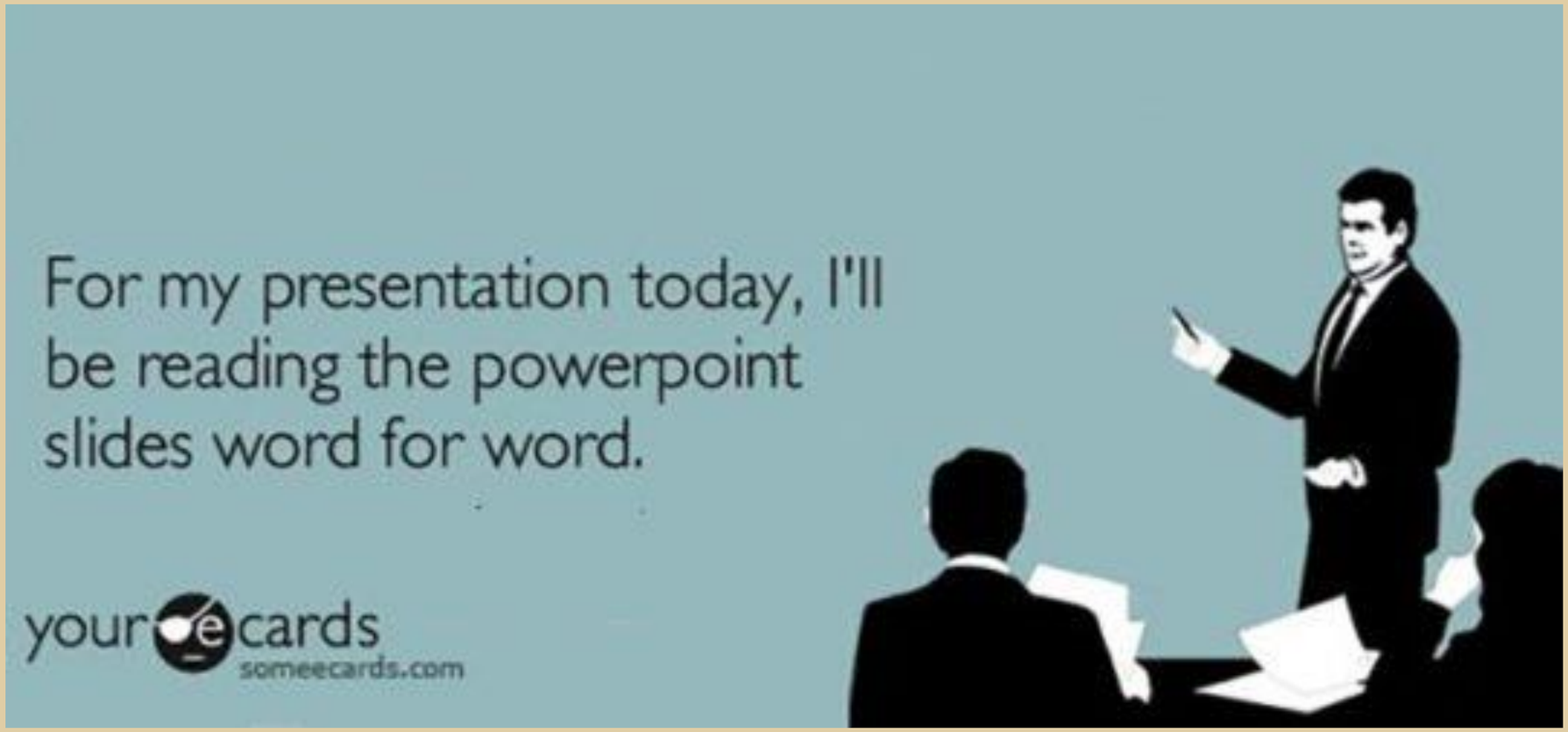
Journal Club

May 10th, 2019

Dr. Melanie Breau and Dr. Gautam Kumar

Disclosures

- We have no relationships with for-profit or not-for-profit organizations
- This session has NOT received financial support or in-kind support from another organization
- A single disclosure to adjust your expectations for this talk:



Probiotic use in acute gastroenteritis

Do you recommend the use of probiotics for children with acute gastroenteritis?

1. No
2. Yes
3. No, unless there's probiotics in wine (for the parents of course!)

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Session ID: Peds2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis

Stephen B. Freedman, M.D.C.M., Sarah Williamson-Urquhart, B.Sc.Kin., Ken J. Farion, M.D., Serge Gouin, M.D.C.M., Andrew R. Willan, Ph.D., Naveen Poonai, M.D., Katrina Hurley, M.D., Philip M. Sherman, M.D., Yaron Finkelstein, M.D., Bonita E. Lee, M.D., Xiao-Li Pang, Ph.D., Linda Chui, Ph.D., David Schnadower, M.D., M.P.H., Jianling Xie, M.D., M.P.H., Marc Gorelick, M.D., and Suzanne Schuh, M.D., for the PERC PROGUT Trial Group*

N Engl J Med 2018;379:2015-26

Acute gastroenteritis

- **1.7 million** yearly visits to the ED in USA

- Considerable non-medical costs - lost parental income, daycare, etc…

the pros of probiotics

WHAT ARE PROBIOTICS? [proh-bahy-ot-ix]
Probiotics are bacteria that help maintain the natural balance of organisms (microflora) in the intestines.

There are more than **25** different **diseases and syndromes** — including **ALZHEIMER'S**, **ARTERIOSCLEROSIS**, **DEPRESSION** & **RHEUMATISM** that have been linked to **bacterial imbalance**

An estimated **100 TRILLION** microorganisms representing more than **500 DIFFERENT SPECIES** inhabit every normal, healthy bowel, **REDUCING THE GROWTH OF HARMFUL BACTERIA** and **PROMOTING A HEALTHY DIGESTIVE SYSTEM.**

save paper

Probiotics reduced antibiotic-associated diarrhea by **64%**

(Cochrane Database of Systematic Reviews, 2013)

probiotics + aloe

43% REDUCTION IN TOTAL CHOLESTEROL LEVELS

12% INCREASE IN HDL (GOOD) CHOLESTEROL

(Journal Nutrition, March 2013)

34%

reduction in Upper Respiratory Infections

In healthy young adults following 12 weeks of oral administration of *Lactobacillus rhamnosus*

(British Journal of Nutrition, 2013)

Oral administration of probiotics has shown to **REDUCE CHOLESTEROL LEVELS BY AS MUCH AS 33%** in animal and human studies.

(World Health Organization)

50% INCREASE

In immune function following two weeks of probiotics supplementation

(British Journal of Nutrition)

Two particular strains of probiotics — *Lactobacillus helveticus and Bifidobacterium longum* — **improved "levels of psychological distress, including measures of depression, anger-hostility, anxiety and problem solving."**

(British Journal of Nutrition, March 2011)

CureJoy

NUTRITION CURE FITNESS BEAUTY GENERAL HEALTH

NUTRITION / PROBIOTICS

Probiotics: Why Women Need To Put Their Microbiome Health Front And Center!

