Non-differential Misclassification of **Outcome**

Truth	Measured
P	P

Truth	Measured
P	P

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
P	N

Truth	Measured
P	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Radiotherapy Only

True risk of progression: 4/10
Measured in the study: 2/10

Truth	Measured
P	P

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
P	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Truth	Measured
N	N

Radiotherapy + chemotherapy

True risk of progression: 2/10
Measured in the study: 1/10

True RR = (2/10)/(4/10)= 1/2
True RD = (2/10)-(4/10)= -1/5

Measured RR =(1/10)/(2/10)= 1/2
Measured RD=(1/10)-(2/10)= -1/10

Closer Look at RR & RD

	Radio + Chemo	**Radiotherapy Only**	
Progression	1	2	3
No Progression	9	8	17
	10	10	20

RR = (1/10) / (2/10) = 1/2 TRUE: 1/2 No bias
RD = (1/10) – (2/10) = -1/10 TRUE: -1/5 Bias toward null (0)

<u>Change the referent group:</u>
1/RR = 2 TRUE: 2 No bias
RD = (2/10) – (1/10) = 1/10 TRUE: 1/5 Bias toward null (0)
Even though RD is positive it's still closer to zero!

What is Snoopy's Problem?
Detection or Correct Assignment of Status?

	Truth		
	Progression	**No Progression**	
Progression	3	0	3
No Progression	3	14	17
	6	14	20

Detection:

Sensitivity = P(T+|D+)
= 3/6
= 50% → true positive rate
1-Sensitivity = 1-P(T+|D+)
= P(T-|D+)
= 1-50% → false negative rate

Correct Assignment of Status:

Specificity = P(T-|D-)
= 14/14
= 100% → true negative rate
1-Specificity = 1-P(T-|D-)
= P(T+|D-)
= 1-100%
= 0 → false positive rate

What is Snoopy's Problem?

	Truth		
	Progression	**No Progression**	
Progression	3	0	3
No Progression	3	14	17
	6	14	20

- Snoopy has a problem **detecting** disease progression
  - Sensitivity= 50% → finds 50% of the cases
  - 1-Sensitivity = 50% → misses 50% of the cases
- But when Snoopy sees a case that hasn't progressed he's correctly identifies this every time
  - Specificity = 100%
  - 1-Specificity = 0 False positives → Never mistakenly identifies a progression

What if specificity was < 1?

Truth	Measured
P	P
P	P
N	P
N	P
N	N

Truth	Measured
P	P
P	P
N	P
N	P
N	N

Truth	Measured
P	P
N	P
N	P
N	N
N	N

Truth	Measured
P	P
N	P
N	P
N	N
N	N

Radiotherapy Only

True risk of progression: 4/10
Measured in the study: 7/10

Radiotherapy + chemotherapy

True risk of progression: 2/10
Measured in the study: 6/10

True RR = (2/10)/(4/10)= 1/2
True RD = (2/10)-(4/10)= -1/5

Measured RR =(6/10)/(7/10)= 6/7
Measured RD=(6/10)-(7/10)= -1/10

Closer Look at RR & RD

	Radio + Chemo	**Radiotherapy Only**	
Progression	6	7	13
No Progression	4	3	7
	10	10	20

RR = (6/10) / (7/10) = 6/7 TRUE: 1/2 Bias toward null (1)
RD = (6/10) – (7/10) = -1/10 TRUE: -1/5 Bias toward null (0)

<u>Change the referent group:</u>
1/RR = 7/6 = 1.2 TRUE: 2 Bias toward null (1).
RD = (7/10) – (6/10) = 1/10 TRUE: 1/5 Bias toward null (0)

Even though RD is positive it's still closer to zero!

What is Snoopy's Problem?
Detection or Correct Assignment of Status?

	Truth		
	Progression	**No Progression**	
Progression	6	7	13
No Progression	0	7	7
	6	14	20

Detection:

Sensitivity = P(T+|D+)
= 6/6
= 100% → true positive rate
1-Sensitivity = 1-P(T+|D+)
= P(T-|D+)
= 0% → false negative rate

Correct Assignment of Status:

Specificity = P(T-|D-)
= 7/14
= 50% → true negative rate
1-Specificity = 1-P(T-|D-)
= P(T+|D-)
= 50% false positive rate

What is Snoopy's Problem?

	Truth		
	Progression	**No Progression**	
Progression	6	7	13
No Progression	0	7	7
	6	14	20

- Snoopy is perfect at detecting disease progression
  - Sensitivity= 100% → finds 100% of the cases
  - 1-Sensitivity = 0% → misses 0% of the cases
- But when Snoopy sees a case that hasn't progressed he has a hard time figuring it out
  - Specificity = 50% → only finds half of the true negatives
  - 1-Specificity = 50% false positive rate! **BAD DOG!**

Misclassification of Outcome in a Cohort Study

Applies to binary outcomes only

- Assuming **non-differential** misclassification
  - All errors occur equally between exposure groups

- Errors in detection (sensitivity < 100%) but not assignment of status (specificity=100%)
  - RR is not biased; RD biased towards null value

- No errors in detection (sensitivity=100%) but errors in assignment of status (specificity < 100%)
  - RR, RD are both biased toward the null value

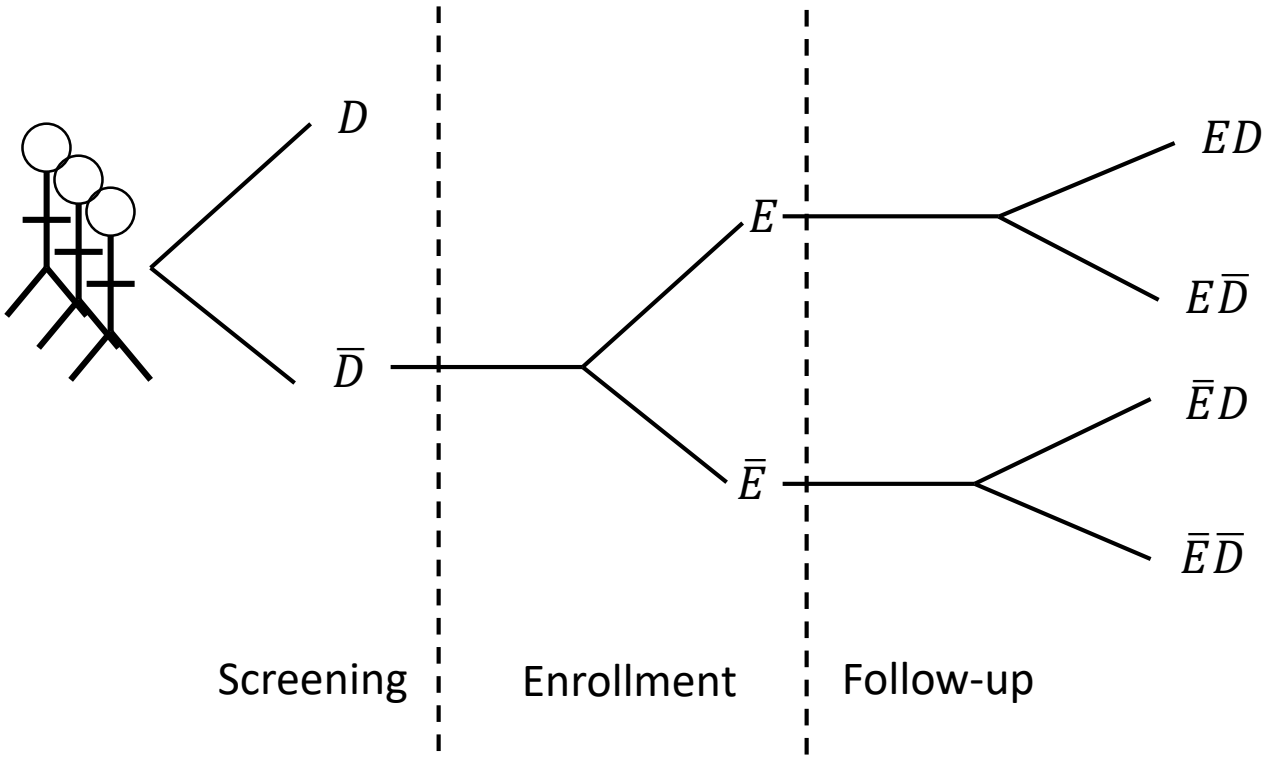
- Errors in detection (sensitivity < 100%) and assignment of status (specificity < 100%)?

