

Faculty Disclosure

Brennan Spiegel, MD receives consulting fees from/is on the Speakers Bureau for Takeda, Prometheus and AstraZeneca and does contracted research for Bristol Meyers Squibb, Takeda, and Amgen.

Controversies in Functional GI: SIBO, Epidemiology, and Non- Pharmacological Treatments

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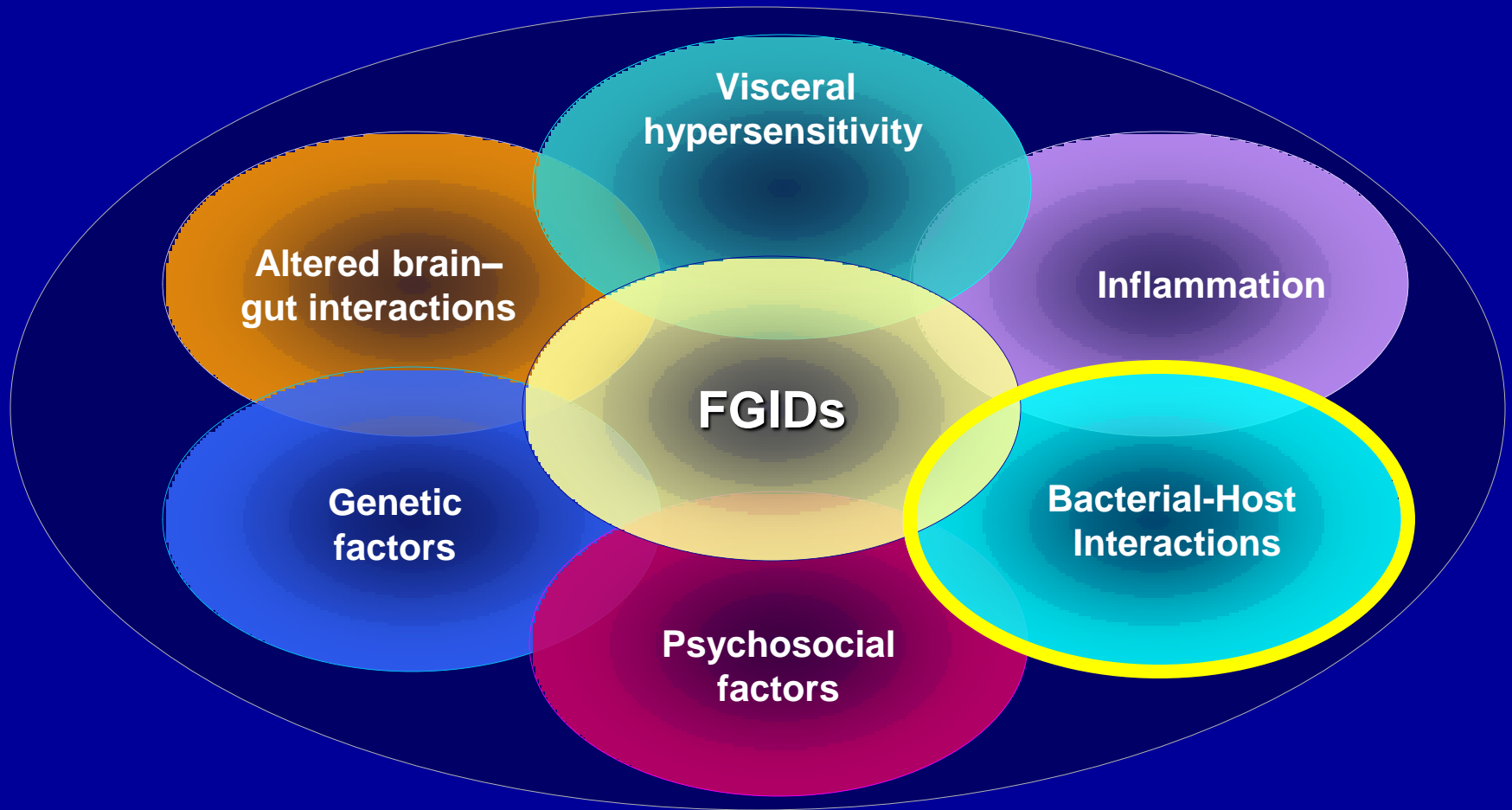
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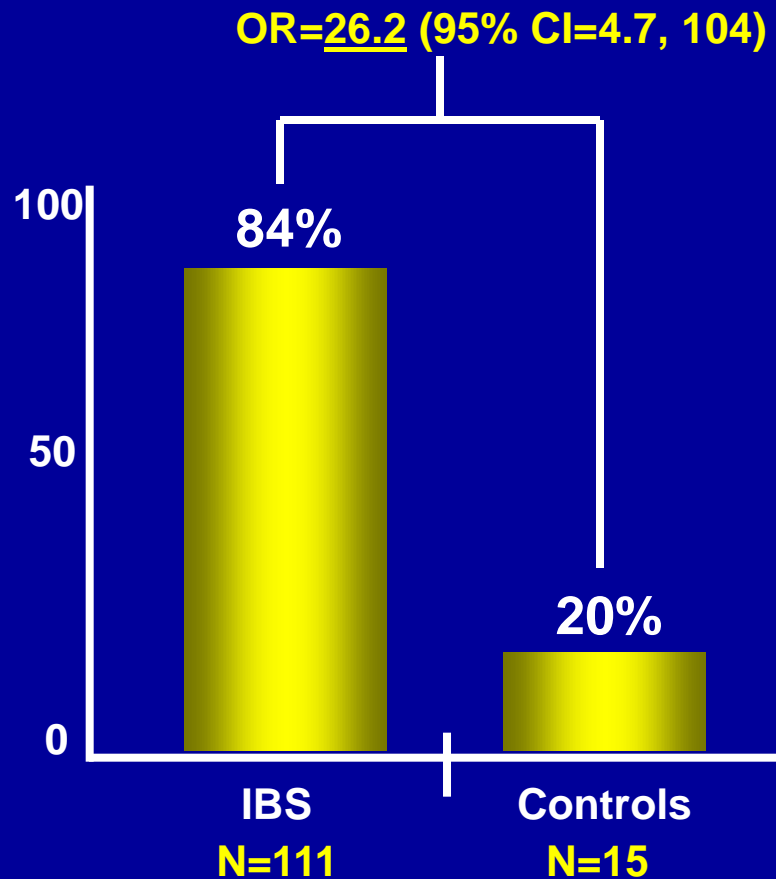


