



Antibiotics

The Good, The Bad, and The Ugly

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Objectives

- Explore the potential causality of early-life antibiotic use as a risk factor for the development of IBD
- Understand the role of antibiotics in the management of established IBD



Case Presentation

- You are seeing a 27 y.o female with a history of long-standing ileocolonic Crohn's disease
- History significant for complicated course
 - Fibrostenosing disease requiring ileocecal resection
 - Perianal fistulas, held in check on anti-TNFs
- Recently gave birth to a baby boy 6 months ago, no complications during pregnancy or delivery



Case Continued

- Recently, her son was diagnosed with a UTI, and investigations reveal Grade 1 ureteropelvic reflux
- Natural history of mild UPR
 - Repeated urinary tract infections, requiring antibiotics to prevent renal damage
 - Most children will grow out of it by age 2-3
 - Can also be treated surgically, though ureteral re-implantation
- Why are we focused on this history



Case Continued

- The mother has recently heard about a possible link between antibiotic use and
- She is wanting your opinion on:
 - Does her son being exposed to multiple courses of Abx early in life increase his risk of developing Crohn's disease
 - She may consider having her son have the operation to reduce antibiotic exposure
 - Surgery is relatively low-morbidity, minimal mortality, and is effective at correcting UPJ



Question 1:

- Do you believe that antibiotic exposure increases one's personal risk of developing IBD later in life?

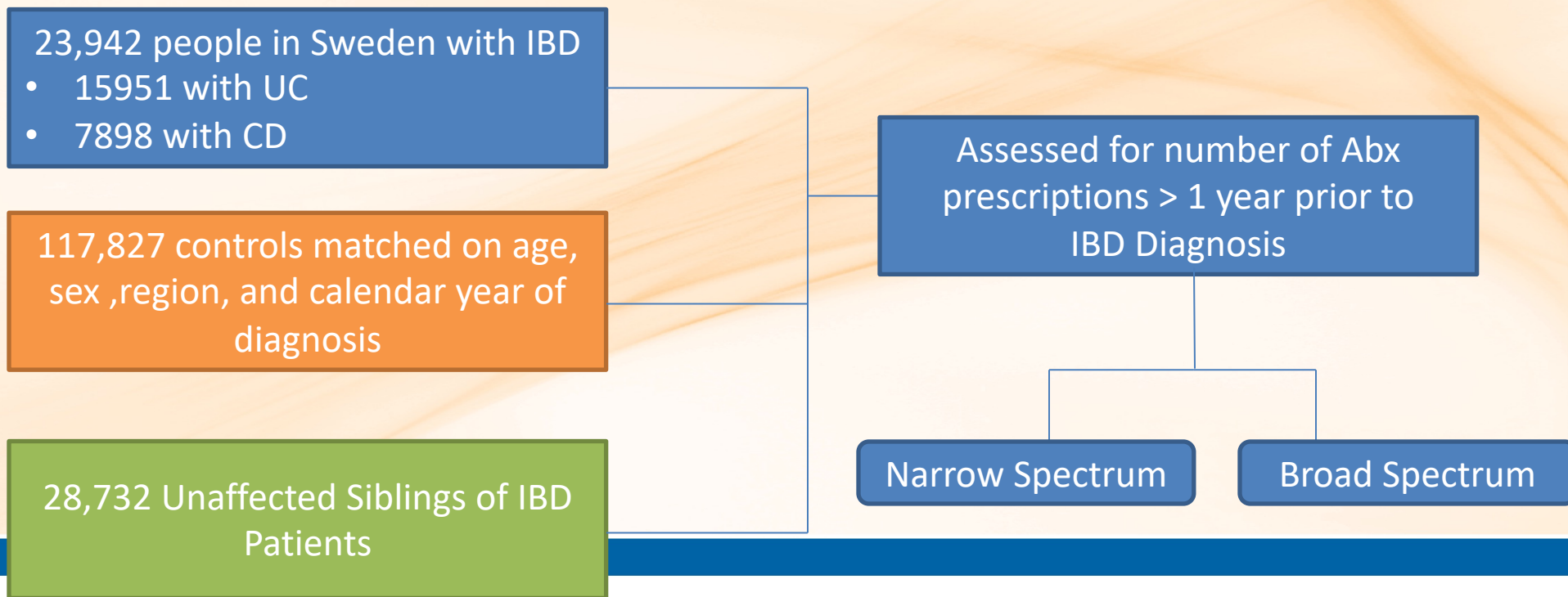
Question 2:

- Would you recommend your patient having surgery?



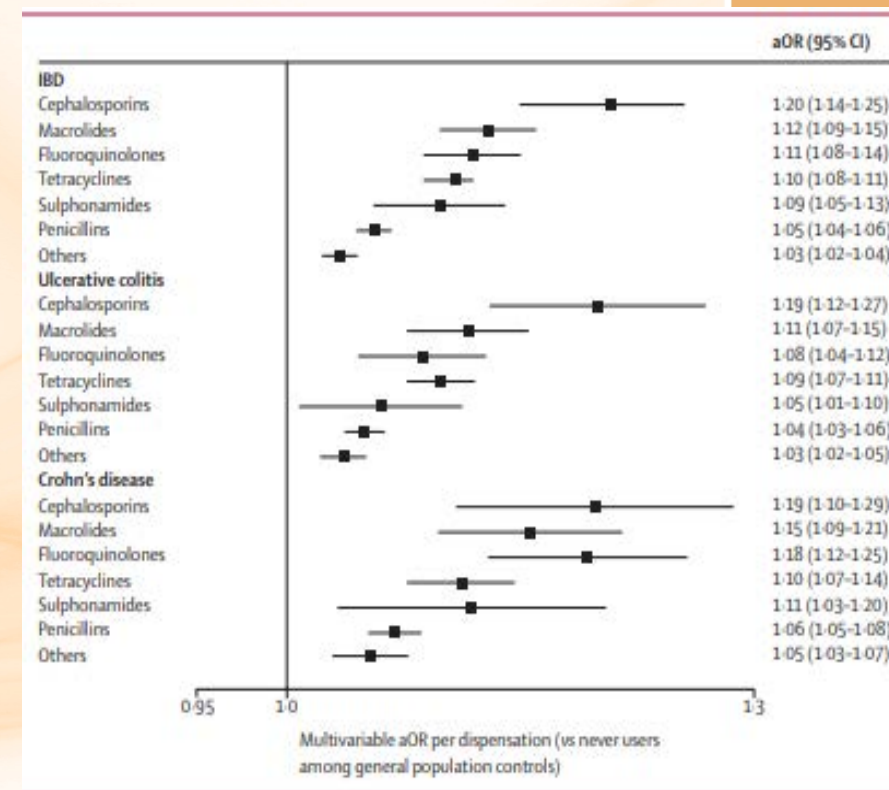
Antibiotic use and the development of inflammatory bowel disease: a national case-control study in Sweden

Long H Nguyen, Anne K Örtqvist, Yin Cao, Tracey G Simon, Bjorn Roelstraete, Mingyang Song, Amit D Joshi, Kyle Staller, Andrew T Chan, Hamed Khalili, Ola Olén, Jonas F Ludvigsson









		1 dispensation	2 dispensation	3 dispensations
IBD	Broad Spectrum	1.31 (1.25 – 1.37)	1.58 (1.48 – 1.68)	1.69 (1.59 – 1.79)
	Narrow Spectrum	1.18 (1.13 – 1.22)	1.37 (1.30 – 1.43)	1.49 (1.43 – 1.56)
CD	Broad Spectrum	1.40 (1.29 – 1.52)	1.79 (1.60 – 2.00)	1.78 (1.59 – 1.99)
	Narrow Spectrum	1.21 (1.13 – 1.30)	1.50 (1.37 – 1.63)	1.57 (1.44 – 1.70)
UC	Broad Spectrum	1.29 (1.22 – 1.36)	1.50 (1.38 – 1.63)	1.57 (1.45 – 1.70)
	Narrow Spectrum	1.20 (1.15 – 1.26)	1.28 (1.21 – 1.36)	1.46 (1.35 – 1.52)