Misclassification of Outcome in a Cohort Study

Applies to binary outcomes only

- If misclassification is differential
  - Misclassification of outcome is unequal between exposure groups
- RR and RD can be biased either toward or away from null
- Direction of the bias depends which group has more misclassification
- We won't cover this in detail in our class

Cohort Study Design



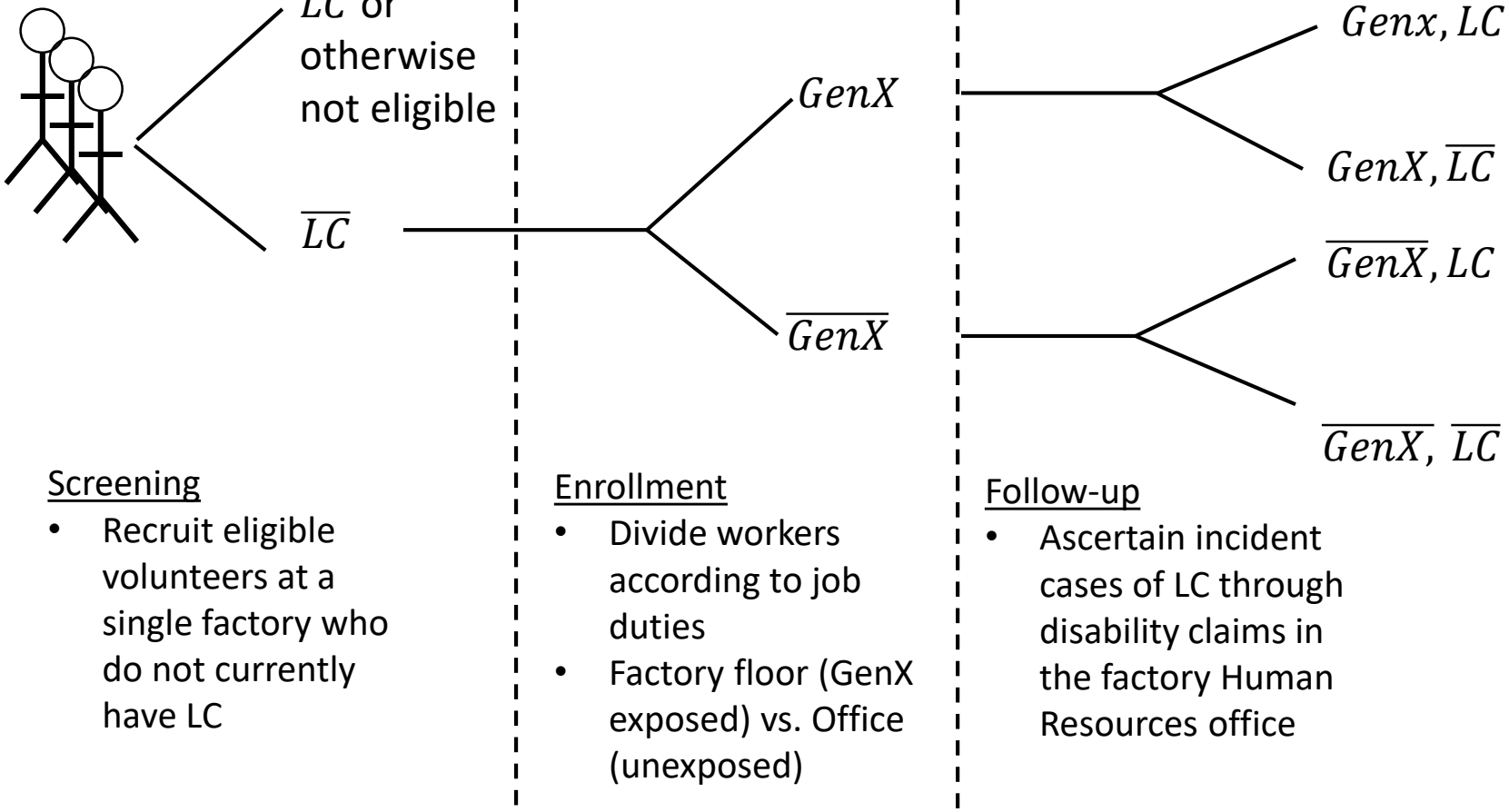
Retrospective vs. Prospective

- Use of these terms is not recommended
  - Meaning is inconsistent in the literature/textbooks
  - Not specific to a single study design
  - Does not necessarily imply weakness
- Instead, consider on a case-by-case basis…
  - Can knowledge of the outcome influence correct classification of the exposure?

See assigned reading by Rothman, et al. Modern Epidemiology, 3rd Ed. Page 95-96.

Example:

Occupational GenX Exposure and Lung Cancer (LC)



Screening

- Recruit eligible volunteers at a single factory who do not currently have LC

Enrollment

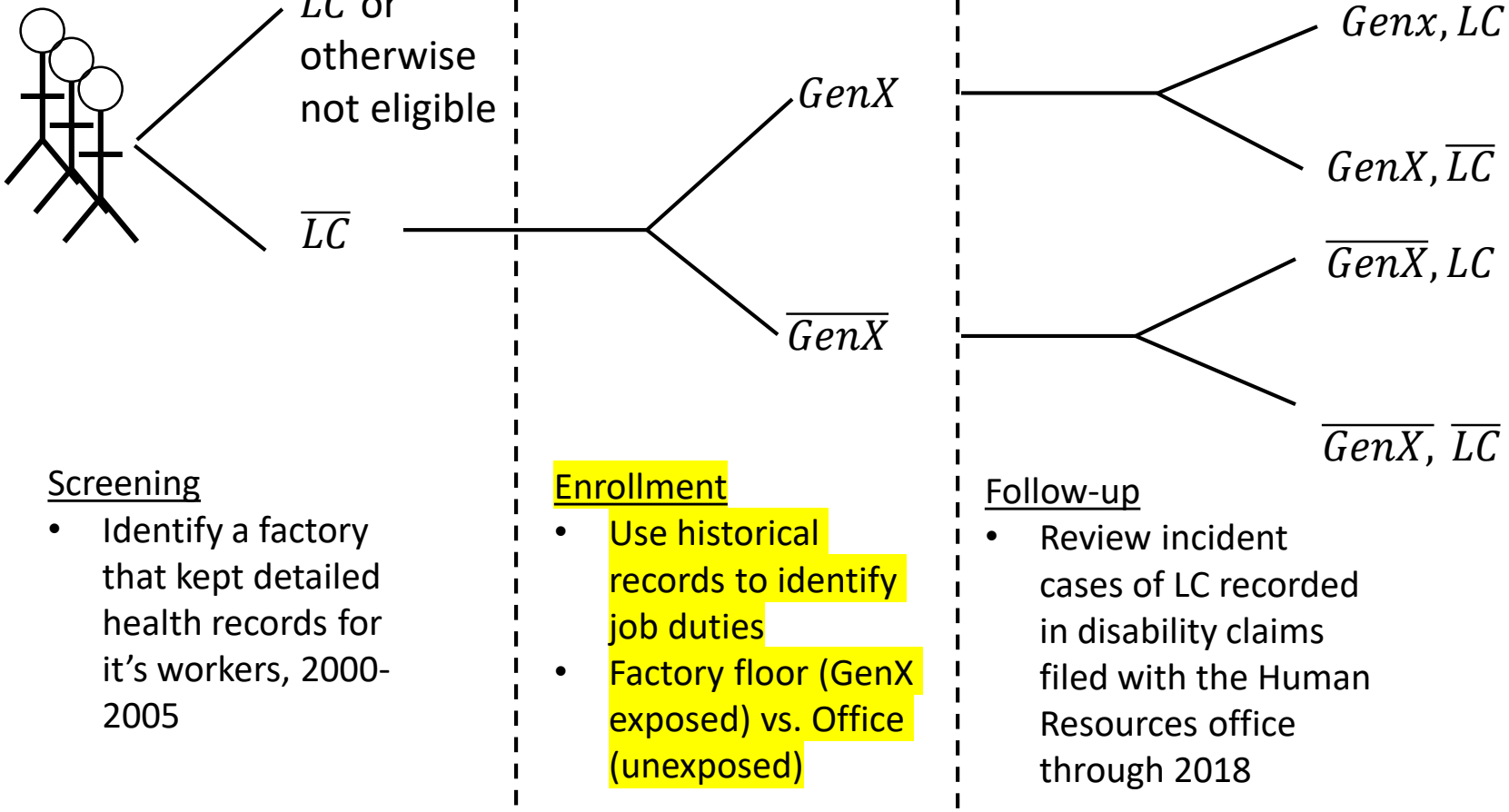
- Divide workers according to job duties
- Factory floor (GenX exposed) vs. Office (unexposed)

