5%
Radiation……....34.1%
Chemotherapy……..16.1%*

p<0.01

*: 2 year survival

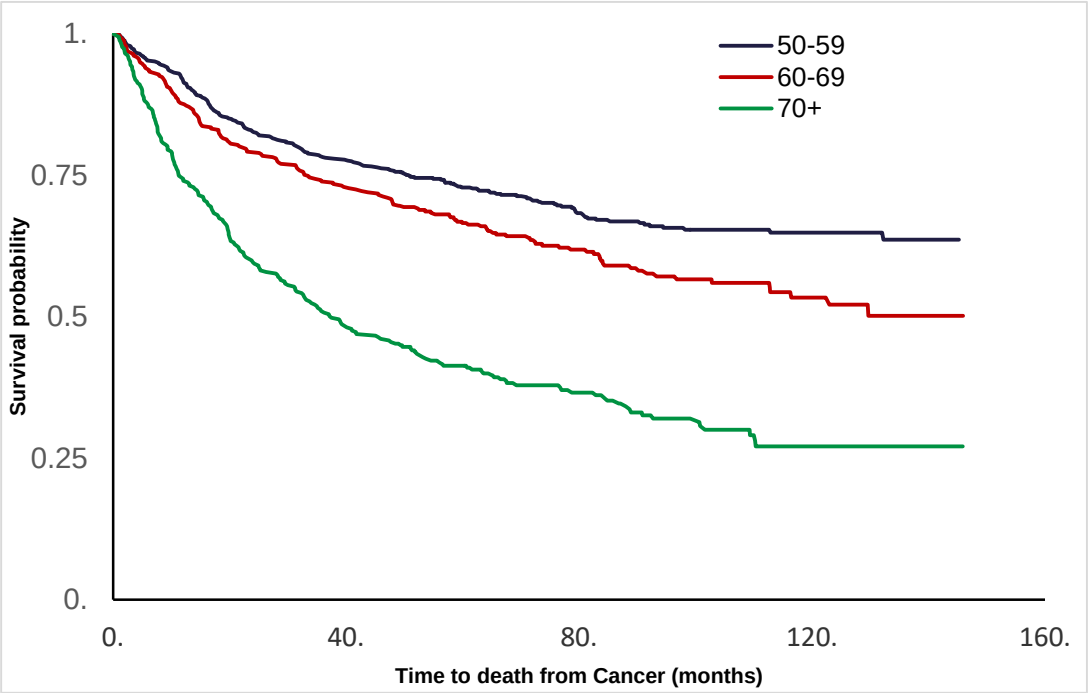
Results: Survival Analysis



4 Year Overall Survival	
No Pap	58.2%
6mo - 3 years	80.3%
3 - 5 years	78.2%
p<0.01	

