

Using Cancer Registry Data for Post Marketing Surveillance of Rare Cancers

Hannah K Weir, PhD

Epidemiology and Applied Research Branch
Division of Cancer Prevention and Control
CDC

NAACCR Annual Conference
June 22, 2011



...the DES story as told by population-based cancer registries....

History of Diethylstilbestrol (DES) use in the US

- ❑ DES, a synthetic oral estrogen, was developed in 1938
- ❑ DES was thought to prevent adverse pregnancy outcomes and was commonly prescribed to pregnant women beginning in the late 1940s
- ❑ In 1971, Herbst et al. reported an association between prenatal DES use and the occurrence of CCA of the vagina in young female offspring
- ❑ Later in 1971, the FDA issued an adverse health effects warning and use was discontinued
- ❑ In 1980, DES was declared a known human carcinogen

History of Diethylstilbestrol (DES) use in the US

- ❑ DES, a synthetic oral estrogen, was developed in 1938
- ❑ DES was thought to prevent adverse pregnancy outcomes and was commonly prescribed to pregnant women beginning in the late 1940s
- ❑ In 1971, Herbst et al. reported an association between prenatal DES use and the occurrence of CCA of the vagina in young female offspring
- ❑ Later in 1971, the FDA issued an adverse health effects warning and use was discontinued
- ❑ In 1980, DES was declared a known human carcinogen
- ❑ **Between 1947-1971, ~1-2% of pregnant women (~5-10 M mothers and their offspring) were exposed**

DES Related Cancers

- ❑ Clear cell adenocarcinoma (CCA)
 - an epithelial tumor that can occur at many sites including the cervix and vagina
 - rare and occurs predominately in postmenopausal women
 - literature supports a strong association between prenatal DES exposure and increased risk of CCA
- ❑ Testicular cancer (TC)
 - predominately germ cell tumors in young men
 - somewhat rare with peak incidence in adolescent and young adult men
 - incidence has been increasing in past several decades (birth cohort effect)
 - literature reports possible increased risk of TC in male offspring with pre natal DES exposure

Methods

❑ **Cancer Registry data:**

- SEER - 9, 1973-2007, 10% US population
- USCS* (NPCR/SEER), 1998-2006, ~64% US population