Follow-up

- Ascertain incident cases of LC through disability claims in the factory Human Resources office

Example:

Occupational GenX Exposure and Lung Cancer (LC)



Screening

- Identify a factory that kept detailed health records for it's workers, 2000-2005

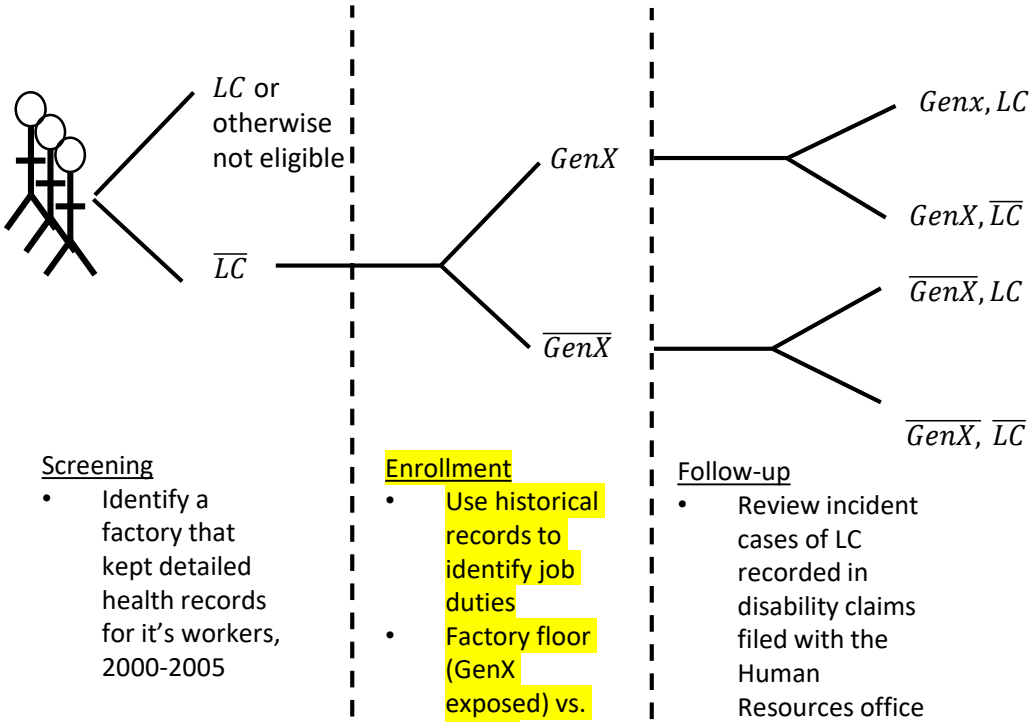
Enrollment

- Use historical records to identify job duties
- Factory floor (GenX exposed) vs. Office (unexposed)

Follow-up

- Review incident cases of LC recorded in disability claims filed with the Human Resources office through 2018

Misclassification of E Related to O



Screening
- Identify a factory that kept detailed health records for it's workers, 2000-2005

Enrollment
- Use historical records to identify job duties
- Factory floor (GenX exposed) vs. Office (unexposed)

Follow-up
- Review incident cases of LC recorded in disability claims filed with the Human Resources office through 2018

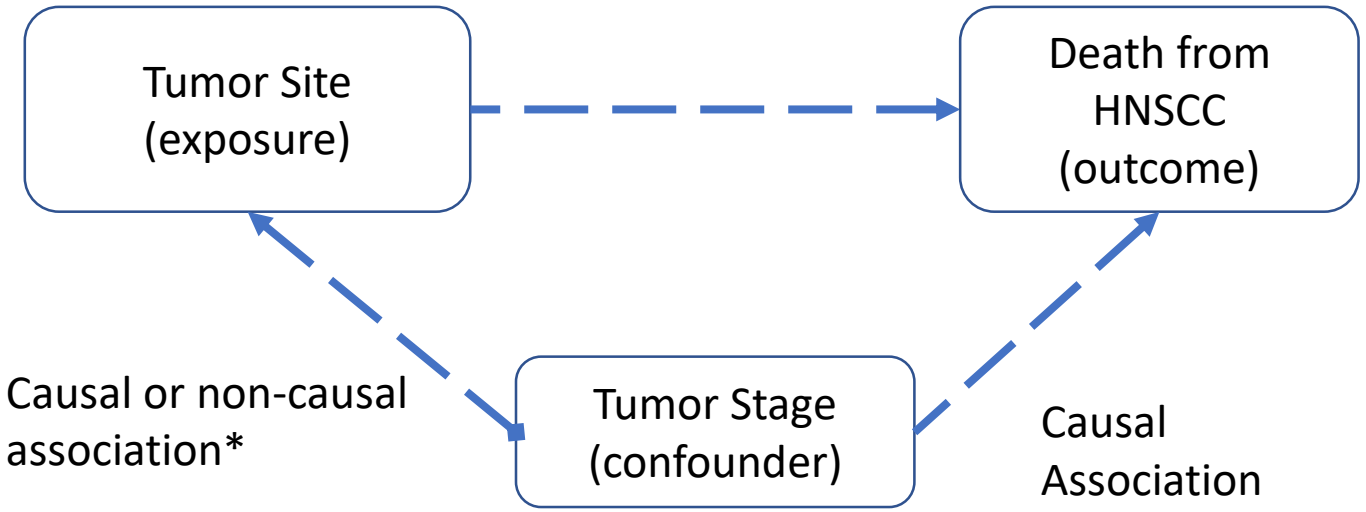
- Exposure and outcome information were not recorded as part of a research study protocol
- Job duties (exposure) might be more accurately recorded only for workers who had cancer and filed a disability claim
- Cohort studies based on records are often subject to this type of bias

Confounding

- Baseline prognostic factor imbalance between exposure groups
- Arises from….
  - Chance (sampling variability; see Altman paper from the BIOSTAT 702 class)
  - Biased selection of treatment or other systematic differences between exposure groups
- To deal with a confounder you have to measure it!

Confounding in a Cohort Study

- Oral cavity
- Oropharynx



*Old literature says “non-causal.” New literature requires “causal” to define confounding. Practically speaking, imbalance might induce concerning amount of bias whether causal or not.

Methods to Deal with Confounding in Cohort Studies

- Study Design
  - Restriction
  - Matching
  - Cannot estimate or test the confounder
- Analysis
  - Direct and indirect standardization (not covered)
  - Stratified analysis (detailed example)
  - Multivariable regression (covered in your other classes)
  - Propensity score (covered in your other classes)

Restriction

- All studies have eligibility criteria that define the population studied
- These criteria can be used to create a *homogenous* group with respect to a confounder
  - Example: Include only stage I/II disease
- This eliminates (or reduces) the possibility of confounding
  - Residual confounding due to distribution of Stage I and II between exposure groups

Matching

- Frequency match
  - Recruit patients such that the frequency (%) of the confounder is similar in the study groups
- Individual match
  - For each exposed patient recruit an unexposed patient with identical values for the confounding factor
- Not often done in cohort studies; logistically difficult unless using a database

Greenland and Morgenstern. Matching and efficiency in cohort studies. *American Journal of Epidemiology.* 1990. 131(1):151-159.