Figure 4. Overall Survival: Interval from last Pap smear

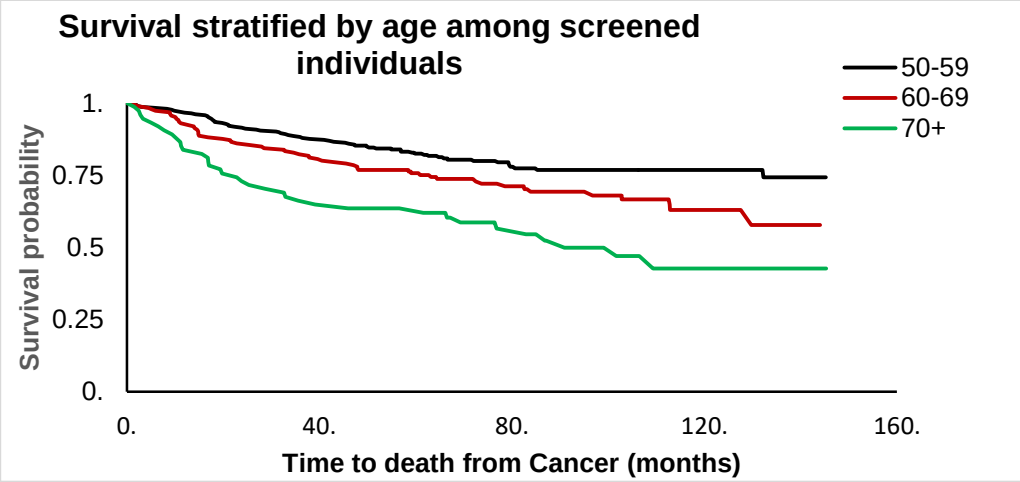
Results: Survival Analysis



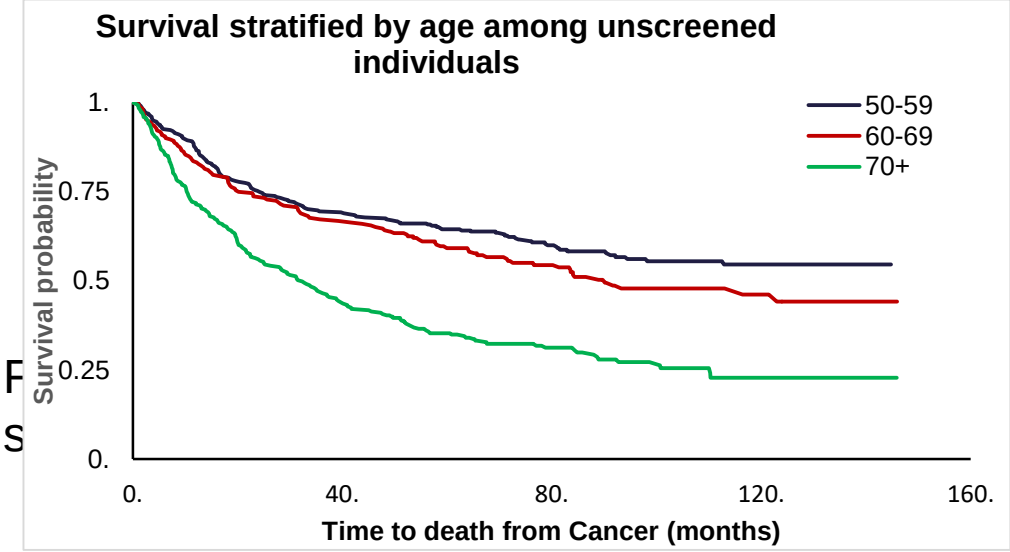
4 Year Overall Survival	
50-59 years	75.8%
60-69 years	70.1%
≥70 years	45.5%
p<0.01	