JENNIFER KANAAN | OCT 25, 2018 9 Min Read

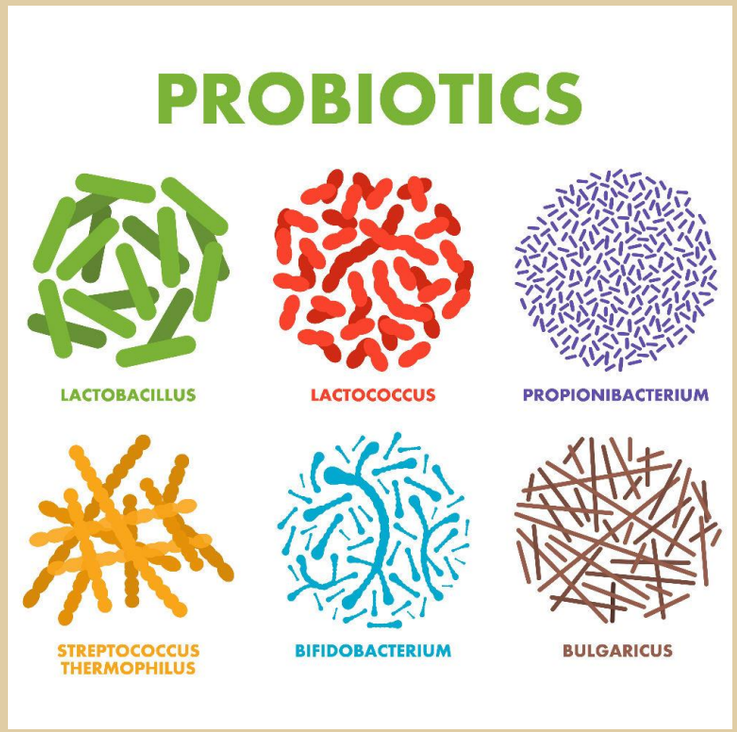
Share Tweet Pin It +

As a woman, you are constantly wearing multiple hats. Whether it's juggling parenting duties and work deadlines, packing lunches and looking after family members, churning out top-notch presentations and mentoring a team, or running an immaculate home, for most women, every day is filled with some madness and a million things to do. And let's not forget, you also have to make it all seem completely effortless! But then, after a point, something's got to give.

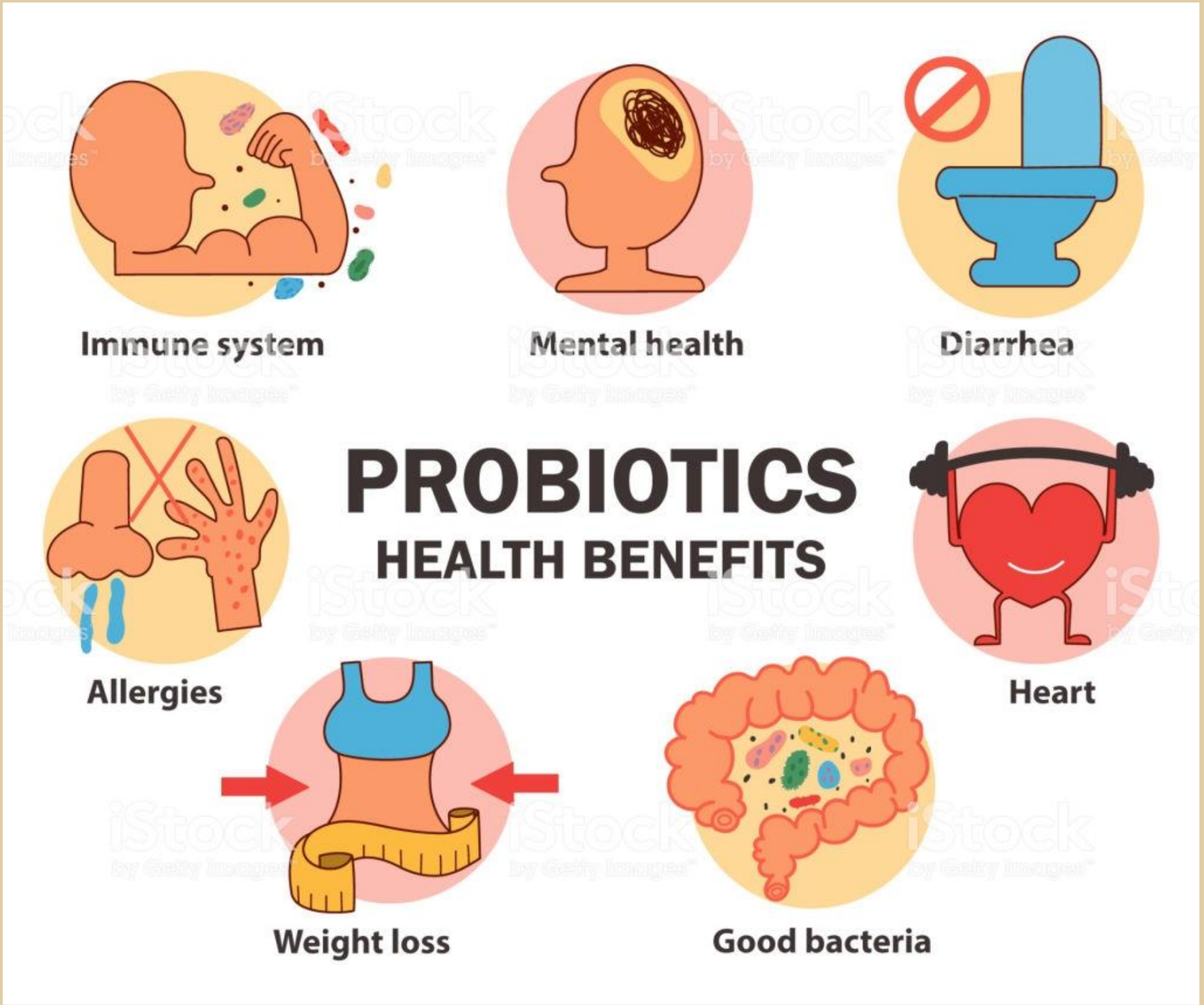
Poor immunity or failing health is often a telltale sign that you aren't looking after yourself as well as you should. And even when you do manage to squeeze in a little time to watch your health, chances are you focus on things like cardiac health, blood sugar levels, or reproductive health. In the middle of all this, a tiny world known as your microbiome is unlikely to be on your radar. In fact, every other organ and system, including your skin and nails, probably gets more attention than this microscopic ecosystem that thrives within you.

Probiotics

- Probiotic global market - $ 37 billion (estimated $64 billion by 2023)
- Live micro-organisms that alter gut microflora



Fact or Fiction?