Effect of Confounding on RR

	Dead at 5 Years	Alive at 5 Years	
Oral Cavity	38	51	89
Oropharynx	40	98	138
			227

RR= (38/89) / (40/138) = 1.47 (95% CI: 1.03, 2.10)

After adjustment for tumor stage:

RR = 1.22 (95% CI: 0.78, 1.92)

Magnitude of confounding:

$(RR_{crude} – RR_{adjusted}) / Rr_{crude}$

(1.47-1.22/1.47)*100 = 17%

Based on an example from *Nephron Clin Pract* 2010;116:c143–c147

Could Tumor Stage be a Confounder?

	Dead at 5 years	**Alive at 5 Years**	
Oral Cavity	38	51	89
Oropharynx	40	98	138
			227

	Stage I/II			**Stage III/IV**		
	Dead	**Alive**	**Total**	**Dead**	**Alive**	**Total**
Oral Cavity	7	25	32	31	26	57
Oropharynx	17	67	84	23	31	54
Total	24	92	**116**	54	57	**111**

Based on an example from *Nephron Clin Pract* 2010;116:c143–c147

Summary of the Problem

- Initial Observation (without stratifying)
  - The risk of death is nearly 50% higher in oral cavity compared with oropharyngeal cancer (RR=1.47)
- BUT (after stratifying)…
  - Patients who have Stage III/IV cancer are more likely to have oral cavity cancer (58%) than patients with Stage I/II cancer (28%)
  - The risk of death in patients with Stage III/IV (49%) is nearly 2.5 times that of Stage I/II (20%)
- SO…do you still think that patients with oral cavity cancer have higher risk of death than patients with oropharyngeal cancer??

Stratified Analysis of Tumor Stage

	Stage I/II			Stage III/IV		
	Dead	**Alive**	**Total**	**Dead**	**Alive**	**Total**
Oral Cavity	7	25	32	31	26	57
Oropharynx	17	67	84	23	31	54
Total	24	92	**116**	54	57	**111**

RR=1.08 (0.5, 2.36)

RR=1.28 (0.86, 1.89)

- Two observations suggest confounding may be present
- Crude RR of 1.47 is outside the range of the stratum-specific estimates (1.08 to 1.28)
- Stratum-specific RR are not significantly different from 1

Based on an example from Nephron Clin Pract 2010;116:c143–c147

Breslow-Day Test for Homogeneity of the RR

H0: RR are homogenous
HA: RR are heterogeneous

	Outcome	No Outcome	
Exposed	a	b	N1
Unexposed	c	d	N0
	M1	M0	T

RR_s = Mantel-Haenszel summary relative risk
K = number of strata
RR_i = relative risk within strata i, where i={1…K}

General form of the test for K strata

$$\chi^2_{df=K-1} = \sum_{i=1}^{K} \frac{(lnRR_i - lnRR_s)^2}{var(lnRR_i)} = \sum_{i=1}^{K} \frac{(lnRR_i - lnRR_s)^2}{\left(\frac{b_i}{a_i N_{i,1}} + \frac{d_i}{c_i N_{i,0}}\right)}$$

For 2 strata

$$\chi^2_{df=1} = \frac{(lnRR_1 - lnRR_s)^2}{\left(\frac{b_1}{a_1 N_{11}} + \frac{d_1}{c_1 N_{10}}\right)} + \frac{(lnRR_2 - lnRR_s)^2}{\left(\frac{b_2}{a_2 N_{21}} + \frac{d_2}{c_2 N_{20}}\right)}$$

<= 3.84: fail to reject H0 (homogenous)
> 3.84: reject H0 (heterogeneous)

Breslow-Day Test for Homogeneity of the RR

H0: RR are homogenous
HA: RR are heterogeneous

	Outcome	**No Outcome**	
Exposed	a	b	N1
Unexposed	c	d	N0
	M1	M0	T

RR_1=1.08 (Stage I/II)

RR_2=1.28 (Stage III/IV)

RR_s=1.22

$$\chi^2_{df=1} = \frac{(lnRR_1 - lnRR_s)^2}{\left(\frac{b_1}{a_1 N_{11}} + \frac{d_1}{c_1 N_{10}}\right)} + \frac{(lnRR_2 - lnRR_s)^2}{\left(\frac{b_2}{a_2 N_{21}} + \frac{d_2}{c_2 N_{20}}\right)} = 0.14 < 3.84$$

Fail to reject H0; i.e., there is insufficient evidence against the hypothesis of homogeneity. Thus, we can report the summary relative risk that adjusts for tumor stage.

Mantel-Haenszel Summary RR

	Outcome	No Outcome	
Exposed	a	b	N1
Unexposed	c	d	N0
	M1	M0	T

K = number of strata

$$RR_s = \frac{\sum_{i=1}^{K} a_i N_{0,i}/T_i}{\sum_{i=1}^{K} c_i N_{1,i}/T_i}$$

	Stage I/II			Stage III/IV		
	Dead	**Alive**	**Total**	**Dead**	**Alive**	**Total**
Oral Cavity	7	25	32	31	26	57
Oropharynx	17	67	84	23	31	54
Total	24	92	116	54	57	111

$$RR_s = \frac{\left(7 * \frac{84}{116}\right) + \left(31 * \frac{54}{111}\right)}{\left(17 * \frac{32}{116}\right) + \left(23 * \frac{57}{111}\right)} = 1.22$$

(95% CI: 0.79, 1.89)

Summary

- Crude RR=1.47 (95% CI: 1.03, 2.10)
  - Risk of death is 47% higher in oral cavity vs. oropharyngeal HNSCC
  - Statistically significant
- MH RR=1.22 (95% CI: 0.78, 1.92)
  - Risk of death is 22% higher in oral cavity vs. oropharyngeal HNSCC after adjustment for stage at diagnosis
  - Not statistically significant!
- There is insufficient evidence to suggest the risk of death is any different in oral cavity vs. oropharyngeal HNSCC after accounting for differences in distribution of stage at diagnosis between each tumor type

See Elwood pages 514-516 for the formulas and an example.

Heterogeneous RR (interaction)

Crude RR=2.02 (1.47,2.76) [new example; try making the 2x2 table combining the strata!]

	Stage I/II			Stage III/IV		
	Dead	**Alive**	**Total**	**Dead**	**Alive**	**Total**
Oral Cavity	2	30	32	50	7	57
Oropharyngeal	17	67	84	23	31	54
Total	19	97	**116**	73	38	**111**

RR=0.31 (0.08, 1.26)

RR=2.10 (1.49, 2.85)

- Crude RR is in between straum-specific estimates – clue to interaction
- Breslow-Day Chi-square = 7.89 > 3.84 ➔ reject null hypothesis of homogenous RR
- Mantel-Haenszel summary RR is not appropriate here
- There is no confounding by tumor stage
- Instead, there is *interaction*

Heterogeneous RR (interaction)

Crude RR=2.02 (1.47,2.76) [new example; try making the 2x2 table combining the strata!]