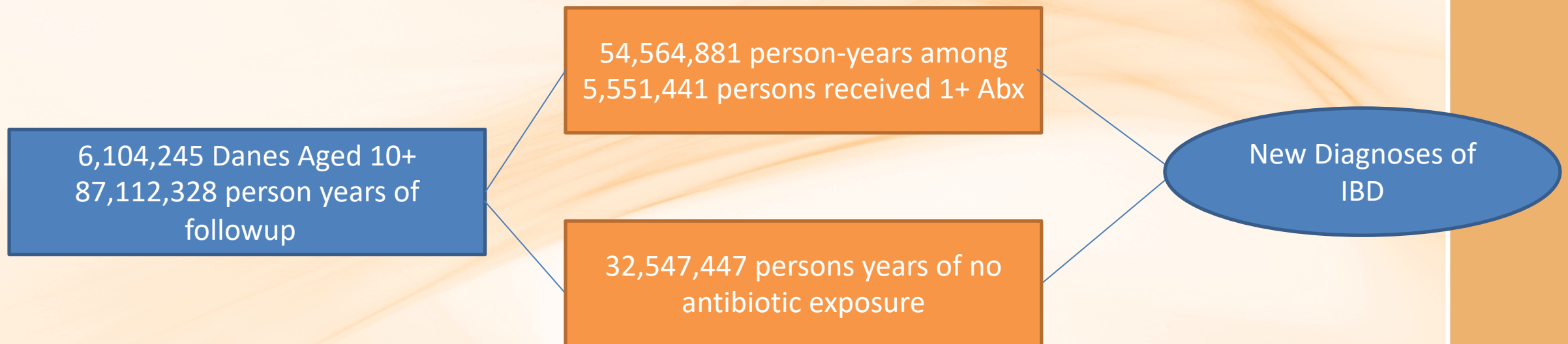


	1 dispensation	2 dispensation	3 dispensations
IBD vs Siblings	1.06 (1.01 – 1.12)	1.32 (1.24 – 1.41)	1.35 (1.28 – 1.43)
CD vs Siblings	1.13 (1.02 – 1.25)	1.41 (1.26 – 1.58)	1.46 (1.23 – 1.62)
UC vs Siblings	1.06 (0.99 – 1.14)	1.23 (1.13 – 1.34)	1.29 (1.20 – 1.39)



Antibiotic use as a risk factor for inflammatory bowel disease across the ages: a population-based cohort study

Adam S Faye ,¹ Kristine Højgaard Allin ,^{2,3} Aske T Iversen,²
Manasi Agrawal ,^{2,4} Jeremiah Faith,⁵ Jean-Frederic Colombel,⁴ Tine Jess ^{2,3}