Probiotics for acute gastroenteritis

- NEJM November 2018 - 2 RCT's designed to look at this question (Canada; USA)
- 6 Canadian tertiary-care, paediatric ED's
- Randomized, double-blind, placebo-controlled trial

Alberta Children's Hospital Research Institute

SickKids

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Université de Montréal

CHEO

Children's Hospital
London Health Sciences Centre

IWK Health Centre

Methods

- 5-day course of combined Lactobacillus rhamnosus R0011/L.helveticus R0052 BID or placebo
- Children 3-48 months in ED:
  - > 3 episodes watery stools in 24 hrs, V or D for less than 72hrs, clinical diagnosis of acute gastro by ED physician
- Parents completed F/U surveys (phone/electronic) every 24hrs until symptoms resolved for 24hrs
- Rectal swabs, stool specimens

Outcomes

1. Occurrence of moderate-severe gastro (modified Vesikari scale, >9/20) at day 14

2. Duration of diarrhea/vomiting, unscheduled visits to HCP, adverse events by day 14

Table 1. Modified Vesikari Scale.*

Scale component	Score on the Vesikari Scale			
	0 Points	1 Point	2 Points	3 Points
Duration of diarrhea (hr)	0	1–96	97–120	≥121
Maximum no. of watery stools per 24 hr	0	1–3	4–5	≥6
Duration of vomiting (hr)	0	1–24	25–48	≥49
Maximum no. of vomiting episodes per 24 hr	0	1	2–4	≥5
Maximum recorded rectal temperature (°C)†	<37.0	37.1–38.4	38.5–38.9	≥39.0
Unscheduled health care visit	None	NA	Primary care	Emergency department
Treatment	None	Rehydration with intravenous fluids	Hospitalization	NA

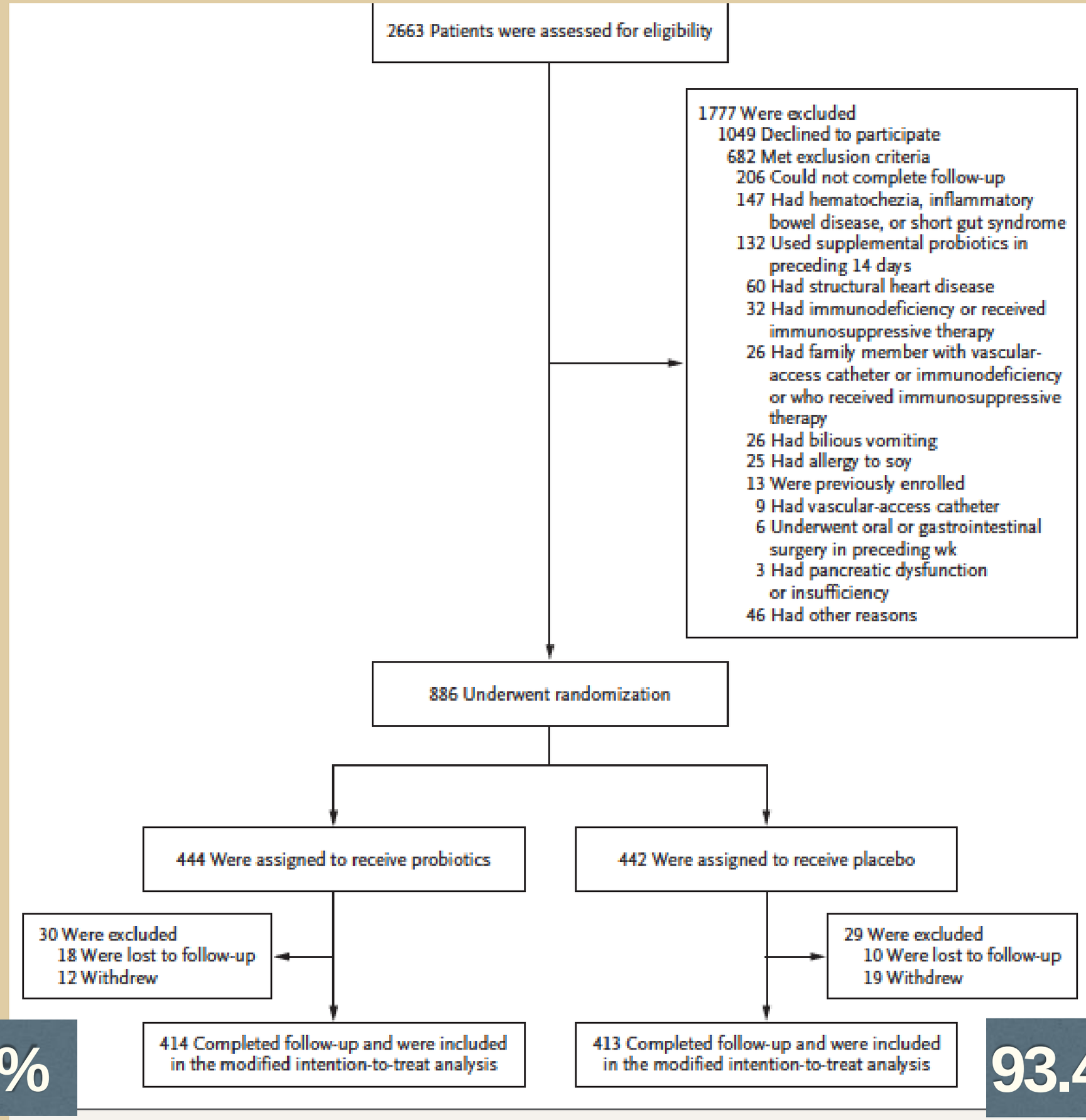


Figure 1. Enrollment, Randomization, and Outcomes.

Table 2. Baseline Characteristics of the Enrolled Participants.*

Characteristic	Probiotic Group (N=440)	Placebo Group (N=437)
Median age (IQR) — mo	16.0 (10.0–24.8)	15.0 (9.5–24.0)
Male sex — no. (%)	243 (55.2)	252 (57.7)
Median weight (IQR) — kg	10.6 (9.0–13.0)	10.7 (8.8–12.6)
Exclusively breast-fed — no. (%)	23 (5.2)	32 (7.3)
Received antibiotics in previous 14 days — no. (%)	56 (12.7)	63 (14.4)
Received rotavirus vaccine — no. (%)	214 (48.6)	213 (48.7)
Median duration of illness (IQR) — hr†	42.5 (26.7–58.1)	43.8 (27.7–58.8)
Median modified Vesikari score (IQR)‡	10 (9–12)	10 (8–12)
Vomiting — no. (%)	345 (78.4)	327 (74.8)
Median no. of vomiting episodes in preceding 24 hr (IQR)§	5 (3–8)	5 (2–8)
Median no. of diarrhea episodes in preceding 24 hr (IQR)	6 (4–8)	6 (4–9)
Febrile — no. (%)¶	198 (45.0)	196 (44.9)
Median clinical dehydration scale score (IQR)‖	1 (0–2)	0 (0–2)
Received ondansetron at index visit — no./total no. (%)	100/440 (22.7)	91/437 (20.8)
Received intravenous rehydration at index visit — no./total no. (%)	40/440 (9.1)	33/437 (7.6)
Admitted to hospital at index visit — no./total no. (%)	11/439 (2.5)	11/437 (2.5)
Stool testing results — no./total no. (%)**		
Norovirus GI or GII	102/432 (23.6)	124/428 (29.0)
Rotavirus A	124/432 (28.7)	85/428 (19.9)
Clostridium difficile toxin A or B	51/432 (11.8)	61/428 (14.3)
Adenovirus 40 or 41	50/432 (11.6)	45/428 (10.5)
Salmonella	11/432 (2.6)	9/428 (2.1)