❑ **Case Definition:** malignant cancers

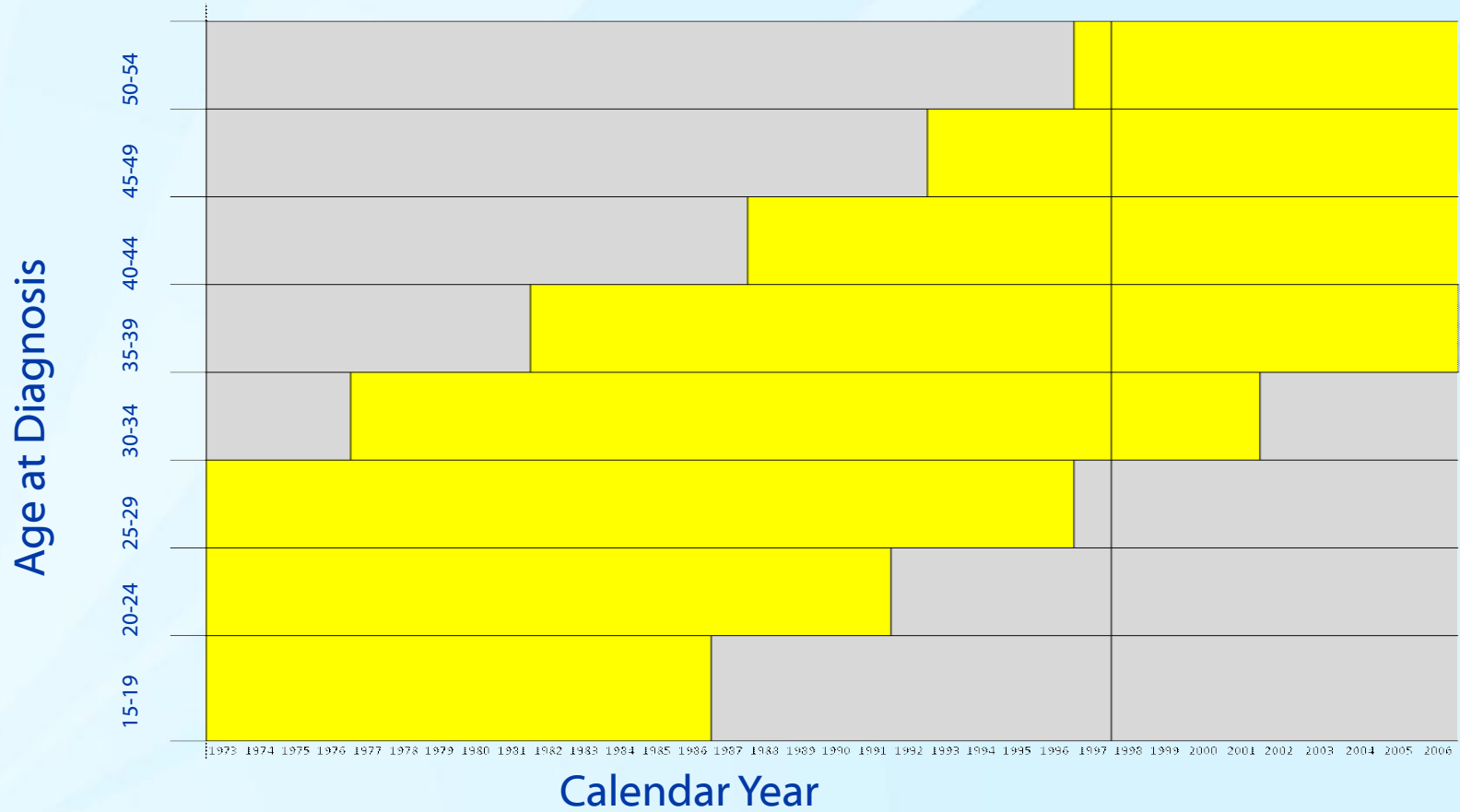
- CCA :M 8310 of the vagina (C52.9) or cervix (C53.0-53.9)
- TC: C62.0-62.9

* United States Cancer Statistics (USCS) database

DES exposed birth cohort by age and calendar year

SEER - 9

USCS



Statistical Methods

- ❑ Indirect standardization method used to compare an expected (E) number of cases to an observed (O) number of cases by gender, age and calendar year of diagnosis
- ❑ Expected case counts generated by applying incidence rates from unexposed populations to counts from potentially exposed populations by gender, age and calendar year
- ❑ O/E ratios and corresponding 95% confidence intervals (CI) calculated for each 5 year age group

**RESULTS: CLEAR CELL
ADENOCARCINOMA (CCA)**

CCA: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	7	3.98	1.8 (0.5, 5.6)
45-49 yrs	1996-2007	6	3.40	1.8 (0.4, 10.9)
40-44 yrs	1991-2007	20	4.39	4.6 (1.1, 40.2)
35-39 yrs	1986-2006	17	12.09	1.4 (0.4, 7.5)
30-34 yrs	1981-2001	8	8.43	1.0 (0.1, 42.1)
25-29 yrs	1976-1996	20	3.30	6.1 (0.9, 251.1)
20-24 yrs	1973-1991	20	6.67	3.0 (1.0, 2.1)
15-19 yrs	1973-1986	8	3.42	2.3 (0.6, 10.6)
USCS				
50-54 yrs	2001-2007	91	40.98	2.2 (1.1, 5.3)
45-49 yrs	1998-2007	104	29.53	3.5 (1.2, 17.4)
40-44 yrs	1998-2007	105	27.54	3.8 (1.1, 31.9)
35-39 yrs	1998-2006	53	53.64	0.9 (0.3, 4.9)
30-34 yrs	1998-2001	13	15.60	0.8 (0.1, 35.4)