Proposed Pathophysiological Mechanisms Involved in FGIDs



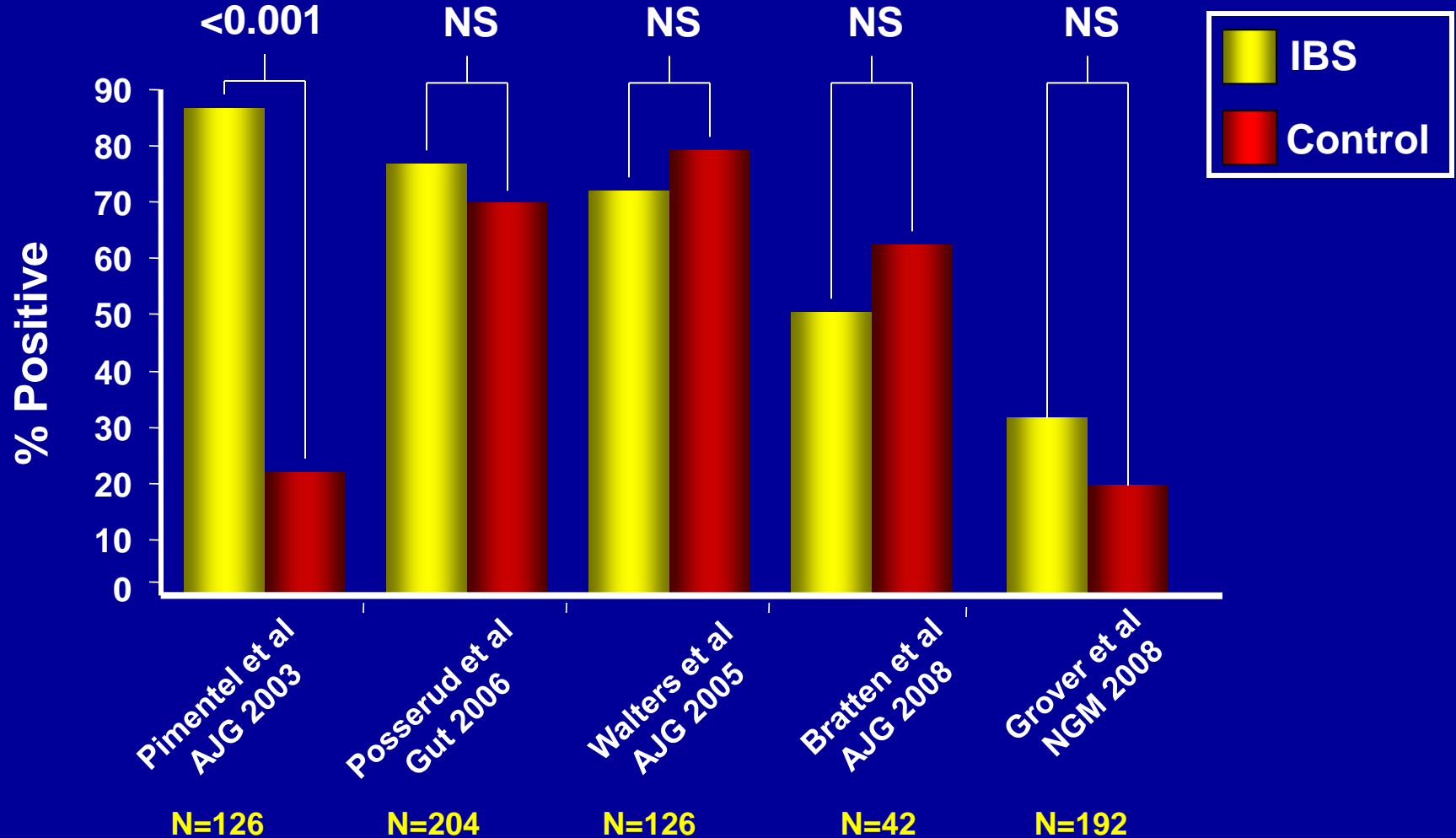
SIBO Update and Controversies

Prevalence of Abnormal* Lactulose Breath Tests in Rome I IBS



*Single peak >20 ppm
rise of H₂ by 90 minutes

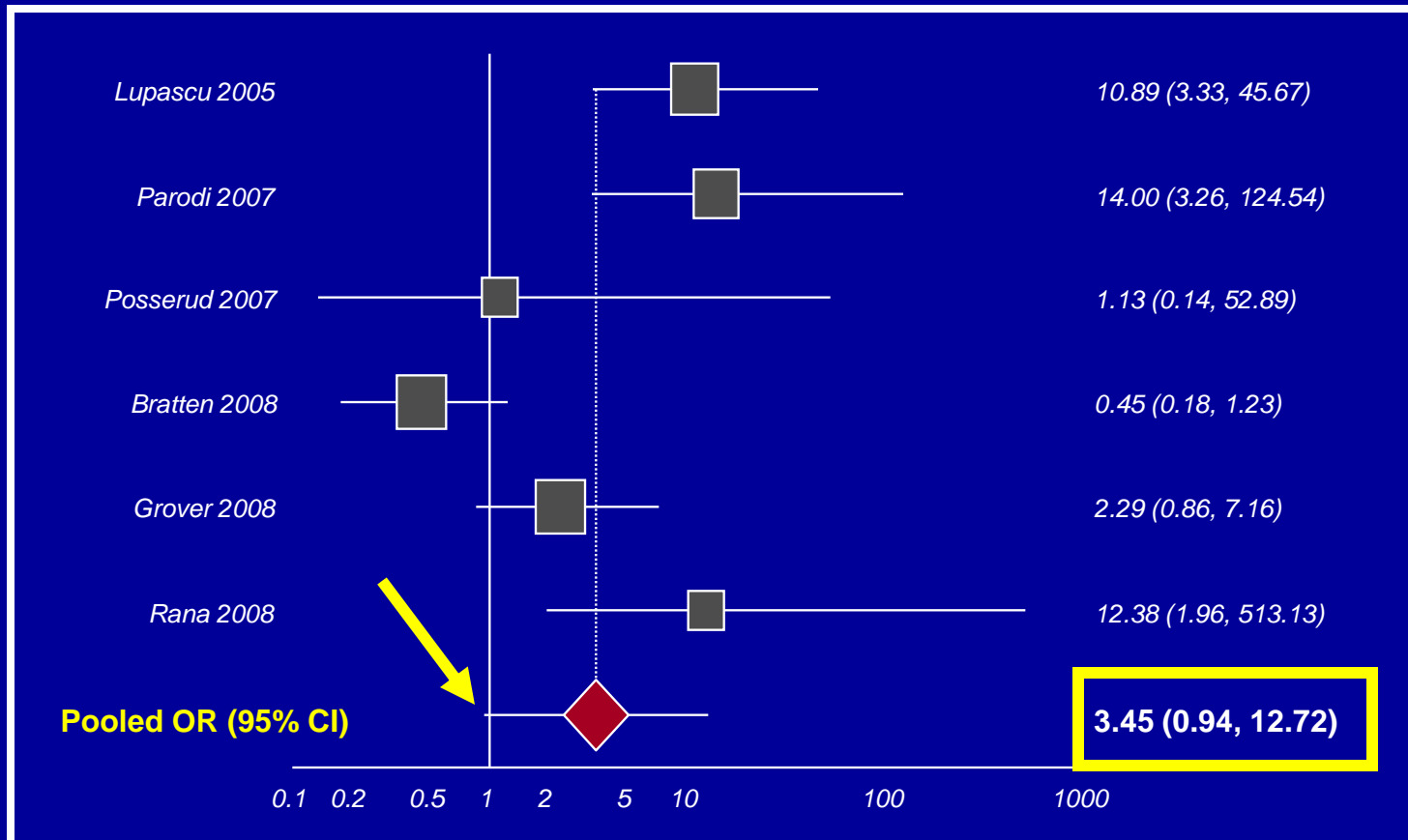
IBS vs. Controls: H₂ rise > 20 ppm by 180



Meta-Analysis of SIBO in IBS

- **Because data are conflicting need to evaluate literature as a whole**
- **Ford et al. conducted meta-analysis to compare prevalence of SIBO in IBS vs. controls**
- **Looked for evidence of “publication bias”**

Positive Lactulose Breath Test: Odds in IBS vs. Controls



Heterogeneity test: $P < 0.001$

Publication bias test: $P = 0.04$

Ford et al. - Conclusions

- **Prevalence of SIBO in IBS numerically high, but:**
 - Large variation between studies
 - Difference not statistically significant
 - Evidence of publication bias
- **Suggests that a definite role for SIBO in IBS remains debatable**
- **Lack of effect may also reflect inaccuracies of existing diagnostic tests**

Jejunal Cultures in IBS vs. Controls

- Posserud et al (Gut 2007):
 - Compared jejunal aspirates in 162 IBS patients vs. 26 healthy controls
 - Using SIBO definition of $\geq 10^5$ CFU/ml, found 4% prevalence in both groups
 - Mildly increased bacterial counts (10^3) more common in IBS vs. controls (43% vs. 12%; $p=0.002$)

Posserud et al: Questions Raised

- Is jejunal aspirate just a really poor marker for SIBO?
- Are sub-threshold bacterial counts clinically important?
- Or is IBS really not marked by SIBO?