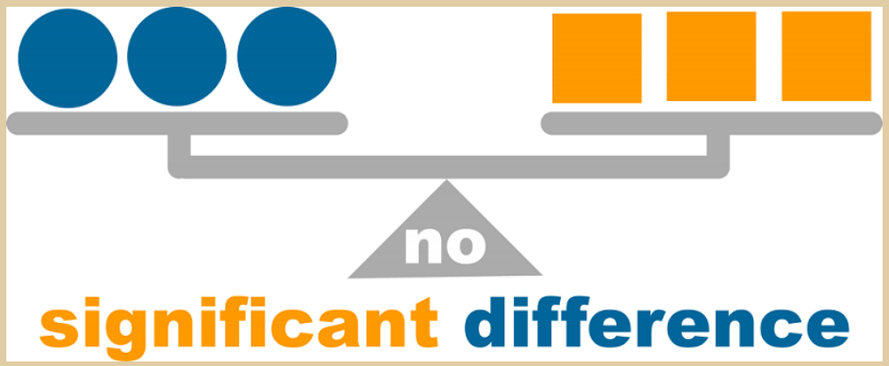
Results

Table 3. Trial Outcomes and Subgroups.*

Outcome and Subgroup	Probiotic Group	Placebo Group	Odds Ratio (95% CI)	P Value
Primary efficacy outcome: modified Vesikari score of ≥9†‡				
All participants — no./total no. (%)	108/414 (26.1)	102/413 (24.7)	1.06 (0.77–1.46)	0.72
Age <1 yr — no./total no. (%)	45/134 (33.6)	48/150 (32.0)	1.01 (0.60–1.71)	0.97
Exclusively breast-fed — no./total no. (%)	7/22 (31.8)	10/31 (32.3)	0.82 (0.18–3.61)	0.79§
Receipt of antibiotics within 14 days before index visit — no./total no. (%)	12/51 (23.5)	17/59 (28.8)	0.86 (0.35–2.11)	0.74¶
Adherence to trial regimen, defined as having received >70% of doses prescribed — no./total no. (%)	72/295 (24.4)	66/303 (21.8)	1.16 (0.79–1.71)	0.45
Secondary efficacy outcomes				
Median duration of diarrhea in 827 participants (IQR) — hr	52.5 (18.3–95.8)	55.5 (20.2–102.3)		0.31
Median duration of vomiting in 409 participants (IQR) — hr‖	17.7 (0–58.6)	18.7 (0–51.6)		0.18
Visit to health care provider — no./total no. (%)†	125/414 (30.2)	110/413 (26.6)	1.19 (0.87–1.62)	0.27
Any adverse event — no./total no. (%)**	136/414 (32.9)	152/413 (36.8)	0.83 (0.62–1.11)	0.21
Tertiary efficacy outcomes				
Median no. of days of day care missed in 331 participants (IQR)††	1.0 (0–2.0)	1.0 (0–2.0)		0.55
Median no. of hours of work missed by parent or guardian of 653 participants (IQR)‡‡	0 (0–8.0)	0 (0–8.8)		0.18
Repeat visit to ED				
No. of participants/total no. (%)†	83/414 (20.0)	76/413 (18.4)	1.11 (0.77–1.60)	0.56
With administration of intravenous fluid — no./total no. (%)†	36/414 (8.7)	26/413 (6.3)	1.57 (0.75–3.28)§§	0.23
With hospitalization — no./total no. (%)†	33/414 (8.0)	22/413 (5.3)	1.65 (0.66–4.12)¶¶	0.28

Results

- **Severity of symptoms:**
  - Probiotic 108/414 (26.1%) vs Placebo 102/413 (24.7%), P 0.72
- **Secondary outcomes**
  - No difference in anything….



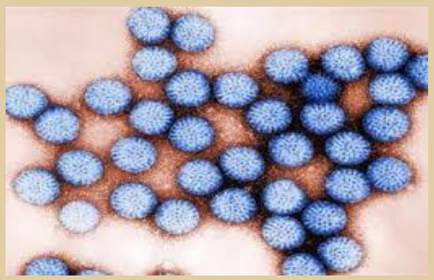
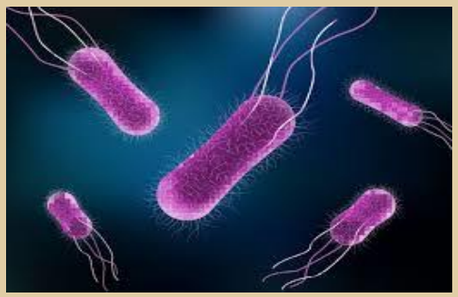
Similar results found in the US study (Schnadower, et al)

Take home message

- No evidence to support use of probiotics to decrease severity of acute gastroenteritis in children

Will this article change your practice?

1. Less probiotics (more wine)
2. Probiotics for everyone!
3. Probiotics are hocus pocus…. I never recommended them anyways
4. Will think about it

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Early introduction of solids and infant sleep

4 mos old not sleeping…

- Exhausted parents in your office
- They read a lot of parent blogs
- ? starting solids will help their baby sleep longer/better

Do you recommend starting solids earlier to help with infant sleep?

1. No
2. Yes
3. I'm an exhausted parent… I don't remember the question…

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JAMA Pediatrics | Original Investigation

Association of Early Introduction of Solids With Infant Sleep
A Secondary Analysis of a Randomized Clinical Trial

Michael R. Perkin, PhD; Henry T. Bahnson, MPH; Kirsty Logan, PhD; Tom Marrs, MB, BS; Suzana Radulovic, MD; Joanna Craven, MPH; Carsten Flohr, PhD; Gideon Lack, MB, BCh

JAMA Pediatr. 2018;172(8):e180739

Current recommendations

- WHO, CPS and AAP recommend exclusive breastfeeding for 6 months

- Complementary foods should be introduced at around six months of age

- Early introduction of complementary foods may be associated with higher risk of obesity and autoimmune diseases (ex. Celiac, T1DM)

Agostoni, C. Complementary feeding: a commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2008 Jan;46(1):99-110.

Nucci, A Infant Feeding and Timing of Complementary Foods in the Development of Type 1 Diabetes. Curr Diab Rep. 2015 Sep; 15(9)

Pluymen, L. Early introduction of complementary foods and childhood overweight in breastfed and formula-fed infants in the Netherlands: the PIAMA birth cohort study. Eur J Nutr. 2018 Aug;57(5):1985-1993. doi: 10.1007/s00394-018-1639-8. Epub 2018 Feb 22.

But what really happens??

- 55% of US families introduce complementary foods before six months

Barrera, CM. Timing of Introduction of Complementary Foods to US Infants, National Health and Nutrition Examination Survey 2009-2014. J Acad Nutr Diet. 2018 Mar;118(3):464-470.

- 75% of British parents introduce solids before 5 months

McAndrews, F. Infant Feeding Survey 2010. Leeds, England: Health and Social Care Information Centre, 2012.