		1 dispensation	2 dispensation	3 dispensations	4 dispensations	5+ dispensations
IBD						
	Age 10-40	1.15 (1.11 – 1.19)	1.24 (1.20 – 1.30)	1.48 (1.32 – 1.45)	1.49 (1.41 – 1.58)	1.69 (1.61 – 1.76)
	Age 40-60	1.27 (1.21 – 1.33)	1.43 (1.36 – 1.61)	1.57 (1.48 – 1.67)	1.69 (1.57 – 1.81)	2.12 (2.01 – 2.23)
	Age 60+	1.21 (1.15 – 1.27)	1.43 (1.36 – 1.50)	1.50 (1.41 – 1.59)	1.72 (1.61 – 1.84)	1.95 (1.85 – 2.04)
CD						
	Age 10-40	1.20 (1.13 – 1.27)	1.36 (1.25 – 1.45)	1.53 (1.41- 1.65)	1.71 (1.56 – 1.87)	2.01 (1.87 – 2.16)
	Age 40-60	1.25 (1.14 – 1.37)	1.56 (1.42 – 1.72)	1.70 (1.52 – 1.90)	2.12 (1.67 – 2.39)	2.54 (2.31 – 2.80)
	Age 60+	1.20 (1.09 – 1.32)	1.45 (1.31 – 1.61)	1.52 (1.35 – 1.70)	1.91 (1.68 – 2.16)	2.07 (1.68 – 2.27)
UC						
	Age 10-40	1.12 (1.07 – 1.170)	1.18 (1.12 – 1.24)	1.29 (1.22 – 1.37)	1.37 (1.27 – 1.47)	1,49 (1.41 – 1.56)
	Age 40-60	1.28 (1.21 – 1.34)	1.29 (1.31 – 1.48)	1.53 (1.43 – 1.64)	1.54 (1.41 – 1.67)	1.97 (1.85 – 2.10)
	Age 60+	1.22 (1.15 – 1.29)	1.43 (1.34 – 1.51)	1.50 (1.40 – 1.61)	1.67 (1.54 – 1.80)	1.92 (1.81 – 2.03)

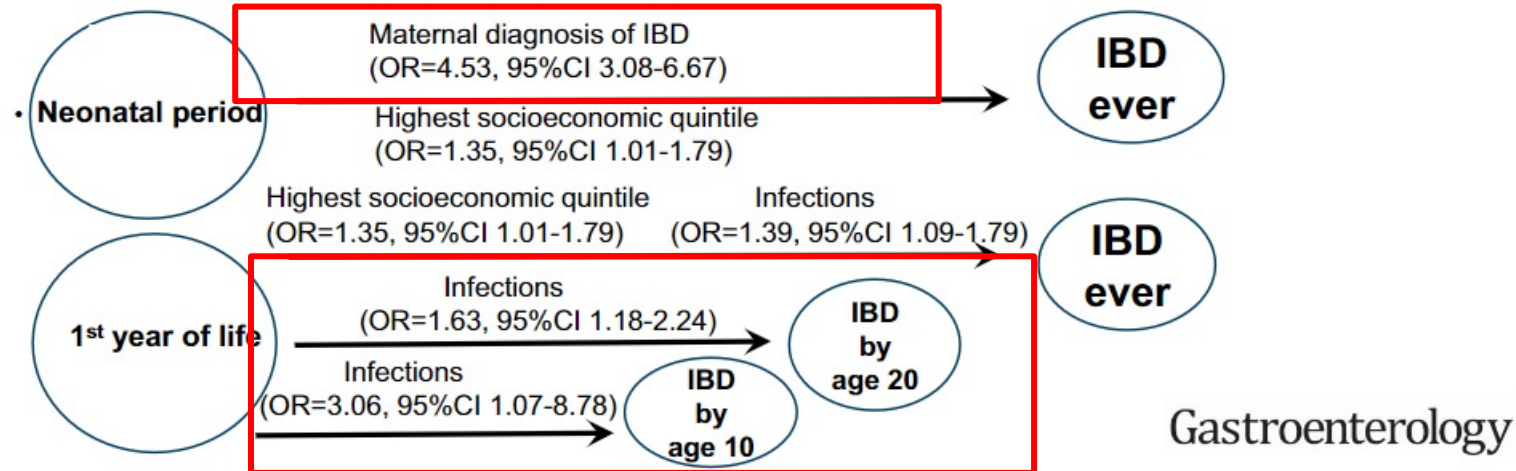
- Risk increases with number of dispensations of antibiotics
- Strength of association higher for CD

Events Within the First Year of Life, but Not the Neonatal Period, Affect Risk for Later Development of Inflammatory Bowel Diseases