CCA: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	7	3.98	1.8 (0.5, 5.6)
45-49 yrs	1996-2007	6	3.40	1.8 (0.4, 10.9)
40-44 yrs	1991-2007	20	4.39	4.6 (1.1, 40.2)
35-39 yrs	1986-2006	17	12.09	1.4 (0.4, 7.5)
30-34 yrs	1981-2001	8	8.43	1.0 (0.1, 42.1)
25-29 yrs	1976-1996	20	3.30	6.1 (0.9, 251.1)
20-24 yrs	1973-1991	20	6.67	3.0 (1.0, 2.1)
15-19 yrs	1973-1986	8	3.42	2.3 (0.6, 10.6)
USCS				
50-54 yrs	2001-2007	91	40.98	2.2 (1.1, 5.3)
45-49 yrs	1998-2007	104	29.53	3.5 (1.2, 17.4)
40-44 yrs	1998-2007	105	27.54	3.8 (1.1, 31.9)
35-39 yrs	1998-2006	53	53.64	0.9 (0.3, 4.9)
30-34 yrs	1998-2001	13	15.60	0.8 0.1, 35.4)

CCA: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	7	3.98	1.8 (0.5, 5.6)
45-49 yrs	1996-2007	6	3.40	1.8 (0.4, 10.9)
40-44 yrs	1991-2007	20	4.39	4.6 (1.1, 40.2)
35-39 yrs	1986-2006	17	12.09	1.4 (0.4, 7.5)
30-34 yrs	1981-2001	8	8.43	1.0 (0.1, 42.1)
25-29 yrs	1976-1996	20	3.30	6.1 (0.9, 251.1)
20-24 yrs	1973-1991	20	6.67	3.0 (1.0, 2.1)
15-19 yrs	1973-1986	8	3.42	2.3 (0.6, 10.6)
USCS				
50-54 yrs	2001-2007	91	40.98	2.2 (1.1, 5.3)
45-49 yrs	1998-2007	104	29.53	3.5 (1.2, 17.4)
40-44 yrs	1998-2007	105	27.54	3.8 (1.1, 31.9)
35-39 yrs	1998-2006	53	53.64	0.9 (0.3, 4.9)
30-34 yrs	1998-2001	13	15.60	0.8 (0.1, 35.4)

CCA: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	7	3.98	1.8 (0.5, 5.6)
45-49 yrs	1996-2007	6	3.40	1.8 (0.4, 10.9)
40-44 yrs	1991-2007	20	4.39	4.6 (1.1, 40.2)
35-39 yrs	1986-2006	17	12.09	1.4 (0.4, 7.5)
30-34 yrs	1981-2001	8	8.43	1.0 (0.1, 42.1)
25-29 yrs	1976-1996	20	3.30	6.1 (0.9, 251.1)
20-24 yrs	1973-1991	20	6.67	3.0 (1.0, 2.1)
15-19 yrs	1973-1986	8	3.42	2.3 (0.6, 10.6)
USCS				
50-54 yrs	2001-2007	91	40.98	2.2 (1.1, 5.3)
45-49 yrs	1998-2007	104	29.53	3.5 (1.2, 17.4)
40-44 yrs	1998-2007	105	27.54	3.8 (1.1, 31.9)
35-39 yrs	1998-2006	53	53.64	0.9 (0.3, 4.9)
30-34 yrs	1998-2001	13	15.60	0.8 (0.1, 35.4)

RESULTS: TESTICULAR CANCER (TC)

TC: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	260	204	1.3 (1.1-1.5)
45-49 yrs	1996-2007	750	535	1.4 (1.3-1.6)
40-44 yrs	1991-2007	1,621	970	1.7 (1.5-1.9)
35-39 yrs	1986-2006	2,512	1,519	1.7 (1.5-1.9)
30-34 yrs	1981-2001	2,710	1,519	1.8 (1.5-2.1)
25-29 yrs	1976-1996	2,333	2,845	0.8 (0.7-0.9)
20-24 yrs	1973-1991	1,306	1,616	0.8 (0.7-0.9)
15-19 yrs	1973-1986	284	405	0.7 (0.6-0.8)
USCS				
50-54 yrs	2001-2007	2,549	2,094	1.2 (1.1-1.4)
45-49 yrs	1998-2007	6,236	4,639	1.3 (1.2-1.5)
40-44 yrs	1998-2007	9,609	6,087	1.6 (1.4-1.8)
35-39 yrs	1998-2006	11,028	6,752	1.6 (1.5-1.8)
30-34 yrs	1998-2001	5,301	2,842	1.9 (1.6-2.2)