- In both countries, a large proportion occurred because of sleeping difficulties

Enquiring About Tolerance (EAT) study

- Large randomized clinical trial in UK
- Examined effects of early introduction of 6 allergenic foods
- Secondary analysis of sleep data

EAT
Enquiring About Tolerance

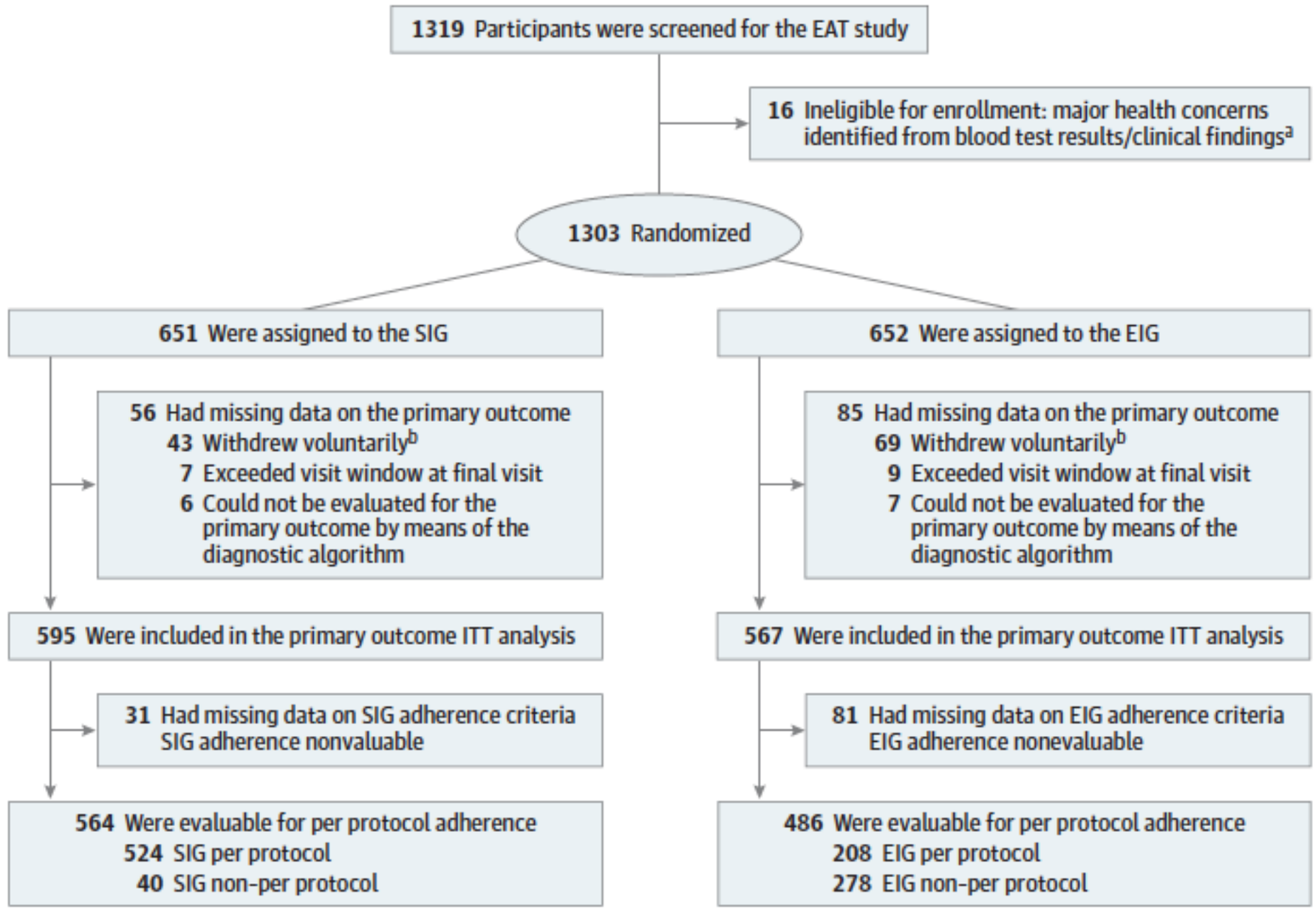
Method

- Randomized 1303 infants into standard vs. early allergenic food introduction groups
- All families completed Brief Infant Sleep Questionnaire and maternal QOL questionnaire monthly until 1 yr, then q3months until 3 yrs

eTable 1. Brief Infant Sleep Questionnaire (BISQ)[8]

BISQ Question	Response options	Variable
Sleeping arrangement	Infant crib in a separate room Infant crib in parents' room In parents' bed Infant crib in room with sibling Other, Specify:	Sleeping Location
In what position does your child sleep most of the time?	On his/her belly On his/her side On his/her back	Sleep Position
How much time does your child spend in sleep during the NIGHT (between 7 in the evening and 7 in the morning)?	Hours: _____ Minutes: _____	Nocturnal Sleep Duration
How much time does your child spend in sleep during the DAY (between 7 in the morning and 7 in the evening)?	Hours: _____ Minutes: _____	Daytime Sleep Duration
Average number of night wakings per night		Number of Night Wakings
How much time during the night does your child spend in wakefulness (from 10 in the evening to 6 in the morning)?	Hours: _____ Minutes: _____	Nocturnal Wakefulness
How long does it take to put your baby to sleep in the evening?	Hours: _____ Minutes: _____	Settling Time
How does your baby fall asleep?	While feeding Being rocked Being held In bed alone In bed near parent	Soothing Method
When does your baby usually fall asleep for the night:	Hours: _____ Minutes: _____	Sleep Onset Time
Do you consider your child's sleep as a problem?	A very serious problem A small problem Not a problem at all	Sleep Problem Rating