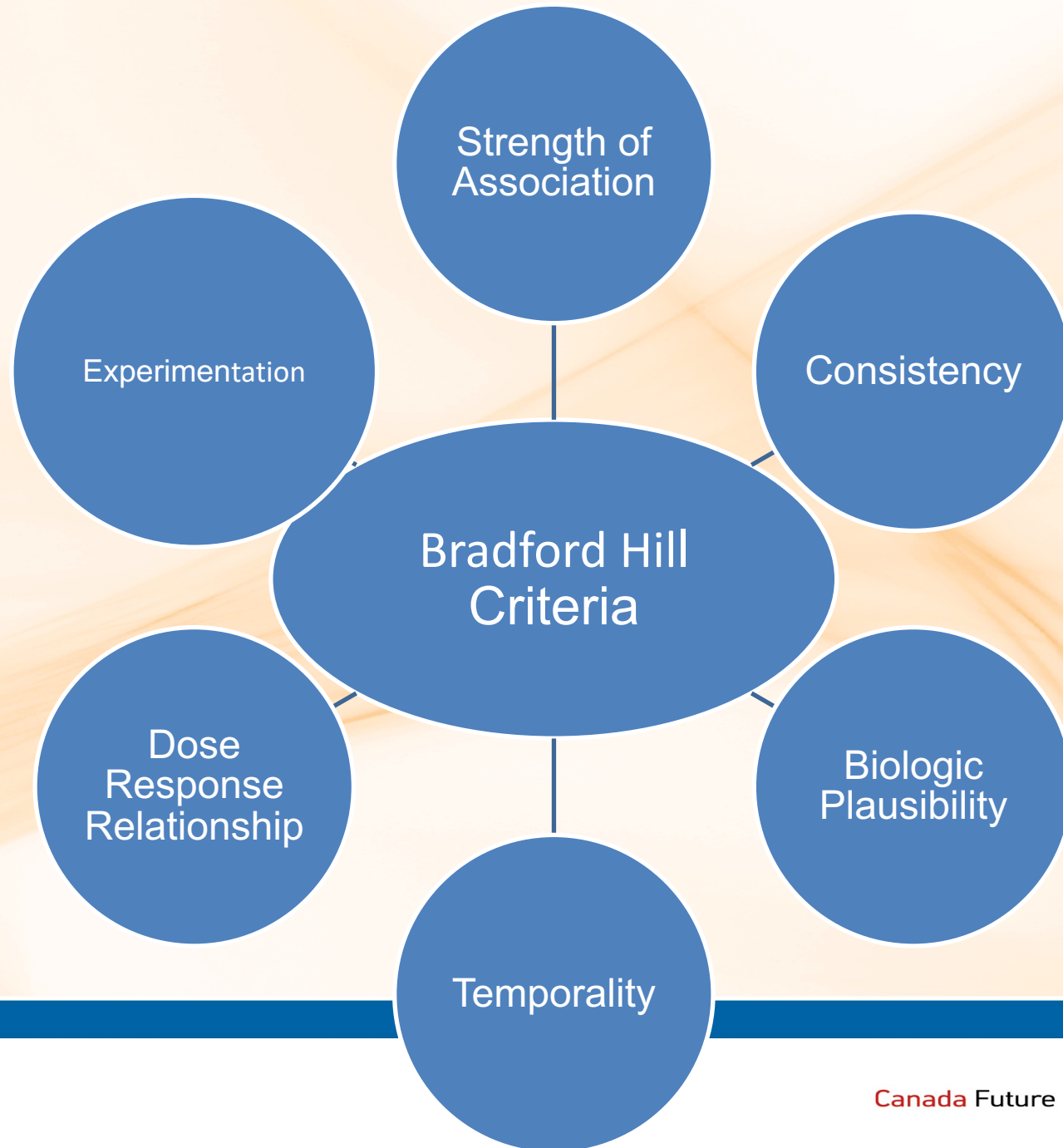
Charles N. Bernstein,^{1,2} Charles Burchill,³ Laura E. Targownik,^{1,2} Harminder Singh,^{1,2,4} and Leslie L. Roos^{3,4}