	Stage I/II			Stage III/IV		
	Dead	**Alive**	**Total**	**Dead**	**Alive**	**Total**
Oral Cavity	2	30	32	50	7	57
Oropharyngeal	17	67	84	23	31	54
Total	19	97	**116**	73	38	**111**

RR=0.31 (0.08, 1.26)

RR=2.10 (1.49, 2.85)

- Interpreting interaction in this example:
  - The association between tumor site and death is different depending on the stage of the tumor
  - Patient with advanced stage oral cavity cancer have a higher risk of death than patients with advanced stage oropharyngeal cancer
  - But at early stage the tumor site makes no difference in the risk of death

Stratified Analysis for Tumor Stage

- Estimate the crude (unadjusted) RR
- Estimate the RR within strata of the confounder
- Assess homogeneity of the RR across strata
  - For homogenous RR (may suggest confounding)
    - Calculate a single, adjusted RR (Mantel-Haenszel RR)
  - For heterogeneous RR (interaction)
    - Report stratum-specific RR separately

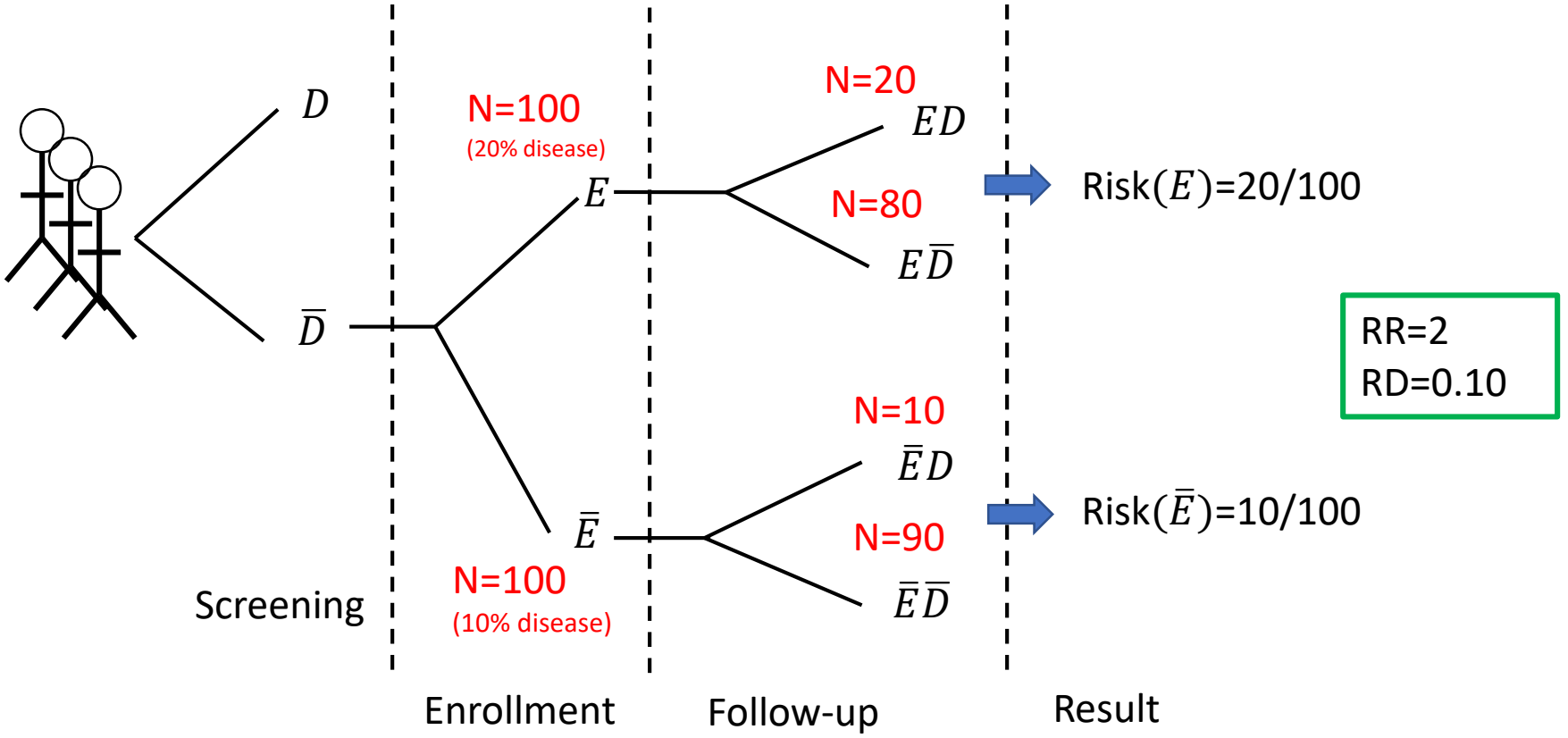
Final Thoughts

- Stratified analyses can be conducted in any study
  - Case-control
  - Cohort
  - Clinical trial
  - Cross sectional
- There is a similar Mantel-Haenszel method for summary odds ratios (e.g., in case-control studies)
- Formulas are in your textbook (p.512-516 for cohort studies)

Selection Bias in Cohort Studies

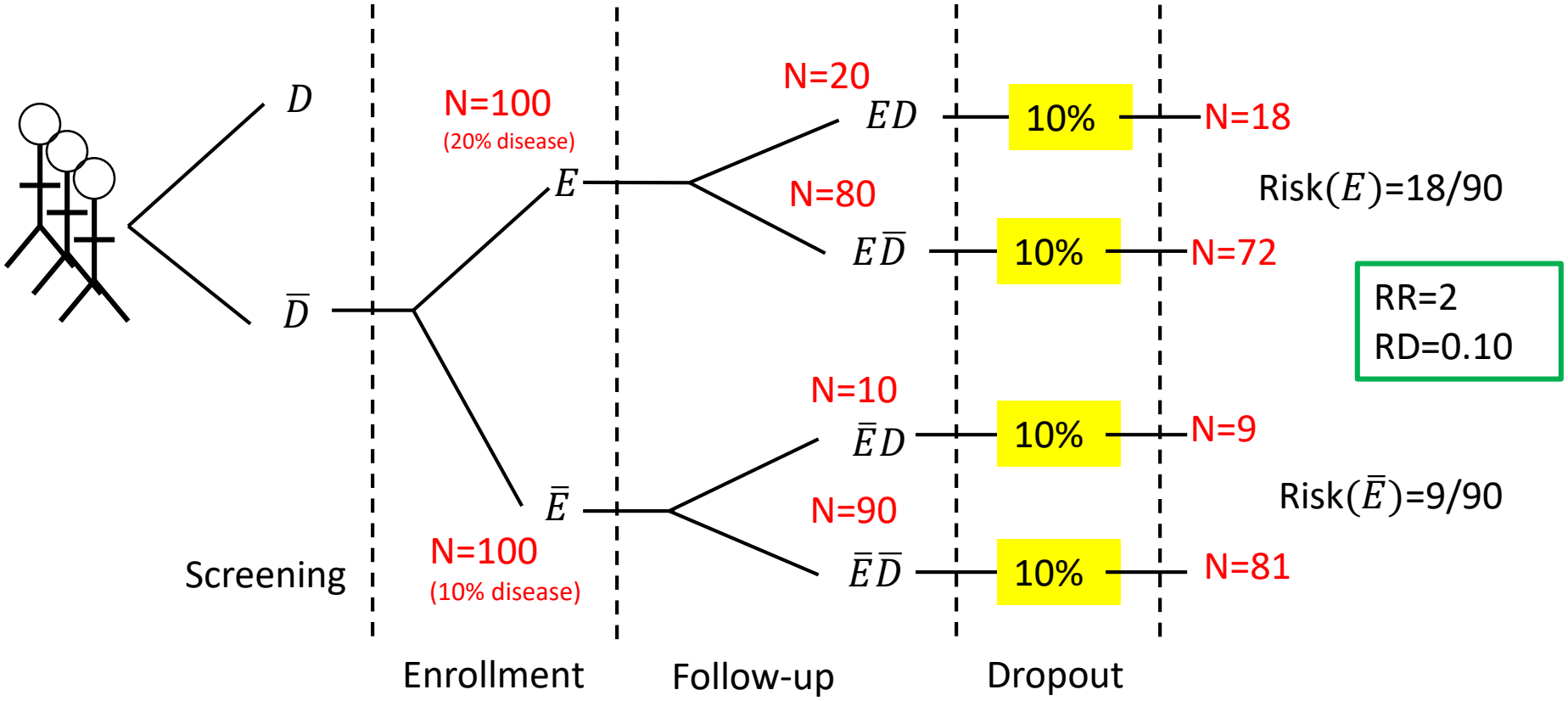
- Loss to follow-up
  - Occurs when patients who join the study leave before the outcome can be ascertained
  - Also called “dropout”
  - Results for completers may not reflect the true result for everyone who joined the study
- Self-selection (volunteer) bias