TC: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	260	204	1.3 (1.1-1.5)
45-49 yrs	1996-2007	750	535	1.4 (1.3-1.6)
40-44 yrs	1991-2007	1,621	970	1.7 (1.5-1.9)
35-39 yrs	1986-2006	2,512	1,519	1.7 (1.5-1.9)
30-34 yrs	1981-2001	2,710	1,519	1.8 (1.5-2.1)
25-29 yrs	1976-1996	2,333	2,845	0.8 (0.7-0.9)
20-24 yrs	1973-1991	1,306	1,616	0.8 (0.7-0.9)
15-19 yrs	1973-1986	284	405	0.7 (0.6-0.8)
USCS				
50-54 yrs	2001-2007	2,549	2,094	1.2 (1.1-1.4)
45-49 yrs	1998-2007	6,236	4,639	1.3 (1.2-1.5)
40-44 yrs	1998-2007	9,609	6,087	1.6 (1.4-1.8)
35-39 yrs	1998-2006	11,028	6,752	1.6 (1.5-1.8)
30-34 yrs	1998-2001	5,301	2,842	1.9 (1.6-2.2)

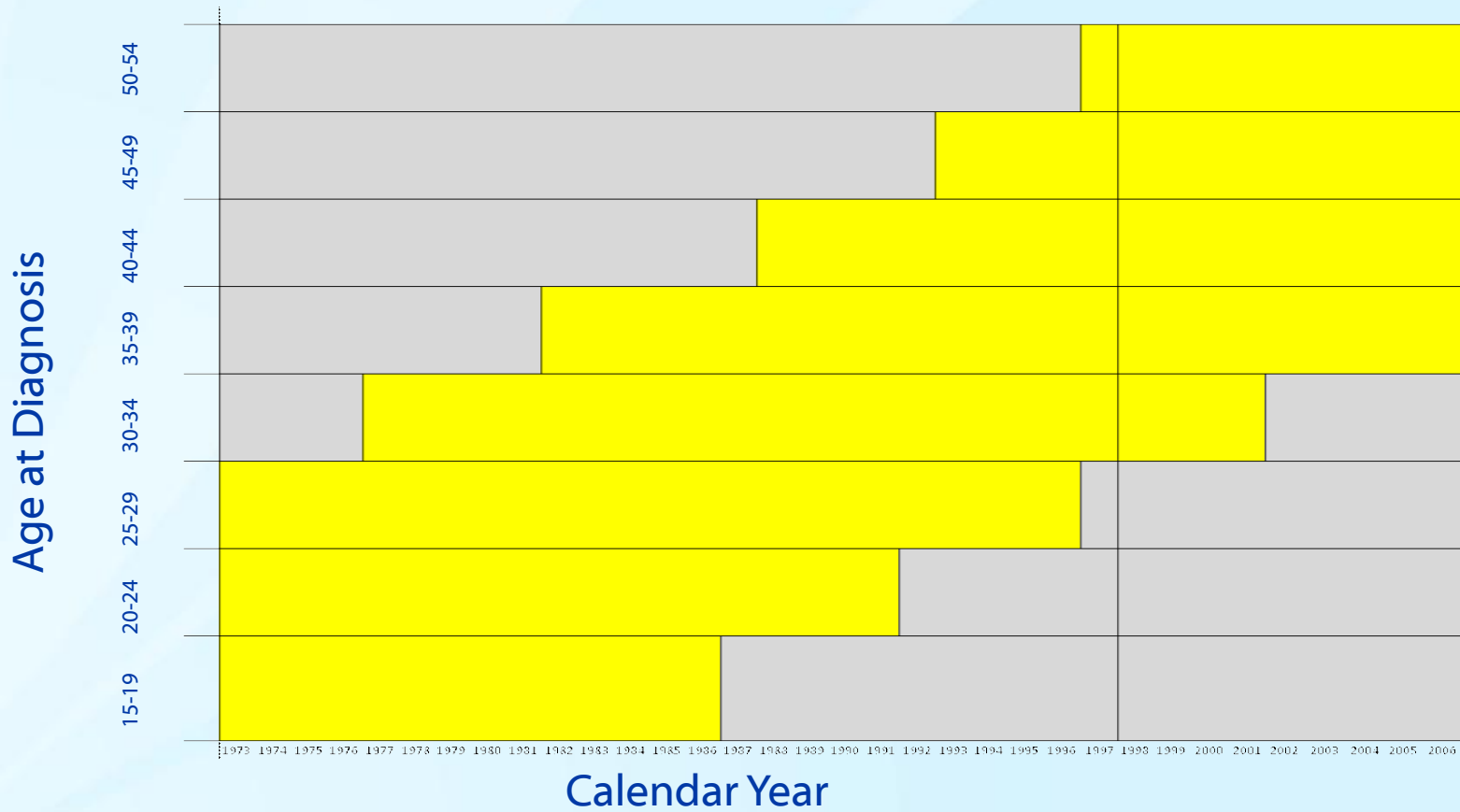
TC: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	260	204	1.3 (1.1-1.5)
45-49 yrs	1996-2007	750	535	1.4 (1.3-1.6)
40-44 yrs	1991-2007	1,621	970	1.7 (1.5-1.9)
35-39 yrs	1986-2006	2,512	1,519	1.7 (1.5-1.9)
30-34 yrs	1981-2001	2,710	1,519	1.8 (1.5-2.1)
25-29 yrs	1976-1996	2,333	2,845	0.8 (0.7-0.9)
20-24 yrs	1973-1991	1,306	1,616	0.8 (0.7-0.9)
15-19 yrs	1973-1986	284	405	0.7 (0.6-0.8)
USCS				
50-54 yrs	2001-2007	2,549	2,094	1.2 (1.1-1.4)
45-49 yrs	1998-2007	6,236	4,639	1.3 (1.2-1.5)
40-44 yrs	1998-2007	9,609	6,087	1.6 (1.4-1.8)
35-39 yrs	1998-2006	11,028	6,752	1.6 (1.5-1.8)
30-34 yrs	1998-2001	5,301	2,842	1.9 (1.6-2.2)