Clinical Relevance of Abnormal SI Bacterial Counts in IBS

- Follow-up study by Posserud et al. to assess relevance of abnormal bacterial counts on IBS symptoms
- Performed aspirates in 126 Rome III IBS patients and LHBT in another 80 patients
- **Compared IBS symptoms** between groups:
 - $\geq 10^5$ **vs.** $< 10^5$ CFU/ml
 - $\geq 10^3$ **vs.** $< 10^3$ CFU/ml
 - LHBT positive **vs.** LHBT negative

Posserud et al. - Results

Diagnosis	%
SIBO by aspirate ($\geq 10^5$ colonic bacteria)	3% (4/126)
Sub-threshold SIBO by aspirate ($\geq 10^3$ colonic bacteria)	9% (11/126)
SIBO by “double peak” LHBT method	6% (5/80)
SIBO by “peak before 90 minutes” method	43% (34/80)

Posserud et al. - Results

“We found no clear association between symptoms and culture verified SIBO, mildly increased small bowel bacteria or abnormal LHBT. A H₂ rise within 90 min was associated with more severe symptoms of diarrhea, possibly as a consequence of faster small bowel transit. Thus, the clinical importance of abnormal small bowel bacterial counts in IBS patients is questionable.”

Question

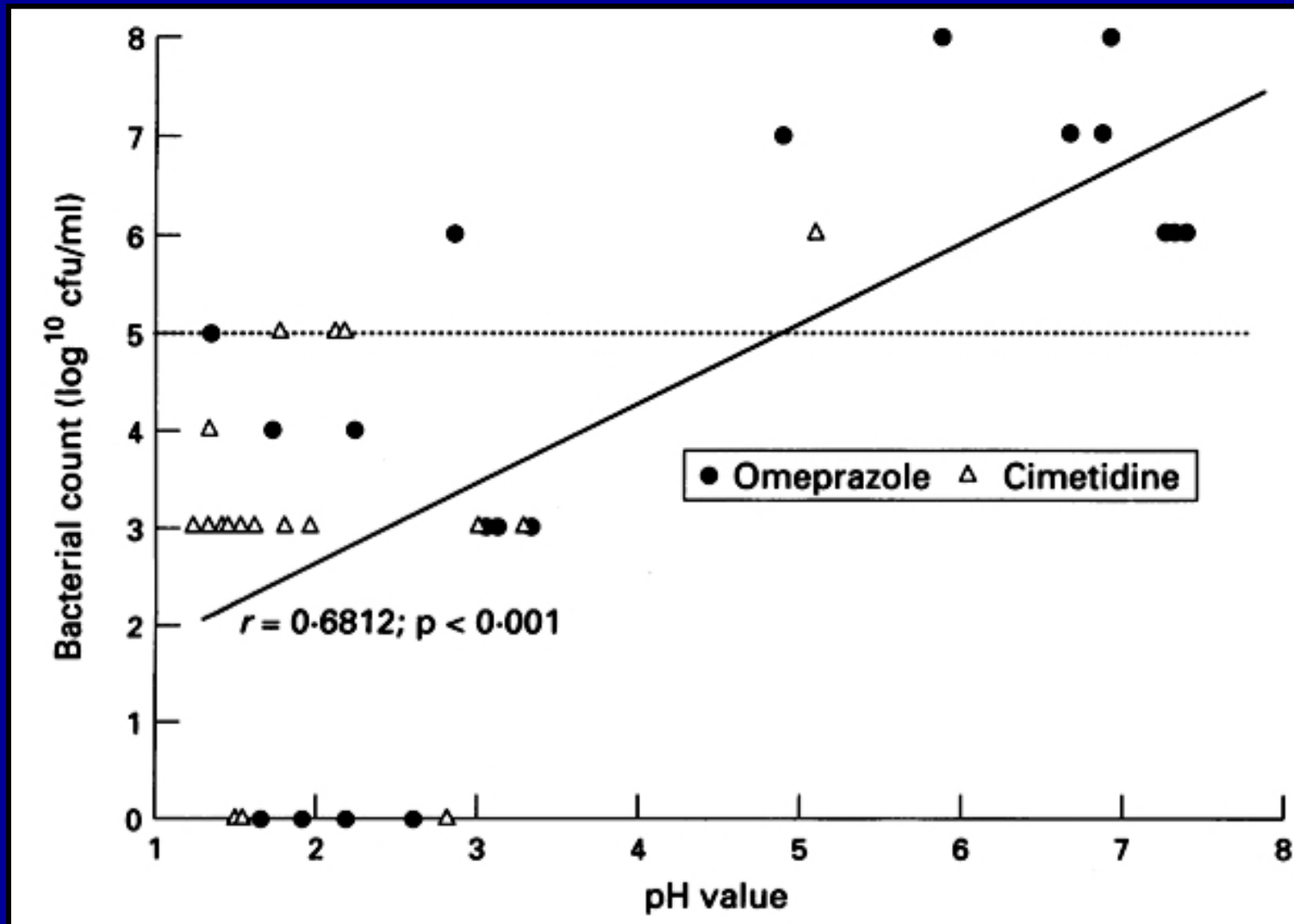
I plan to use antibiotics regardless of the HBT or jejunal aspirate. In fact, I don't check the HBT anyway. Will clearing SIBO with rifaximin lead to a long-term cure? Or will the SIBO just come back?