A Cohort Study with No Losses



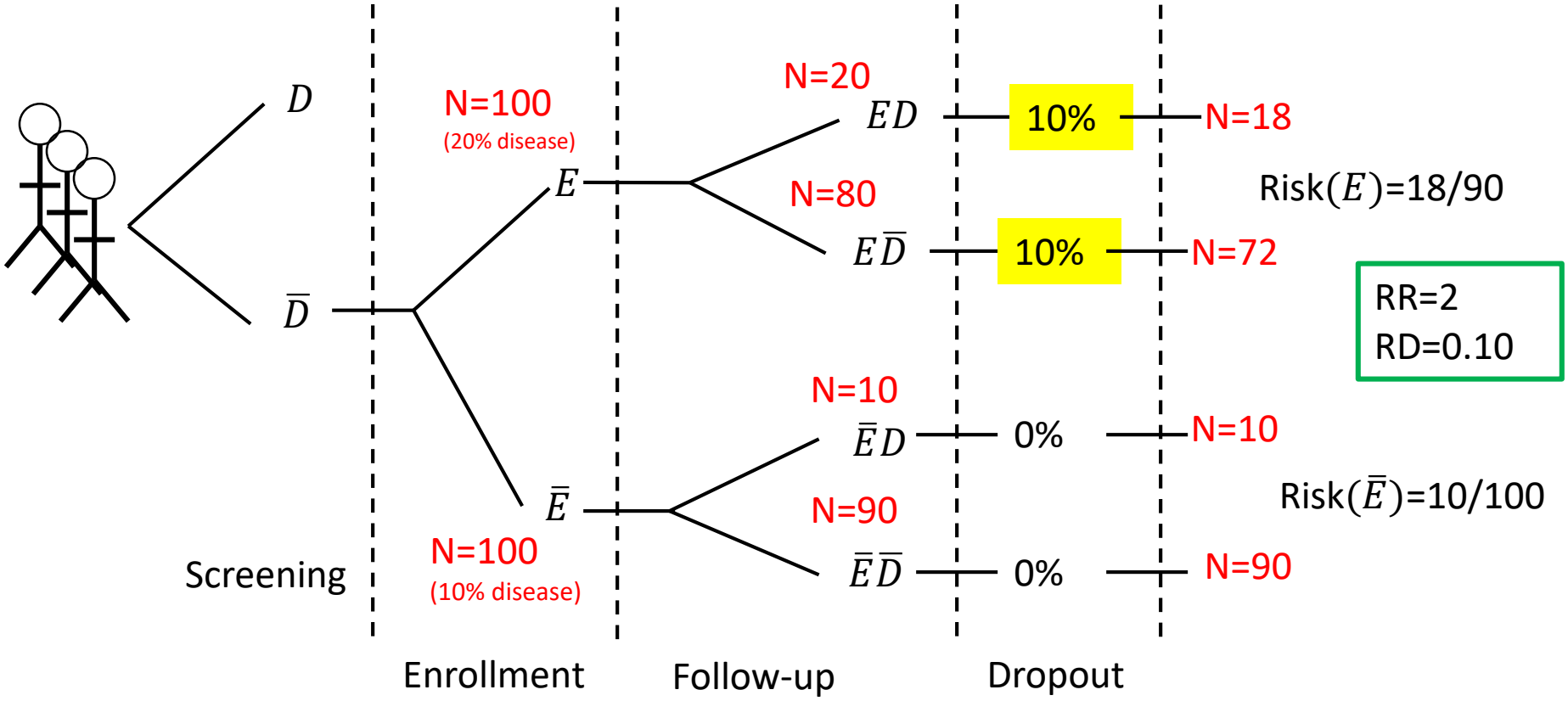
Internally Valid Result
(assuming no confounding or information bias)

Uniform Losses



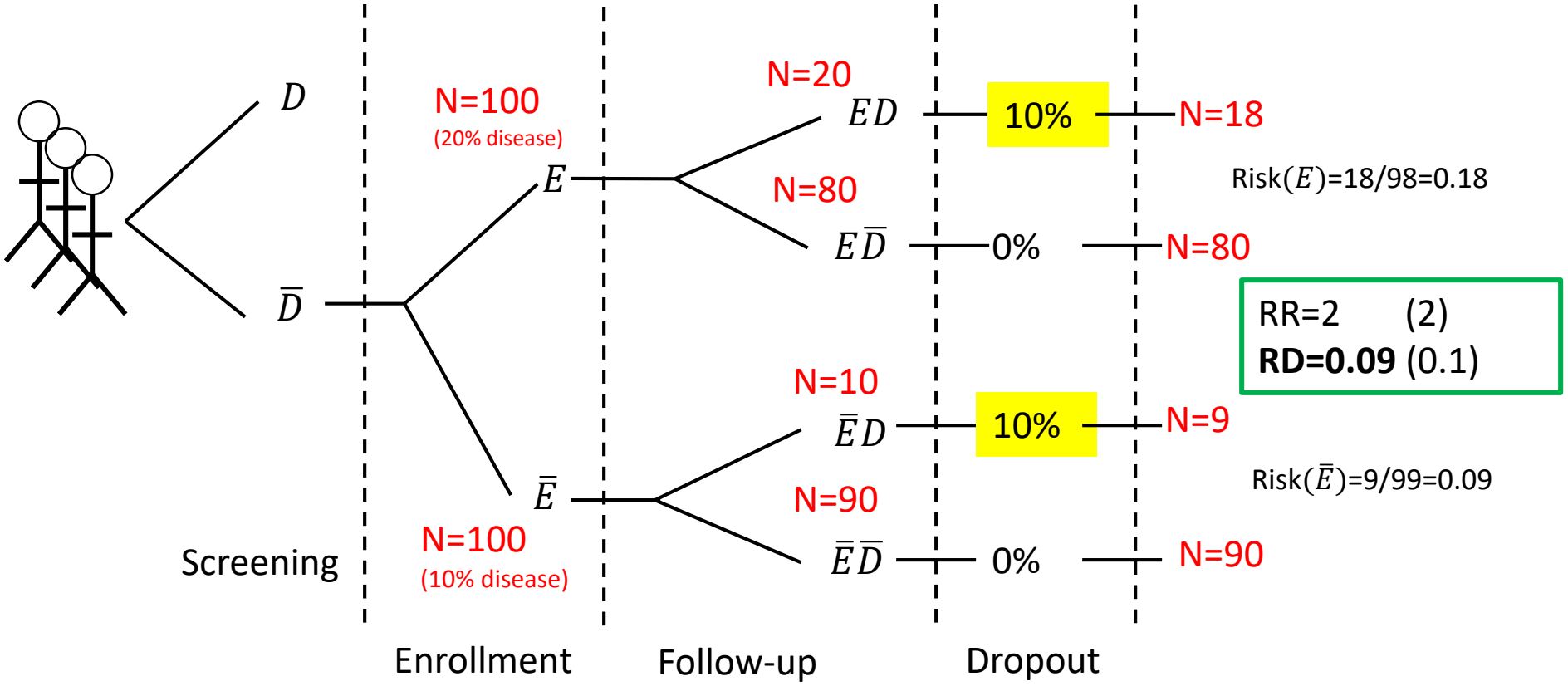
No bias in RR or RD!