DES exposed birth cohort by age and calendar year

SEER - 9

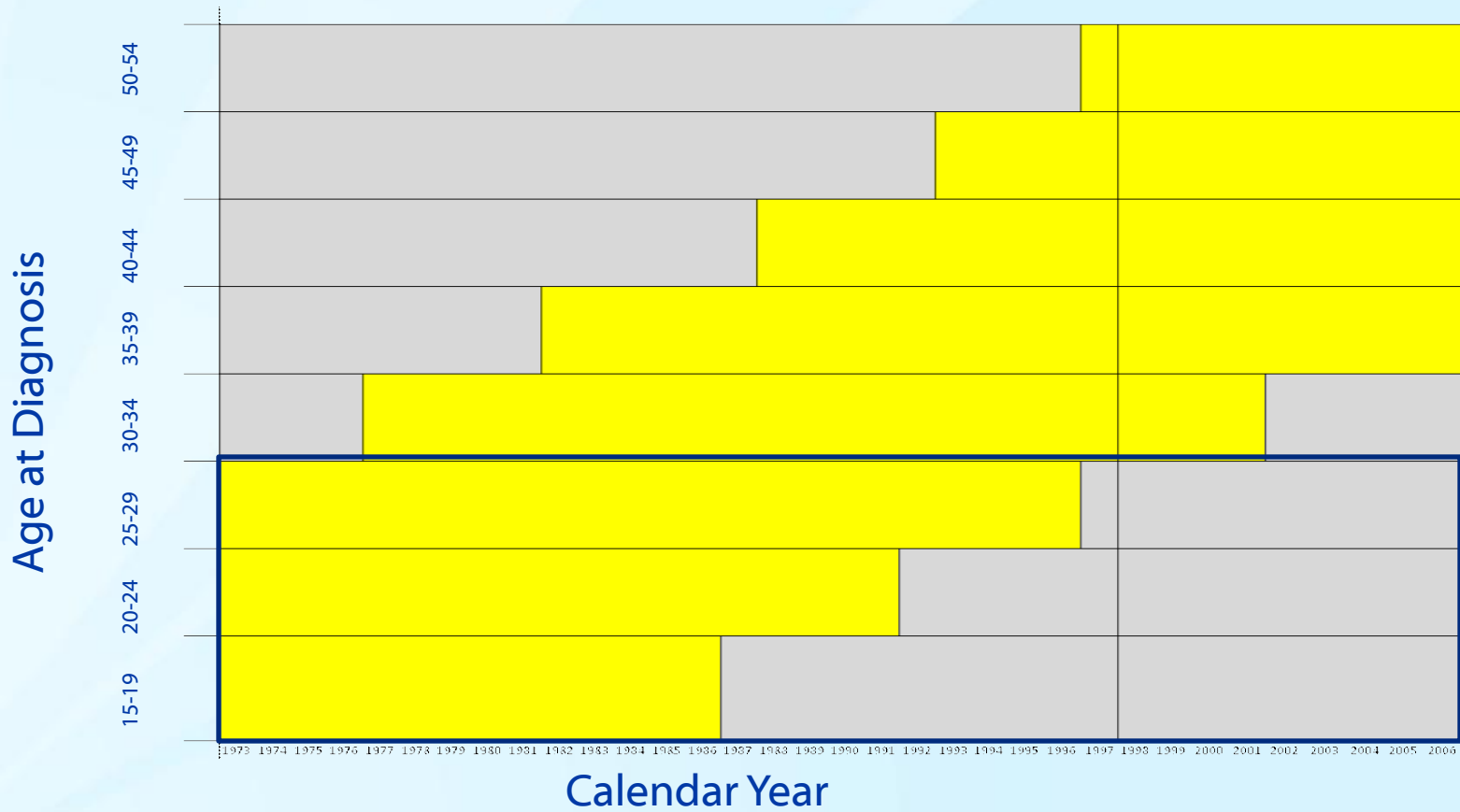
USCS



DES exposed birth cohort by age and calendar year

SEER - 9

USCS



TC: observed (O) and expected (E) case counts and rate ratios by age and calendar year

Age at Diagnosis	Diagnosis year	O	E	O/E (95% CI)
SEER = 9				
50-54 yrs	2001-2007	260	204.	1.3 (1.1-1.5)
45-49 yrs	1996-2007	750	535	1.4 (1.3-1.6)
40-44 yrs	1991-2007	1,621	970.	1.7 (1.5-1.9)
35-39 yrs	1986-2006	2,512	1,519	1.7 (1.5-1.9)
30-34 yrs	1981-2001	2,710	1,519	1.8 (1.5-2.1)
25-29 yrs	1976-1996	2,333	2,845	0.8 (0.7-0.9)
20-24 yrs	1973-1991	1,306	1,616.	0.8 (0.7-0.9)
15-19 yrs	1973-1986	284	405	0.7 (0.6-0.8)
USCS				
50-54 yrs	2001-2007	2,549	2,094	1.2 (1.1-1.4)
45-49 yrs	1998-2007	6,236	4,639	1.3 (1.2-1.5)
40-44 yrs	1998-2007	9,609	6,087	1.6 (1.4-1.8)
35-39 yrs	1998-2006	11,028	6,752	1.6 (1.5-1.8)
30-34 yrs	1998-2001	5,301	2,842	1.9 (1.6-2.2)

Conclusion

- ❑ **Clear Cell Adenocarcinoma of cervix and vagina**
 - Women born during the period of prenatal DES use continue to be at elevated risk for CCA
 - < 30 years: elevated risk
 - 30-39 years: no risk
 - 40-54 years: elevated risk
 - *but only reached statistical significance in all age groups when using USCS data*
 - These women should continue to be monitored carefully for vaginal and cervical cancers
- ❑ **Testicular Cancer**
 - Pattern of risk is consistent with a birth cohort effect

Strengths and Limitations

Strength

- population based study using high quality Incidence data with large nationwide coverage in USCS database
- indirect standardization allowed for investigation of rare cancers

Limitations

- low statistical power
- population of exposed is unknown
- exposure status of cases is unknown
- use of DES varied by region in U.S.

Implications and Future Directions

Nationwide network of population-based cancer registries can be used to:

- monitor the occurrence of adverse and rare events

FDA: Adverse Event Reporting System (AERS) (<http://www.fda.gov>)

- surveillance of rare cancers could provide information to clinicians and patients regarding the burden of rare cancers - rare individually, they constitute ~ 15% of all cancers diagnosed, Rarecare (<http://www.rarecare.eu/>)

Acknowledgements

Trevor Thompson, BS
Emily Smith, MPH
Mary C White, ScD
Lucy Peipins, PhD

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