SIBO Recurrence Following Rifaximin

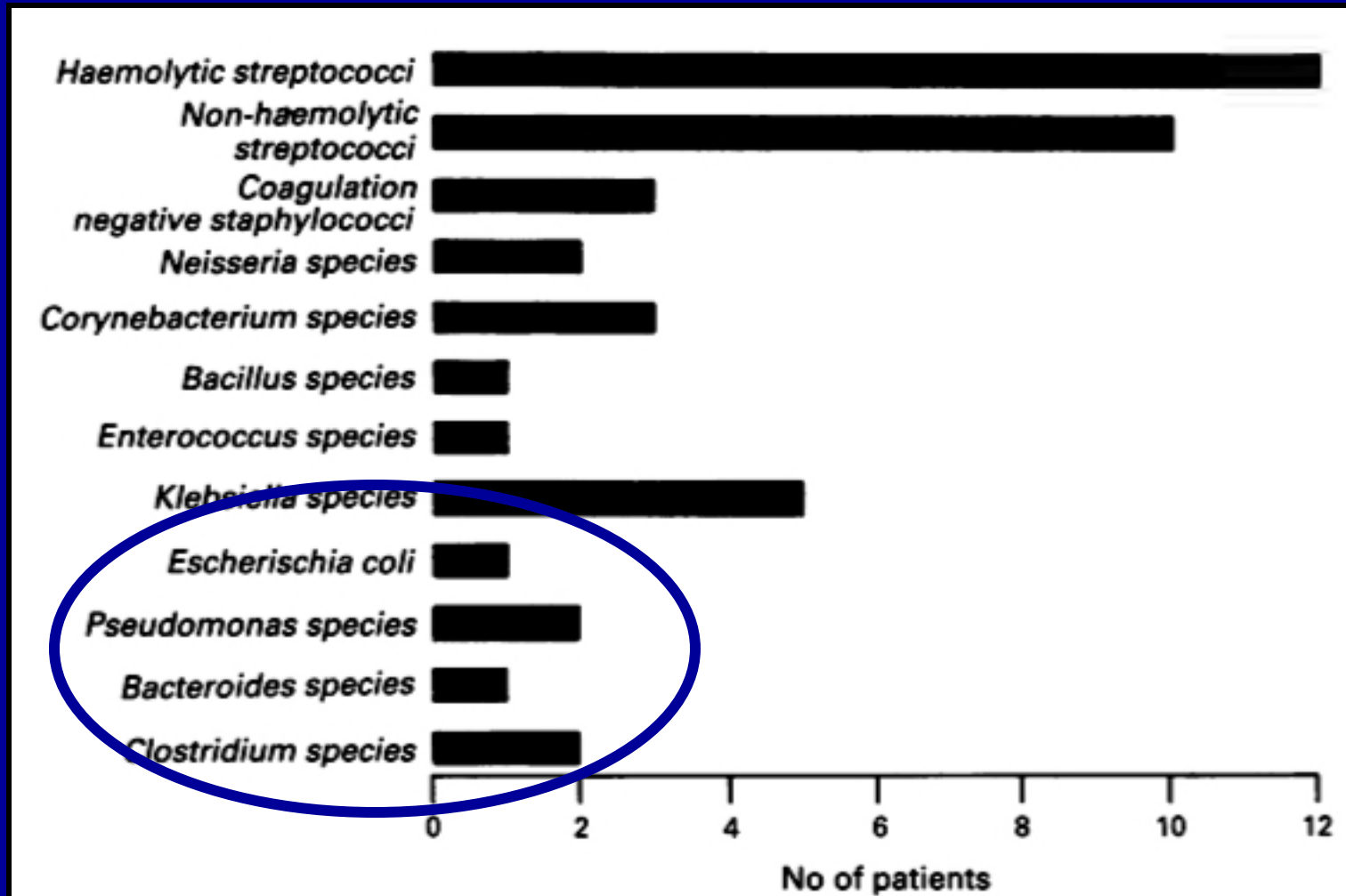
Predictors of SIBO Recurrence:

- Older age (OR=1.09)
- History of appendectomy (OR=5.9)
- Use of **proton pump inhibitors** (OR=3.5)