Figure 1. Enquiring About Tolerance (EAT) Enrollment and Randomization

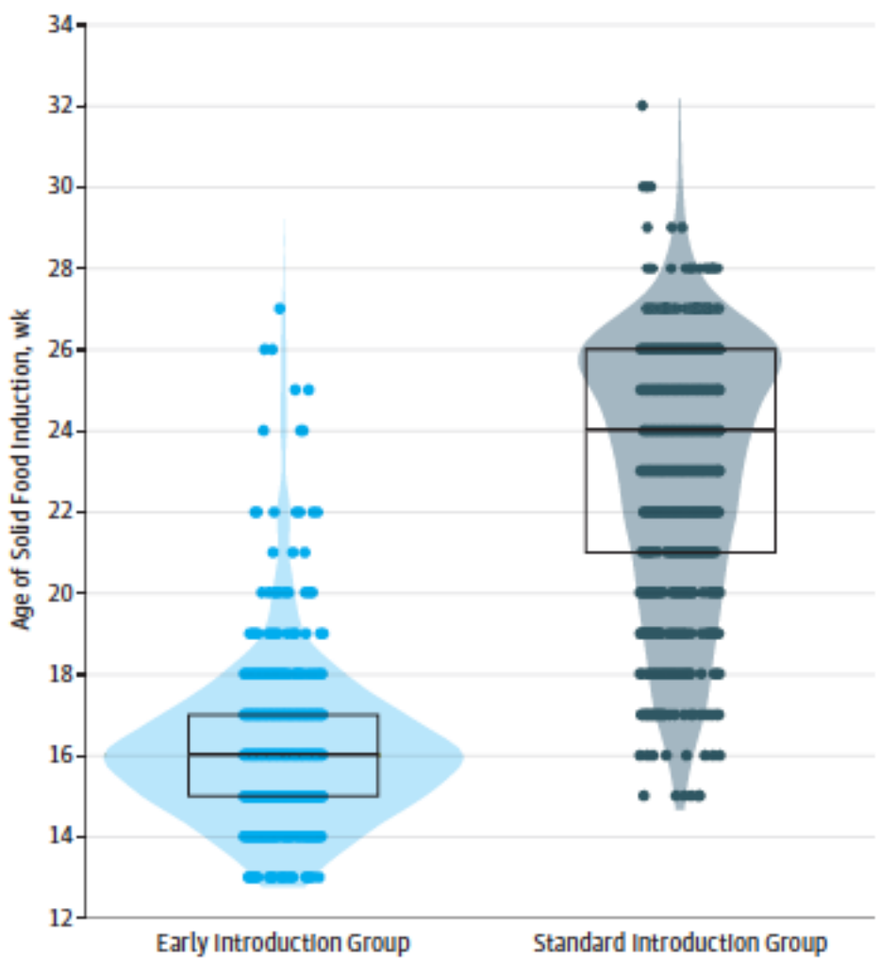


SIG: Standard intro group

EIG: Early intro group

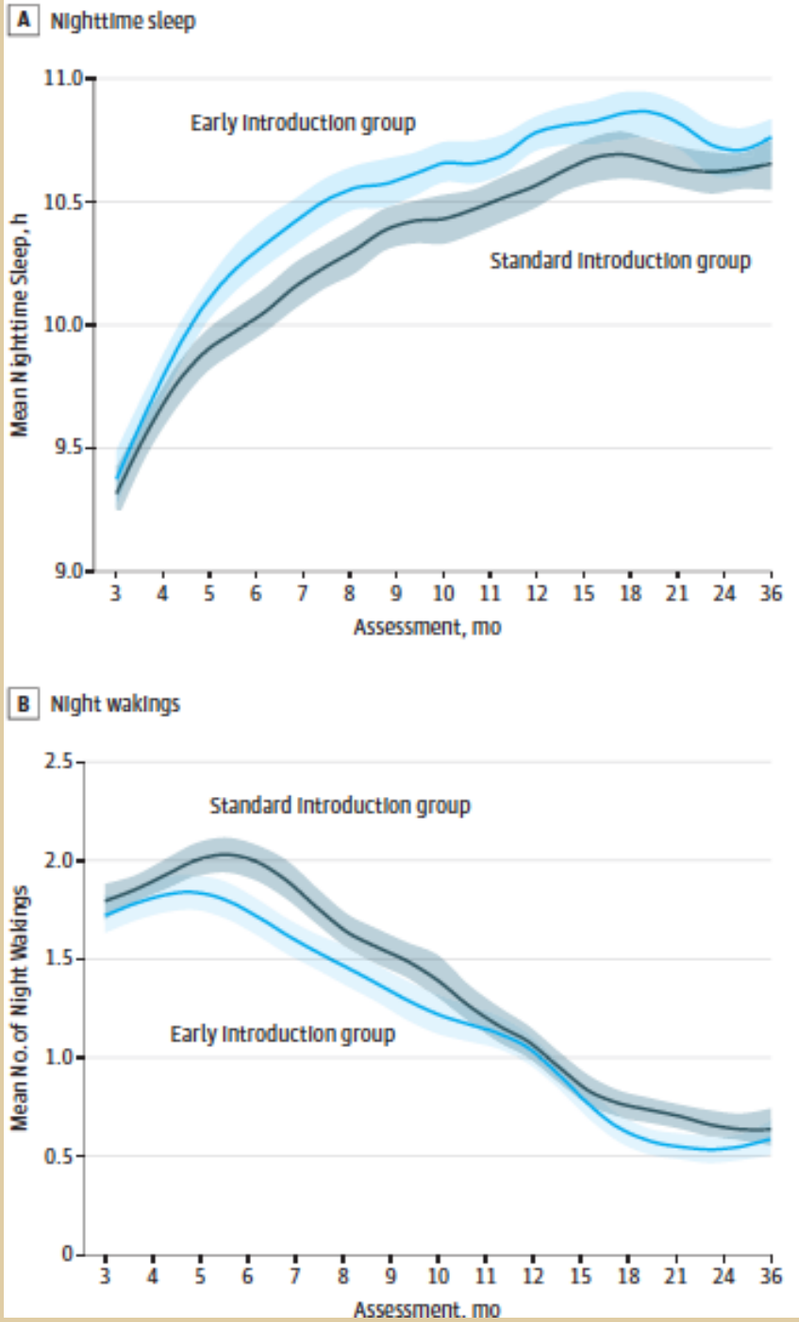
Results

Figure 2. Age of Solid Food Introduction in Infants Participating in the Enquiring About Tolerance (EAT) Study



The black bar indicates the median, the box upper hinge the 75th percentile, and the box lower hinge the 25th percentile.

Figure 3. Nocturnal Sleep Characteristics by Study Group in the Intention-to-Treat Unadjusted Analysis