Figure 5. Overall Survival: Age

Results: Survival Analysis

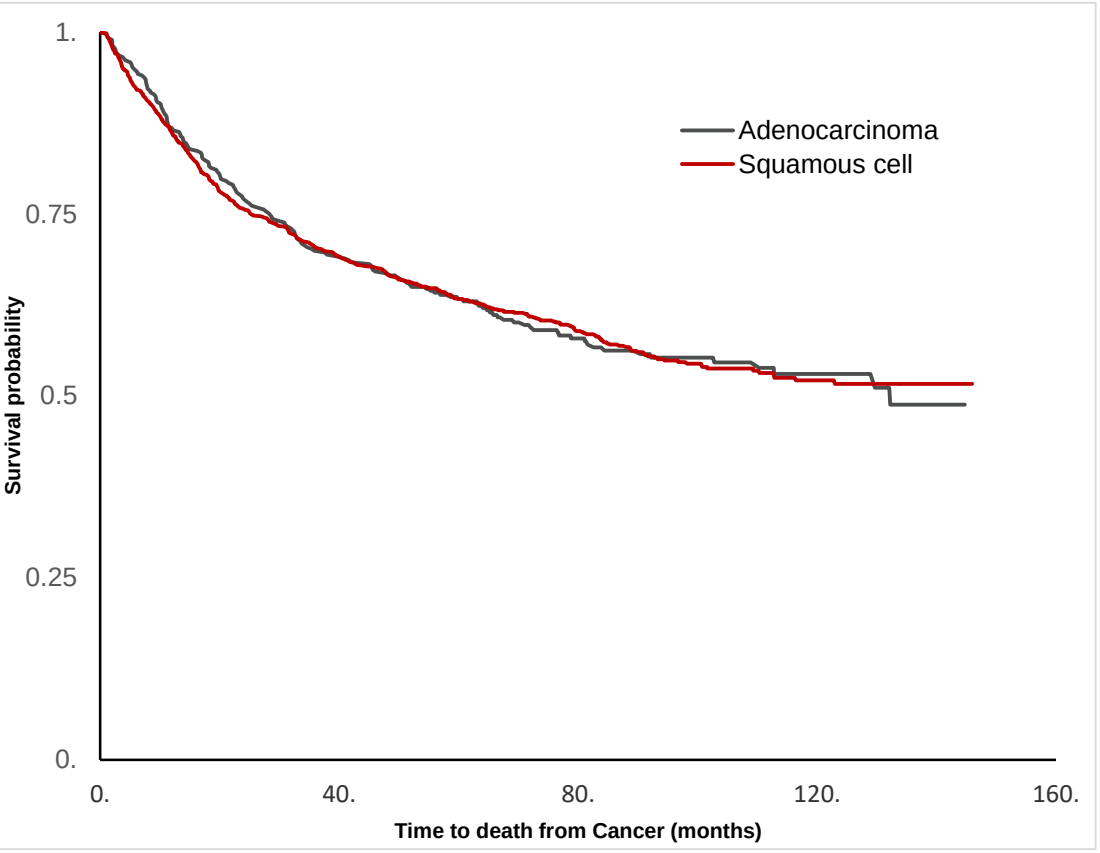


4 Year Overall Survival
50-59 years……..85.3%
60-69 years……77.4%
≥70 years……..63.5%
p<0.01



4 Year Overall Survival
50-59 years……..67.5%
60-69 years……64.2%
≥70 years……..40.7%
p<0.01

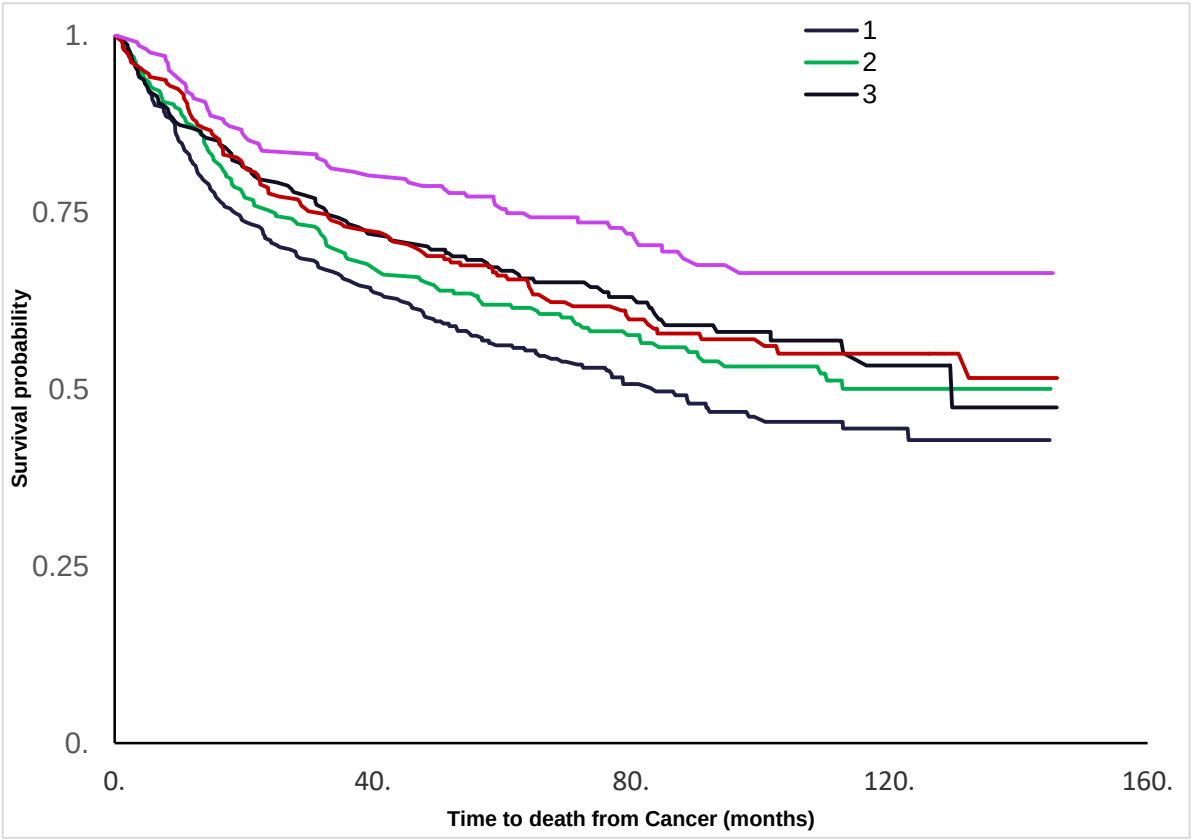
Results: Survival Analysis



4 Year Overall Survival
Adenocarcinoma……..66.8%
Squamous……66.8%
p=0.9

Figure 6. Overall Survival: Histologic sub-type

Results: Survival Analysis



4 Year Overall Survival	
Q1	60.5%
Q2	65.4%
Q3	70.1%
Q4	69.2%
Q5	78.7%
p<0.01	

Figure 7. Overall Survival: Income Quartile

Univariate model for time to death after diagnosis

Characteristics	HR	95% CI	P value
Stage			
IA	1		
IB	1.4	0.8 - 2.6	<0.01
II	3.7	2.1 - 6.4	
III	6.7	3.9 - 11.6	
IV	12	6.9 - 20.9	
Age			
50-59	1		<0.01
60 to 69	1.3	1.1 -1.6	
70+	2.8	2.3 - 3.3	
Income quintiles			
Q5	1		
Q1	1.8	1.4 - 2.4	<0.01
Q2	1.5	1.1 - 2.0	
Q3	1.3	1.0 - 1.8	
Q4	1.4	1.0 - 1.8	
Screened Pap			<0.01
yes	1		
no	2.3	1.9 - 2.7	
PEM			
yes	1		<0.01
no	1.3	1.1 - 1.5	
Treatment			
Only surgery	1		
Concurrent chemoradiation	3.4	2.7 - 4.4	<0.01
Only chemo	13.5	8.3- 21.9	
Only radiation	8.7	6.8 - 11.2	
Surgery + chemo /rad	3.1	2.0 - 4.9	

Multivariate model for time to death after diagnosis (entire cohort)

Characteristics	HR	95% CI	P value
Age			
50-59	1		<0.01
60 to 69	1.2	1.0 - 1.5	
70+	1.6	1.3 - 2.0	
Treatment			