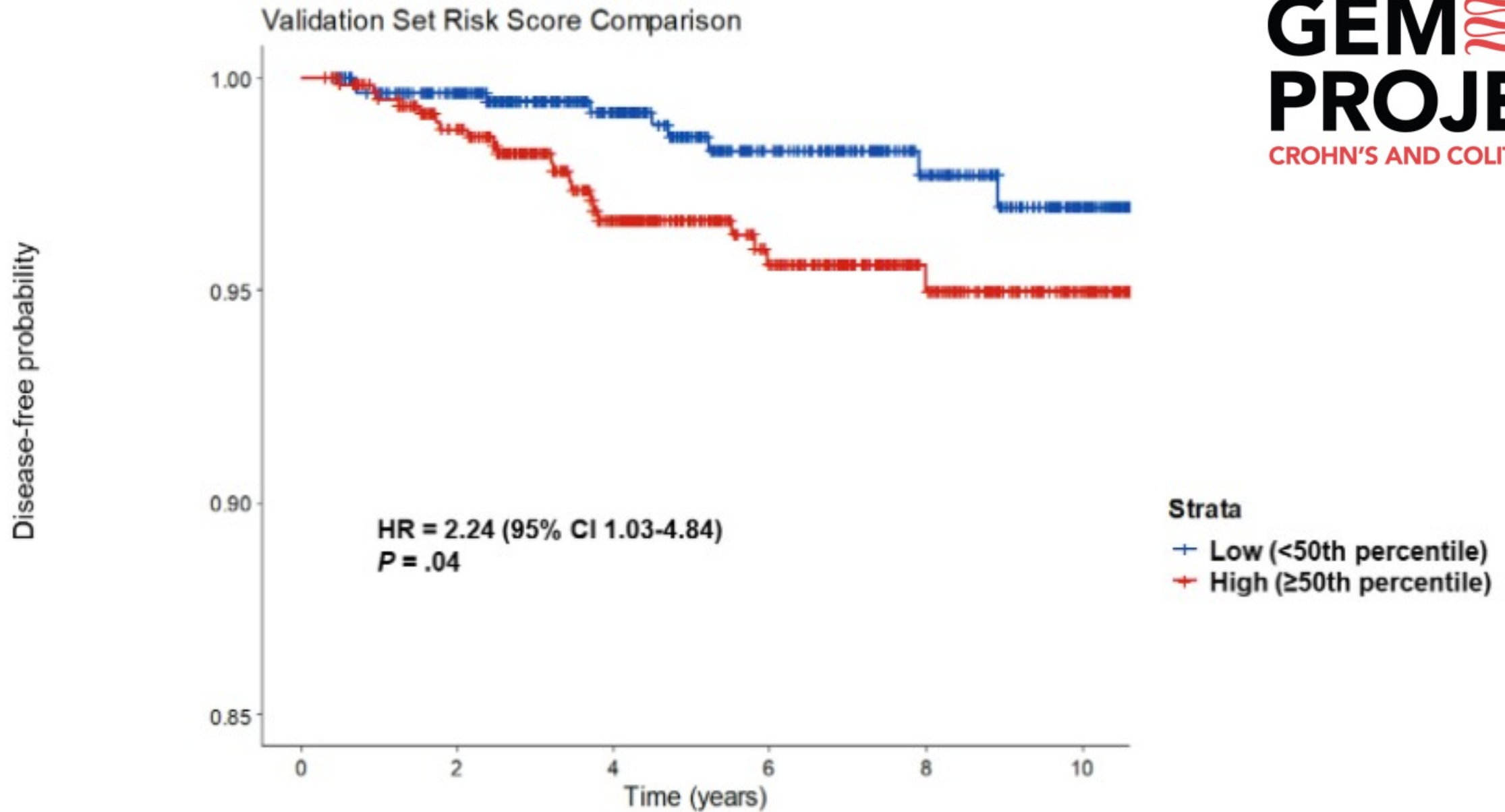
Early Life Predictors of Development of IBD