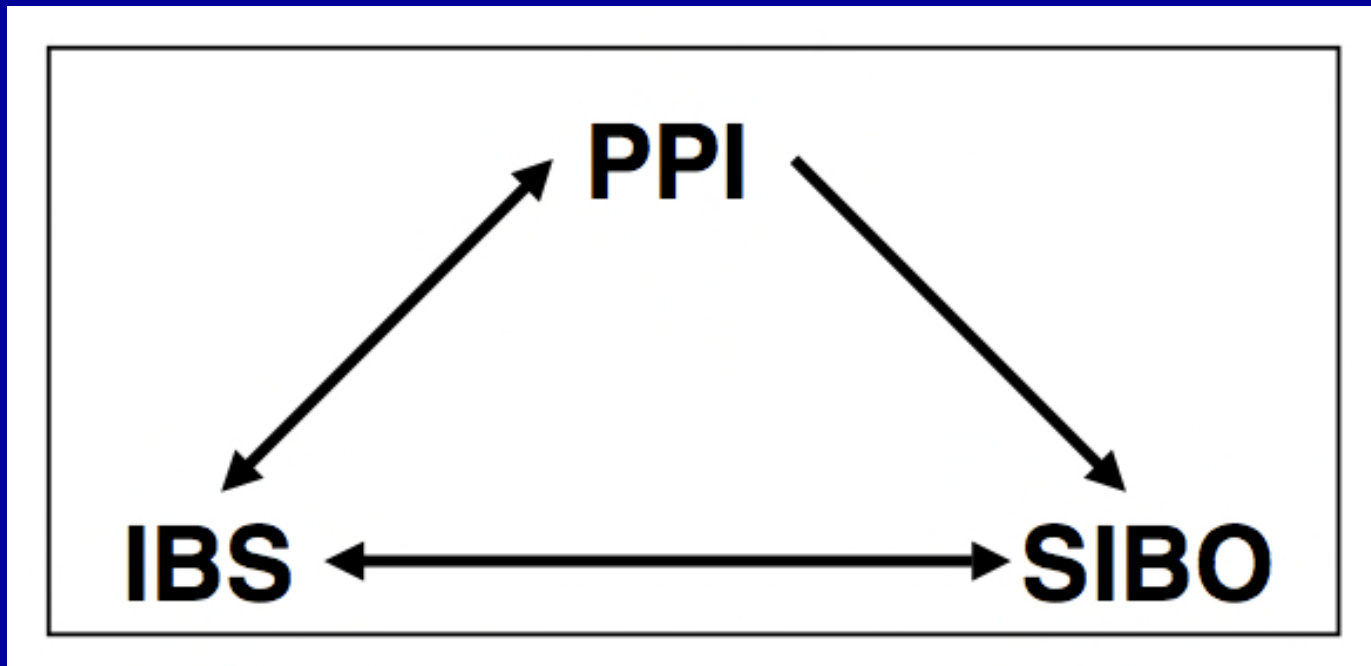
Relationship between PPI Use and Foregut Bacterial Counts



Species Found in Foregut of Patients on PPIs



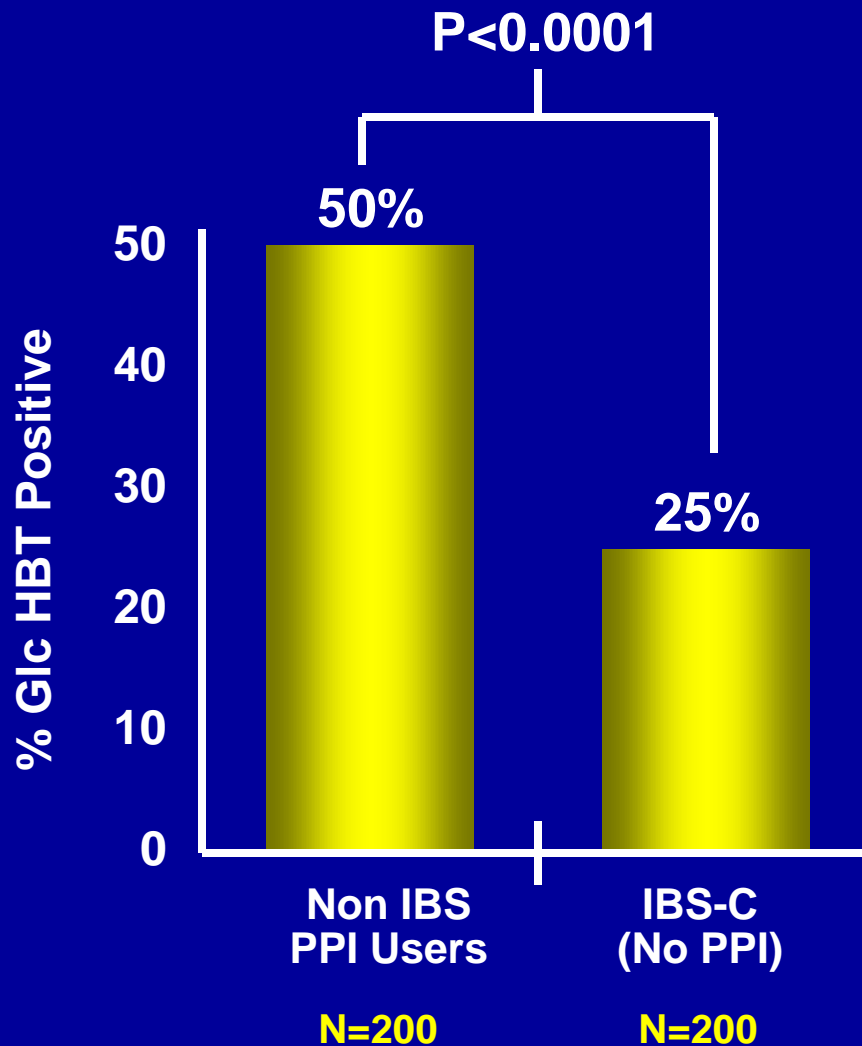
PPIs as the Confounder: Could IBS Be Linked to SIBO Through PPIs?