Non-Differential Losses (exposure)



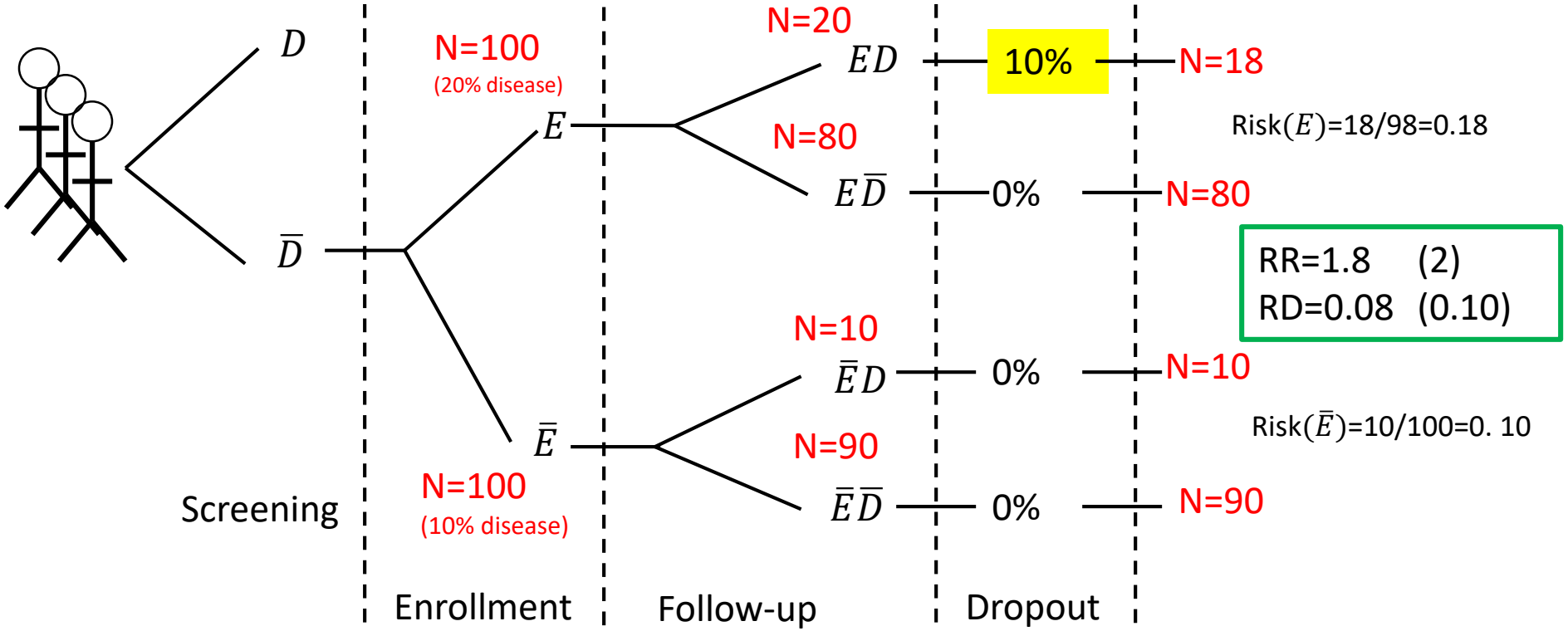
No bias in RR or RD!

Non-Differential Losses (disease)



RR not effected; RD biased toward the null

Differential Losses (exposure/disease)



RR & RD are both biased!

Bias is towards H0 but could be away from H0 if losses are differential by $\bar{E}D$

Risk(E)=0.2 & Risk($\bar{E}$)=.09, RR=2.22, RD=0.11

Summary of Losses to Follow-up in Cohort Studies

- Uniform losses
  - Losses are consistent across all exposure/outcome combinations
  - No bias in RR or RD
- Non-differential losses - exposure
  - Losses related to exposure but not outcome
  - No bias in RR or RD
- Non-differential losses – outcome
  - Losses related to outcome but not exposure
  - RR not effected; RD biased toward H0
- Differential – losses occur in one exposure/disease
  - RR & RD are biased; either toward or away from H0

Cancer Diagnosis

- Anatomic site
- Histopathology
  - Squamous cell, adenocarcinoma, etc.
  - Grade
    - Degree of dysplasia
    - Classification varies by tumor type
- Stage
  - TNM system for most solid tumors
- Prognosis
  - How well the patient is expected to do after diagnosis
  - Considers disease characteristics and the impact of usual care

Staging by TNM

Tumor (T)

Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor > 2 cm but not more than 4 cm in greatest dimension
T3	Tumor > 4 cm in greatest dimension
T4a	Moderately advanced local disease •Lip - Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face •Oral cavity - Tumor invades adjacent structures (eg, through cortical bone into deep extrinsic muscle of the tongue, maxillary sinus, or skin of face)
T4b	Very advanced local disease •Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

Lymph Node (N)

N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node 3 cm or less in greatest dimension
N2	Metastasis in a single ipsilateral lymph node > 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none > 6 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node > 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none > 6 cm in greatest dimension
N3	Metastasis in a lymph node > 6 cm in greatest dimension

Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

https://emedicine.medscape.com/article/2007181-overview

Locoregional Disease and staging by TNM

Locoregionally advanced

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
IVB	T Any	N3	M0
	T4b	N Any	M0
IVC	T Any	N Any	M1

https://emedicine.medscape.com/article/2007181-overview

https://www.uptodate.com/contents/treatment-of-locoregionally-advanced-stage-iii-and-iv-head-and-neck-cancer-the-larynx-and-hypopharynx#H291853305

HPV in HNSCC

- Increasing incidence of OPSCC
  - The majority of these tumors are HPV+
  - Incidence is highest in white males
  - Incidence is lower in females and non-whites
  - Early age at diagnosis compared to non-OPSCC
  - Often diagnosed in patients with little or no smoking hx
- HPV+ OPSCC are associated with improved survival relative to HPV- OPSCC
  - Due to disease epidemiology this is primarily relevant in younger, white males
- Prognostic utility of HPV is uncertain in…
  - Minorities and women with OPSCC
  - Non-OPSCC tumors (rate of HPV+ is very low)

Questions asked by Fakhry, et al.

- Is the association between tumor HPV status and risk of death similar in OPSCC and non-OPSCC?
- Is sex associated with risk of death in OPSCC and non-OPSCC separately? How does HPV positivity influence these associations, if at all?
- Is race associated with risk of death in OPSCC and non-OPSCC separately? How does HPV positivity influence these associations, if at all?

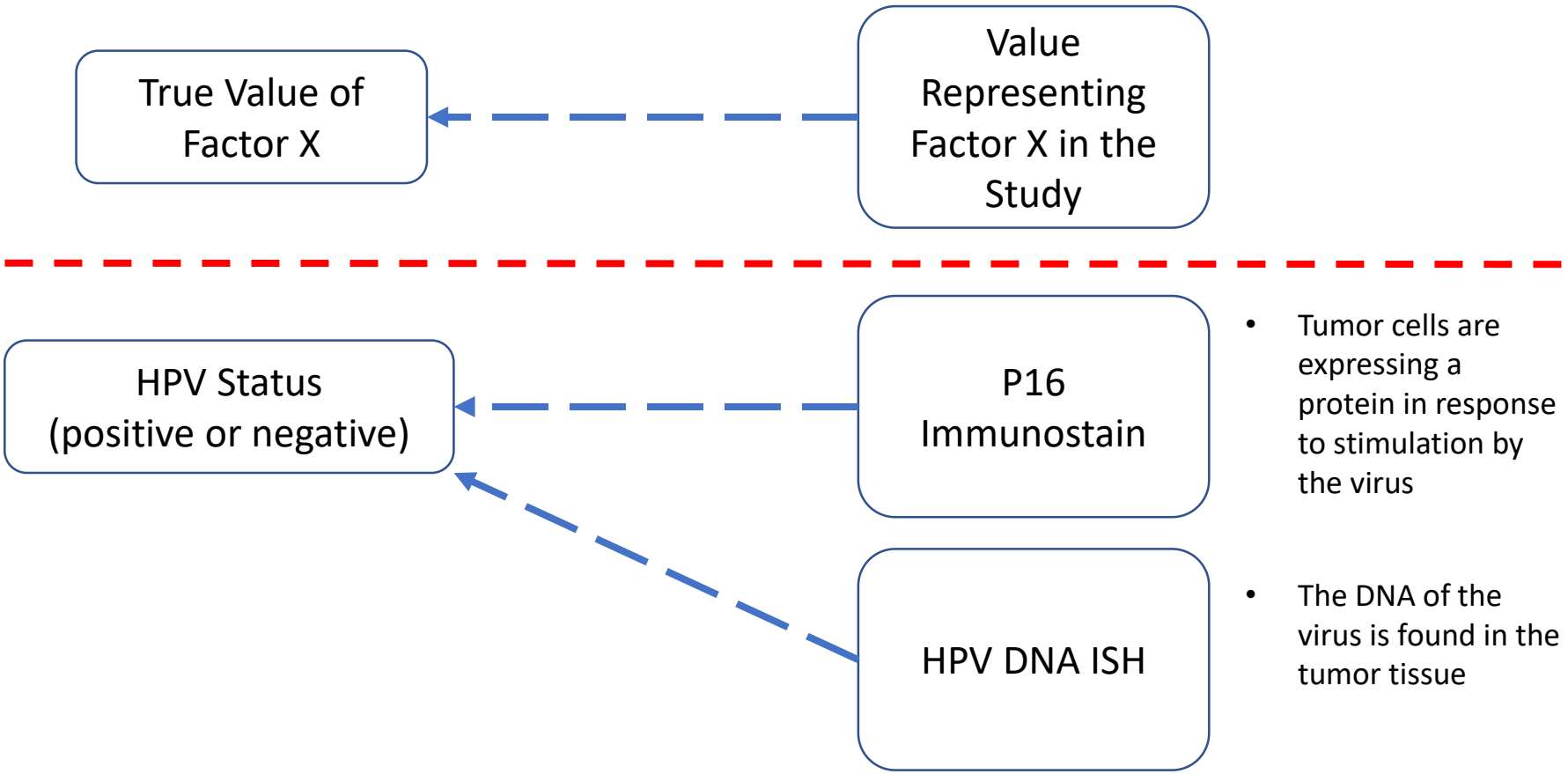
Design of Fakhry, et al.