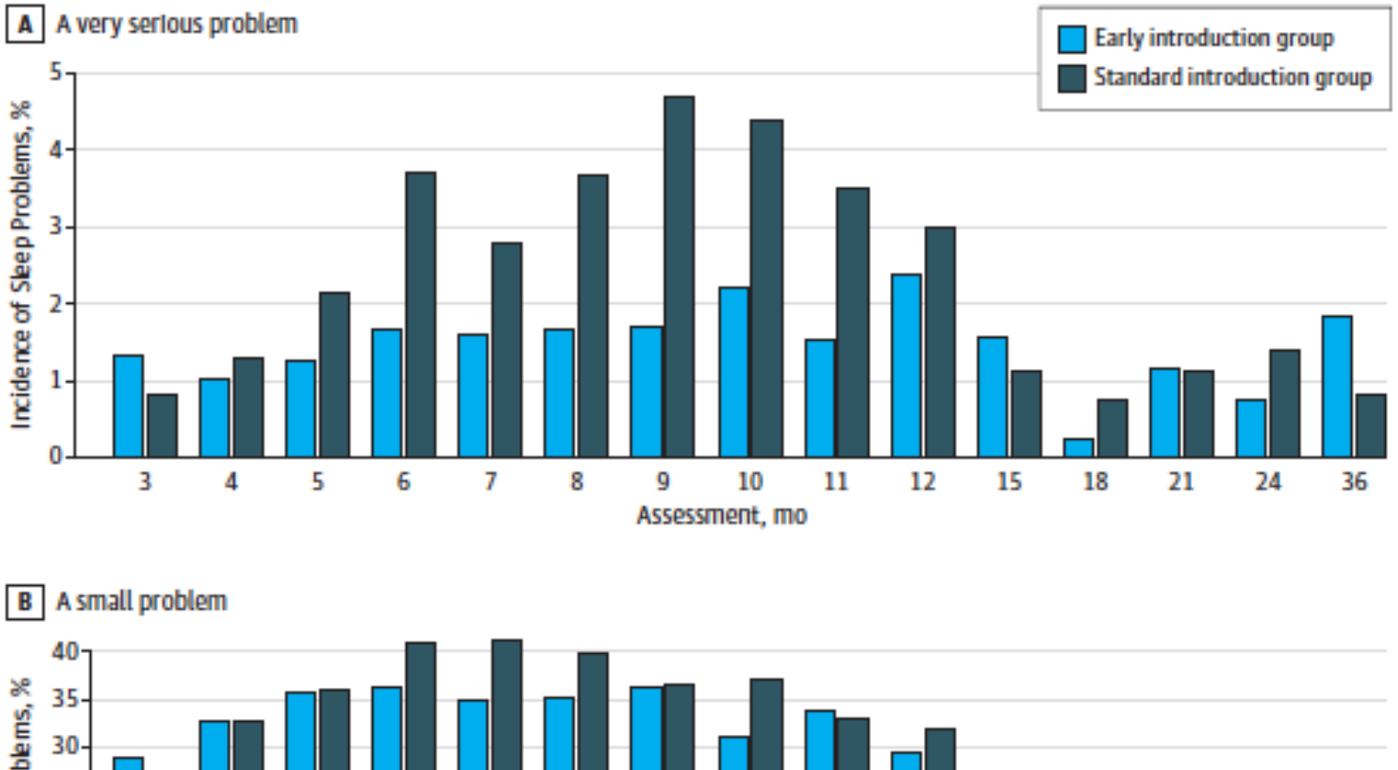


Translation please…

- EIG slept **7.3 minutes more**/night (95% CI, 2-12.5)
  - *A game changing extra 16 minutes/night by 6 months*
- EIG had **9.1% less nighttime awakenings** (95% CI, 4-14%)

But there’s more

Figure 4. Parent Reporting of a Sleep Problem in Their Child by Study Group (Intention-to-Treat Analysis)



Parental perception of sleep problem were significantly correlated with maternal global and sleep QOL

Limitations

- Full adherence to EIG regimen as per protocol in only 42%
- Reporting bias (did parents in EIG *believe* their babies would sleep better?)

Take home message

- Early introduction of solids may have a small improvement in sleep patterns
- No negative impact on BF rates in early introduction of solid group

Will this article change your practice?

1. Parents need sleep and 16 minutes is HUGE. Feed that 2 month old pasta if you have to!

2. Introducing complementary foods at around six months still sounds the most reasonable

3. I think complementary food introduction between 4-6 months is reasonable

4. No vote - I slept through most of your presentation

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Increasing Maintenance glucocorticoids during Asthma Exacerbations

8yo asthmatic on maintenance ICS presents with mild exacerbation from a URTI. In addition to increasing Salbutamol frequency, what do you recommend patients do with their ICS?

1. Trash the ICS because it expired 3 years ago

2. Maintain the current dose of ICS

3. Double the dose of ICS during the flare

4. Quintuple the dose of ICS during the flare

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 8, 2018 VOL. 378 NO. 10

Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations

D.J. Jackson, L.B. Bacharier, D.T. Mauger, S. Boehmer, A. Beigelman, J.F. Chmiel, A.M. Fitzpatrick, J.M. Gaffin, W.J. Morgan, S.P. Peters, W. Phipatanakul, W.J. Sheehan, M.D. Cabana, F. Holguin, F.D. Martinez, J.A. Pongracic, S.N. Baxi, M. Benson, K. Blake, R. Covar, D.A. Gentile, E. Israel, J.A. Krishnan, H.V. Kumar, J.E. Lang, S.C. Lazarus, J.J. Lima, D. Long, N. Ly, J. Marbin, J.N. Moy, R.E. Myers, J.T. Olin, H.H. Raissy, R.G. Robison, K. Ross, C.A. Sorkness, and R.F. Lemanske, Jr., for the National Heart, Lung, and Blood Institute AsthmaNet*

N Engl J Med 2018; 378:891-901

Asthma

- Asthma exacerbations are common
- Guidelines recommend patient be provided with written action plan to guide management at home

CHEO Children's Hospital of Eastern Ontario
Centre hospitalier pour enfants de l'est de l'Ontario

Emergency Department

ASTHMA ACTION PLAN & PRESCRIPTION

ADDRESSOGRAPH

Weight: _____ kg

***PHYSICIAN:** Initial beside selected orders.*

***PHARMACIST:** Label salbutamol as "Take as directed as per asthma action plan". Fill other medications as directed by physician.*

GREEN ZONE — Asthma **under control**

Breathing is good
Run & play normally.
Cough or wheeze less than 4 times a week.

CONTROLLER Medicine:

__ Fluticasone (Flovent®) ____mcg/puff, take ___ puffs, 2 times/day, 3 months, Refill 3
__ Ciclesonide (Alvesco®) ____mcg/puff, take ___ puffs, __times/day, 3 months, Refill 3
__ Montelukast (Singulair®) _____mg, take 1 pill at night, 30 days supply, Refill 3

__ _____

QUICK RELIEF Medicine (blue inhaler):

___ Salbutamol, 2 puffs every 4 to 6 hours as needed, 1 inhaler, Refill 3
___ Salbutamol before exercise: 2 puffs

___ **HOLDING CHAMBER:** dispense __ chamber, Refill __
___ Infant with mask __ Pediatric with mask__ Adult with mouthpiece

YELLOW ZONE — Asthma **not well controlled**

Signs of a cold.
Mild to moderate cough or wheezing.
Waking up because of asthma.

Continue GREEN ZONE CONTROLLER medicine.

Take QUICK RELIEF medicine (blue inhaler) every 4 hours until better.

__ _____

See a doctor if quick relief needed more than 4 days a week.

Today, your child was seen in the Emergency Department for a significant asthma exacerbation. To treat this attack, in addition to your Controller and Quick Relief medicine, also give :

___ Prednisolone liquid ___ mg daily for ___ days, Refill 0 OR ___ Prednisone tablet ___ mg daily for ___ days, Refill 0

Additional discharge instructions: _____

RED ZONE — Asthma **out of control**

Very short of breath.
Severe wheezing.
"Pulling in" of skin between ribs.
Cannot do usual activities.
Severe trouble breathing, walking or talking.
Blueness of lips or skin.
Tired because of effort of breathing.

Take QUICK RELIEF medicine (blue inhaler) every 4 hours.

If you need QUICK RELIEF medicine (blue inhaler) more than every 4 hours, seek medical attention NOW.

If still in Red Zone after 15 minutes or you have not reached your doctor, call 911 *or* go to nearest emergency department NOW. Take QUICK RELIEF medicine (blue inhaler) as needed (even every 10 or 20 minutes if not improving) on way to hospital

☐ Referral to Asthma Specialist ☐ Referral to Asthma Educator

☐ Schedule follow-up appointment with a doctor in _____ weeks

Physician: _____ (print name) **License #** _____ **Signature:** _____ **Date:** _____ (dd/mm/yyyy)

ORIGINAL – PHARMACY, COPY 1 – MEDICAL CHART, COPY 2 – PATIENT

Form No. P5574E, January 2011

Not much evidence what to do here….