Only surgery	1		<0.01
Concurrent chemoradiation	2.9	2.2 - 3.8	
Only chemo	16.7	9.8 - 28.6	
Only radiation	6.4	4.8 - 8.5	
Surgery + chemo /rad	3.2	2.0 - 5.1	
Income quintiles			
Q5	1		0.04
Q1	1.6	1.2 - 2.1	
Q2	1.4	1.0 - 1.9	
Q3	1.4	1.1 - 2.0	
Q4	1.4	1.0 - 1.9	
Screened Pap			
yes	1		<0.01
no	1.5	1.2 - 1.8	
PEM			
yes	1		0.16
no	1.1	1.0 - 1.3	

Multivariate model for time to death after diagnosis (Subset analysis for patients with known stage)

Characteristics	HR	95% CI	P value
Age			
50-59	1		<0.01
60 to 69	1.4	1.0 - 2.0	
70+	2.4	1.7 - 3.5	
Income quintiles			
Q5	1		0.32
Q1	1.5	1.0 - 2.3	
Q2	1.1	0.7 - 1.8	
Q3	1.1	0.6 - 1.8	
Q4	1.3	0.8 - 2.1	
Screened Pap			
yes	1		0.04
no	1.4	1.0 - 1.9	
PEM			
yes	1		0.64
no	1.1	0.8 - 1.5	
Stage			
IA	1		<0.01
IB	1.3	0.7 - 2.6	
II	3	1.6 - 5.5	
III	6	3.3 - 11.1	
IV	12.4	6.6 - 23.0	

Discussion & Recommendations

- Women >50 years old who do not adhere to screening guidelines are 50% more likely to die than their screened counterparts after cancer diagnosis
- Women at the lowest socio-economic level are 60% more likely to die than those at the highest income quintile
- Having a primary care physician was not associated with a survival advantage
- Patients and providers should be mindful of the importance of cervical cancer screening in older women given the significant survival advantage to screening
- Outreach campaigns should consider focusing on women over the age of 50