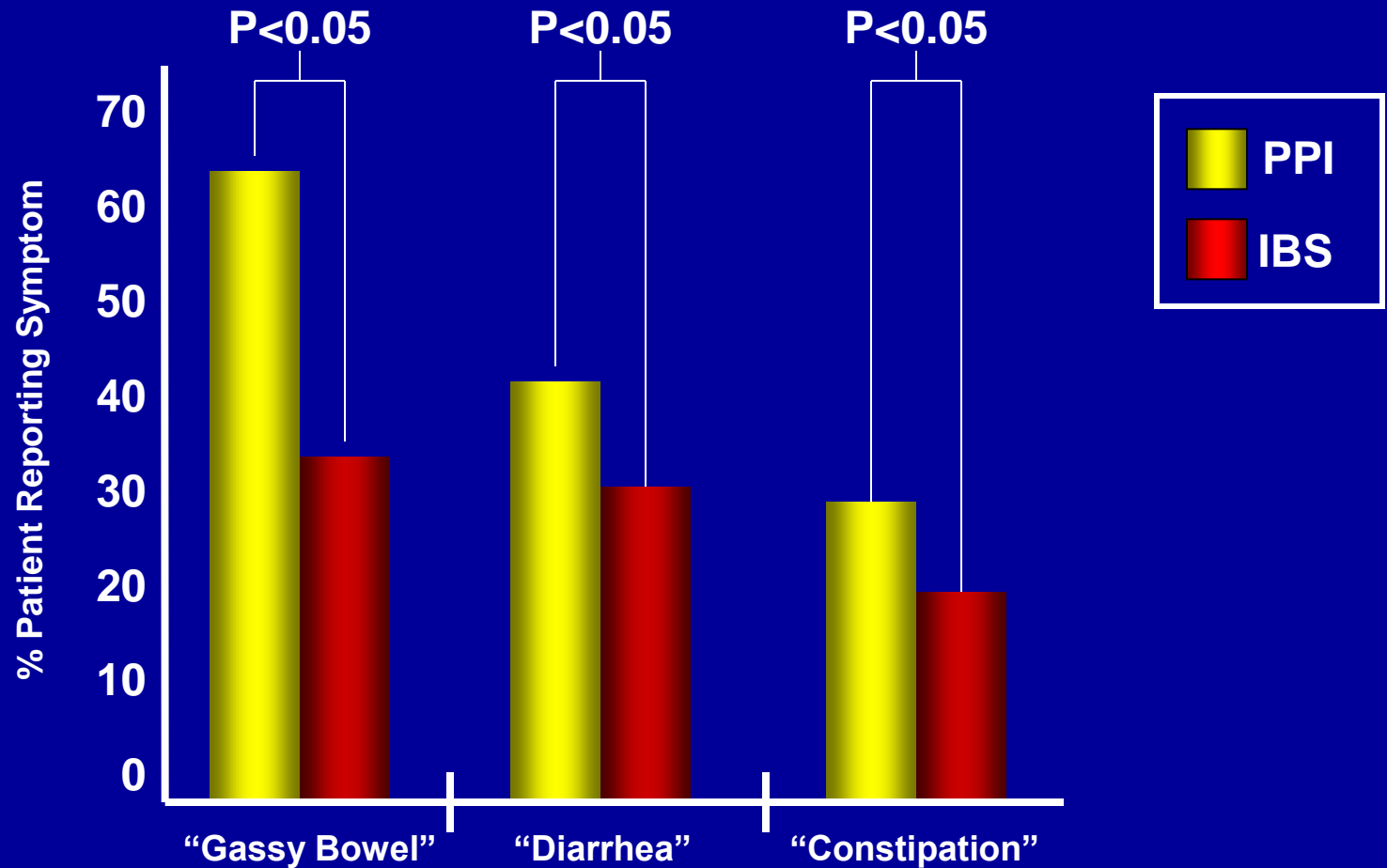
Clinical Significance of PPI-Related SIBO

- Clinical significance of PPI-related SIBO remains uncertain
- Lucio et al. evaluated relationship between PPIs, SIBO, and GI symptoms
- Compared GHBT results and GI symptoms between
 - 200 **non-IBS active PPI users**
 - 200 **IBS-C patients not using PPIs**

HBT Positivity: Non-IBS PPI vs. Non-PPI IBS



GI Symptoms in Patients with SIBO: Non-IBS PPI vs. Non-PPI IBS



Lucio et al - Conclusions

- SIBO is more prevalent in patients on long term PPIs vs. IBS controls
- PPI users with SIBO report higher intensity of GI symptoms than IBS patients with SIBO
- **Supports hypothesis that PPIs may be associated with clinically significant SIBO**
- **Suggest that IBS patients on PPI might consider stopping PPI prior to trying abx.**