Interpreting Observational Studies

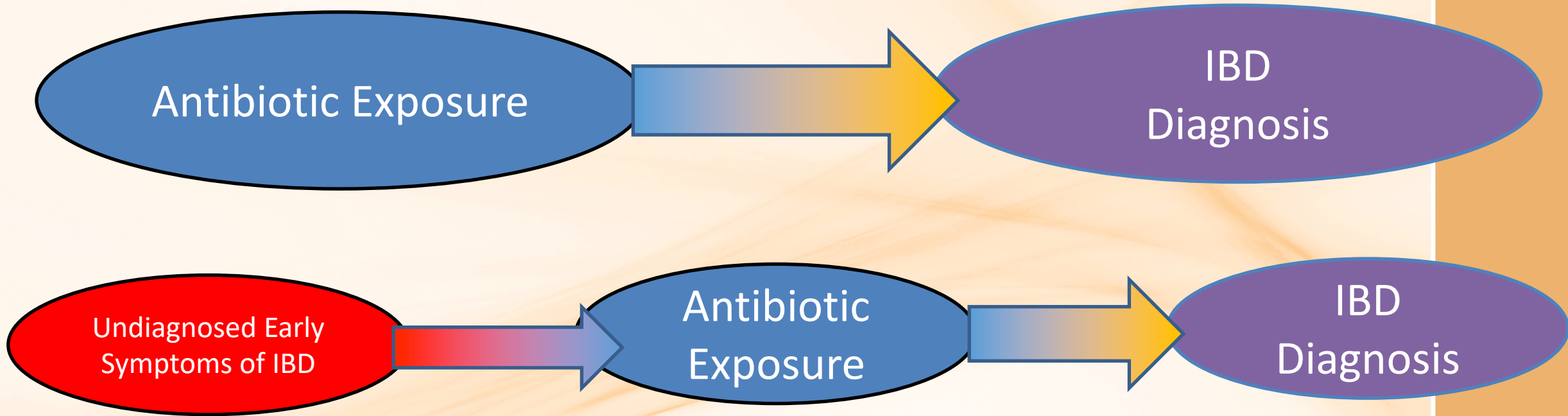
Cannot definitely
assume CAUSALITY
on the basis of
observational studies







Temporality



*****PROTOPATHIC BIAS*****

Age group	antibiotic use	IRR*, IBD	IRR*, CD
10–40 years	No use in the last 5 years	1.00	1.00
10–40 years	4 to 5 years	1.13	1.12
10–40 years	3 to 4 years	1.18	1.23
10–40 years	2 to 3 years	1.24	1.34
10–40 years	1 to 2 years	1.40	1.59
40–60 years	No use in the last 5 years	1.00	1.00
40–60 years	4 to 5 years	1.21	1.22
40–60 years	3 to 4 years	1.36	1.36
40–60 years	2 to 3 years	1.41	1.53
40–60 years	1 to 2 years	1.66	1.89
60+ years	No use in the last 5 years	1.00	1.00
60+ years	4 to 5 years	1.22	1.23
60+ years	3 to 4 years	1.26	1.29
60+ years	2 to 3 years	1.39	1.37
60+ years	1 to 2 years	1.63	1.72



Follow-Up Questions

- Is this association likely to be causal?
- What further evidence can we expect to feasibly collect
- When should we act?



Conclusions

- Antibiotic use (like many early life exposures) **COULD** impact on risks of developing Crohn's disease
- The magnitude of the risk is likely small for any individual
- Would recommend this knowledge should have only a minimal impact of clinical decision making