- Cohort study
- Based on a sample from 2 study centers

The study population was composed of patients with HNSCCs of the oropharynx, oral cavity, larynx, and nasopharynx. For each tumor site, cases were randomly sampled from [each institution's] cancer registry (when there were sufficient numbers to allow this) in sex and race/ethnic groups of interest to oversample nonwhites and women (Fakhry, et al. p. 1567).

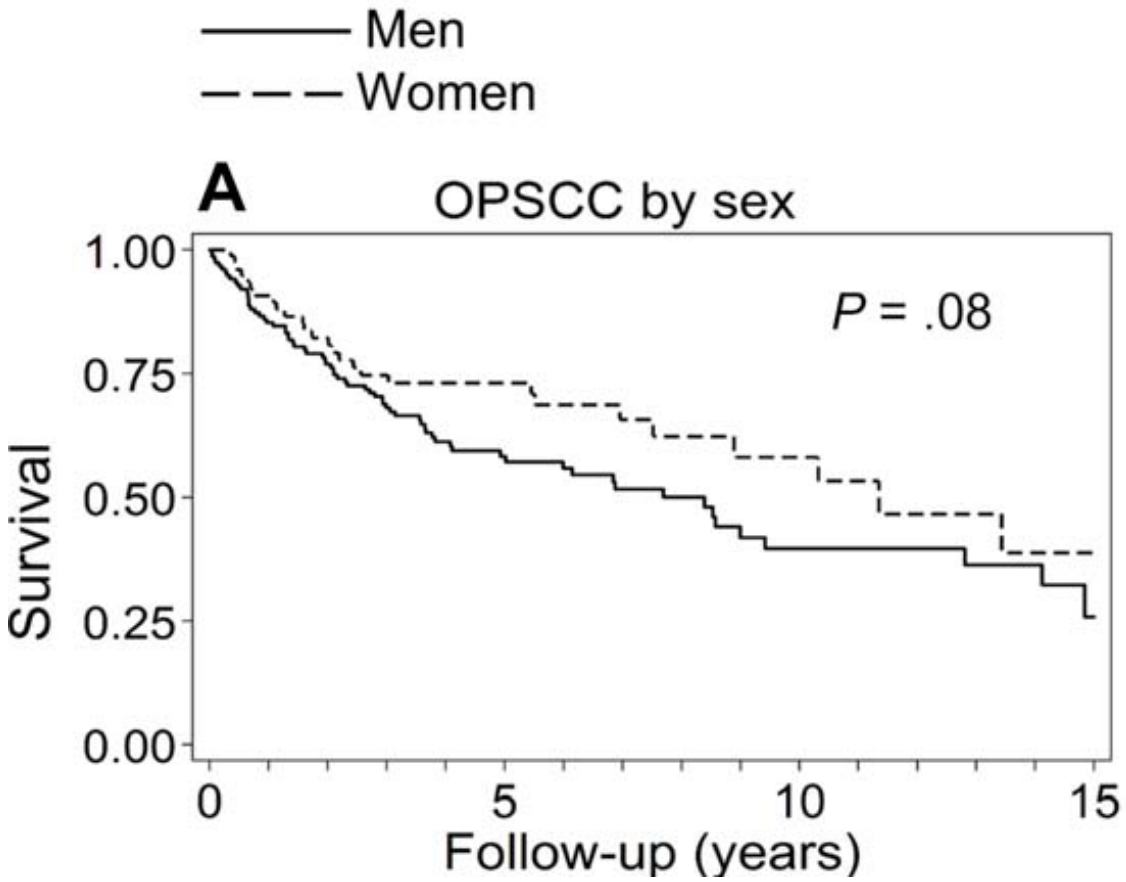
- Exposures: Tumor HPV status, sex, race/ethnicity based on archival tissue for included patients
- Outcome: overall survival (time from diagnosis to death from any cause)

Classification of HPV (exposure)



- Tumor cells are expressing a protein in response to stimulation by the virus
- The DNA of the virus is found in the tumor tissue

Comparing Outcomes across Exposure Groups: How to Read a KM Plot



Losses in a Survival Analysis

- Patients whose status is unknown beyond a given time during follow-up are called *censored*
  - Truly lost (censored prior to end of study)
  - Administrative (finished study, did not have the outcome)
- Valid survival analysis requires losses to be *non-informative*
- Informative means lost participants have different probability of the outcome than completers
  - See *Non-Differential Losses – Disease*
- Especially problematic when this occurs in a single exposure group
  - See *Differential Losses – Exposure/Disease*

https://www.ctspedia.org/do/view/CTSpedia/BiasSelectCohort#Loss_to_Follow_up

Interpreting Model Results

TABLE 3. Univariate and Multivariate Risk Factors for Death Among Patients With Oropharyngeal Squamous Cell Cancer

	Univariate Analysis (n = 239)[a]		Multivariate Analysis (n = 183)[a,b]	
Characteristic at Diagnosis	HR (95% CI)	*P*	aHR (95% CI)	*P*
Age (per 10-y increase)	**1.22 (1.01-1.48)**	**.04**	1.23 (0.95-1.59)	.11
Tumor stage				
T1	1.00		1.00	
T2	1.20 (0.66-2.20)	.55	0.90 (0.43-1.85)	.77
T3	**2.39 (1.32-4.32)**	**.004**	0.92 (0.43-1.97)	.84
T4	**2.74 (1.50-4.99)**	**.001**	1.06 (0.47-2.38)	.89
P for trend		**<.001**		.92
Nodal stage				
N0	1.00		1.00	
N1-N2b	1.07 (0.62-1.87)	.80	1.85 (0.86-3.97)	.12
N2c- N3	1.77 (0.94-3.33)	.08	**2.92 (1.16-7.36)**	**.02**
P for trend		.07		**.01**
Sex				
Men	1.00		**1.00**	
Women	0.68 (0.43-1.05)	.08	**0.48 (0.26 -0.88)**	**.02**

Women with OPSCC have a 32% lower risk of death than men with OPSCC (at any time after diagnosis).

After adjustment for the other factors [confounders] in the model, women with OOPSC have a 52% lower risk of death than men with OOPSC (at any time after diagnosis).

Assignment for the Class Activity

- Read the instructions to prepare for the lab
- Read the required parts of the article
- Follow Elwood's paradigm to…
  - Describe the evidence
  - Identify threats to interval validity
- Think about how the following impact the results
  - What are the main findings?
  - Subject selection (including losses to follow-up)
  - Misclassification of exposure/outcome variables