Update on Epidemiological Controversies and Gender Differences



Air Pollution and Abdominal Pain

- **Unexplained abdominal pain is often associated with depression and headaches**
- **Depression and headaches, in turn, are known to be exacerbated by air pollution**
- **Therefore, could unexplained abdominal pain also be exacerbated by air pollution?**

Kaplan et al – Abstract #1055

- Measured relationship between air pollution and ER visits for nonspecific abdominal pain (NSAP)
- Evaluated 2 cohorts over 10 years of data:
 - 95,173 ER visits for NSAP in **Edmonton**, Canada
 - 25,852 ER visits for NSAP in **Montreal**, Canada
- Tracked daily ozone, nitrogen dioxide, sulfur dioxide, carbon monoxide, and particulates
- Performed time series to estimate relationship between NSAP visits and pollutants

Kaplan et al – Results

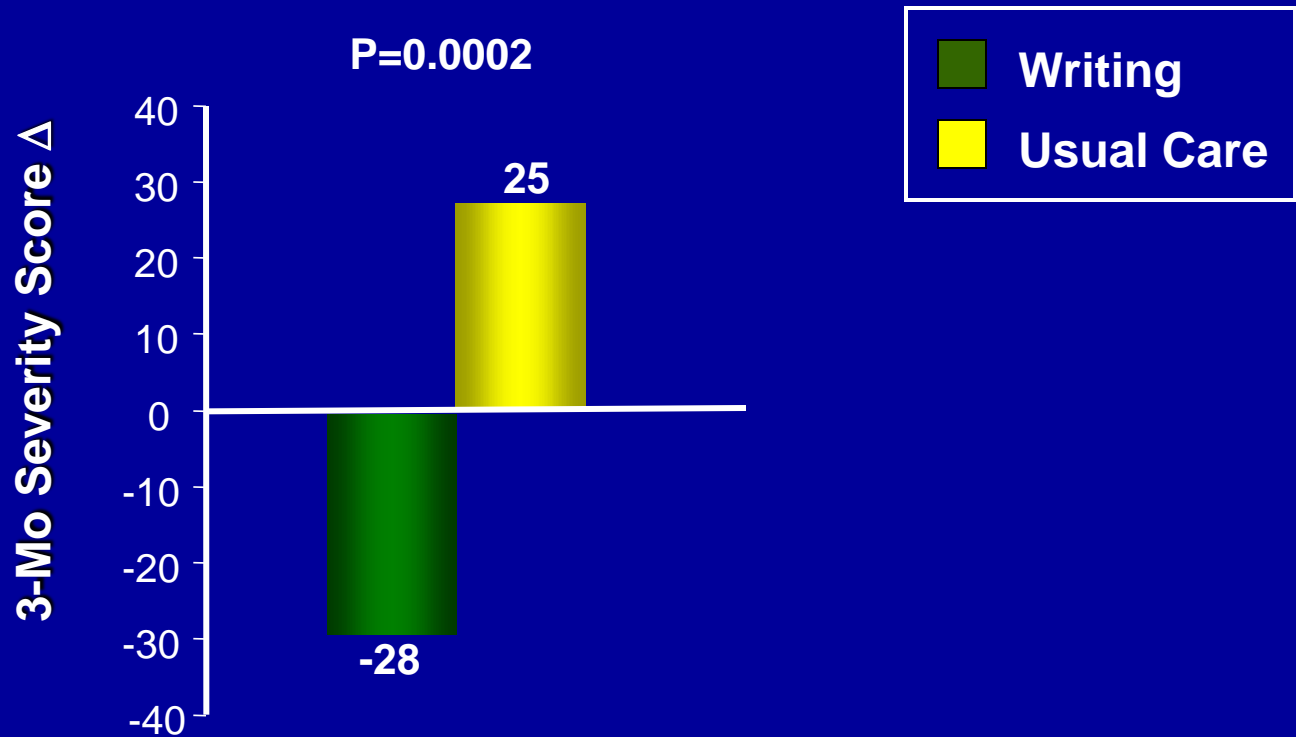
- Two-thirds of ER visits for NSAP were by women aged 15-24 years – probably lots of IBS
- NSAP visits significantly tracked with pollutants in both cities for:
 - Large particulates
 - Nitrogen and sulfur dioxide
 - Carbon monoxide
- Visits tracked negatively with ozone
- Striking that results reproduced in two geographically distinct metropolitan areas

Non-Pharmacological Therapies for IBS

Trial of “Expressive Writing” vs. Usual Care in IBS

- Compared IBS symptom severity and quality of life in between 2 groups:
 1. **Expressive writing group**
 2. **Usual care** without writing intervention
- **Expressive writing group:**
 - Asked to write online about IBS thoughts and feelings for 30 min for 4 consecutive days
 - Encouraged to explore their emotions and the effects of IBS on wellbeing

Results



Take-Home Messages

- Prevalence of SIBO in IBS **numerically high** but **not statistically significant** compared to controls
- No clear association between symptoms and culture verified SIBO, sub-threshold SI bacteria or abnormal LHBT
- Nearly half of SIBO patients treated with rifaximin have recurrence after 9 months
- Long-term PPI users may have higher prevalence of SIBO than IBS patients not on PPI
- Air pollution might be related to functional abdominal pain
- **Expressive writing** might help select patients with IBS