Review of literature

- Previous Cochrane Review in 2010 - sub-group analysis suggested potential benefit in *Adults* of quadrupling their baseline ICS dose during asthma exacerbations

- Global Initiative for Asthma (2017) recommends a short-term increase in dose of inhaled glucocorticoids (2-4x baseline dose)

- Canadian Thoracic Society Guidelines (2012) recommend *against* increasing inhaled corticosteroid during an flare-up

- Updated Cochrane Review (2016) showed no evidence that doubling dose of inhaled glucocorticoids decreased the likelihood of an exacerbation in children

STICS Trial

- Efficacy and safety of increasing dose of inhaled steroids from baseline daily low dose to 5x daily dose x 7 days in school-aged children with mild-to-moderate persistent asthma

- **ST**ep Up Yellow Zone **I**nhaled **C**orticoS**S**teroids to Prevent Exacerbations trial

Yellow PE STICS Trial

***** Consider Name Change:

Yellow zone **P**revention of **E**xacerbations with **St**ep up **I**nhaled **C**orticoS**S**teroids Trial

Methods

- Children 5-11 years with diagnosis of asthma
- Had > 1 exacerbation treated with systemic steroids in the previous year
- Excluded if asthma was too severe (> 2 oral steroid courses in last six months or > 5 in last year)

Method

- Randomized, double-blind, parallel group trial
- 17 trial sites in US (March 2014-March 2016)
- 4 week run-in period to establish adherance
- Had blinded “green zone” and “yellow zone” puffers during the treatment phase (48 wks)
- Patients provided with a standardized asthma education plan and electronic diary with instructions on early initiation of yellow-zone treatment

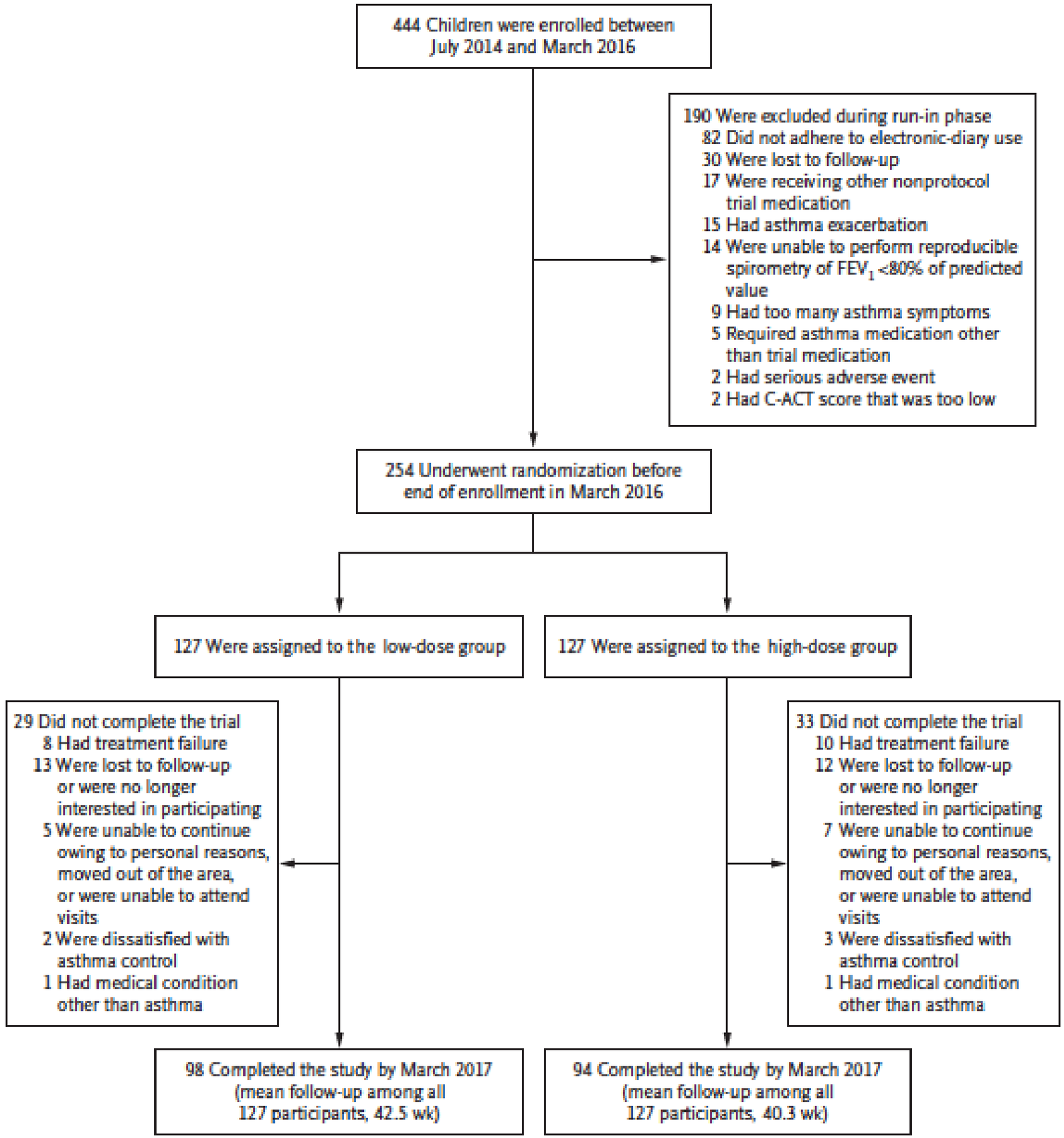
Run-in Phase

A

Run-in Phase: 4 Wk	Treatment Phase: 48 Wk		
	Randomized treatment group	Daily *except* during 7-day yellow zone	Daily *only* during 7-day yellow zone
Fluticasone 44 μg/inhalation, 2 inhalations twice daily	Low dose	Fluticasone 44 μg/inhalation, 2 inhalations twice daily	Fluticasone 44 μg/inhalation, 2 inhalations twice daily
	High dose	Fluticasone 44 μg/inhalation, 2 inhalations twice daily	Fluticasone 220 μg/inhalation, 2 inhalations twice daily

Adherence > 75%

B


444 Children were enrolled between July 2014 and March 2016
190 Were excluded during run-in phase
82 Did not adhere to electronic-diary use
30 Were lost to follow-up
17 Were receiving other nonprotocol trial medication
15 Had asthma exacerbation
14 Were unable to perform reproducible spirometry of FEV1 <80% of predicted value
9 Had too many asthma symptoms
5 Required asthma medication other than trial medication
2 Had serious adverse event
2 Had C-ACT score that was too low
254 Underwent randomization before end of enrollment in March 2016
127 Were assigned to the low-dose group
127 Were assigned to the high-dose group
29 Did not complete the trial
8 Had treatment failure
13 Were lost to follow-up or were no longer interested in participating
5 Were unable to continue owing to personal reasons, moved out of the area, or were unable to attend visits
2 Were dissatisfied with asthma control
1 Had medical condition other than asthma
33 Did not complete the trial
10 Had treatment failure
12 Were lost to follow-up or were no longer interested in participating
7 Were unable to continue owing to personal reasons, moved out of the area, or were unable to attend visits
3 Were dissatisfied with asthma control
1 Had medical condition other than asthma
98 Completed the study by March 2017 (mean follow-up among all 127 participants, 42.5 wk)
94 Completed the study by March 2017 (mean follow-up among all 127 participants, 40.3 wk)

Outcomes

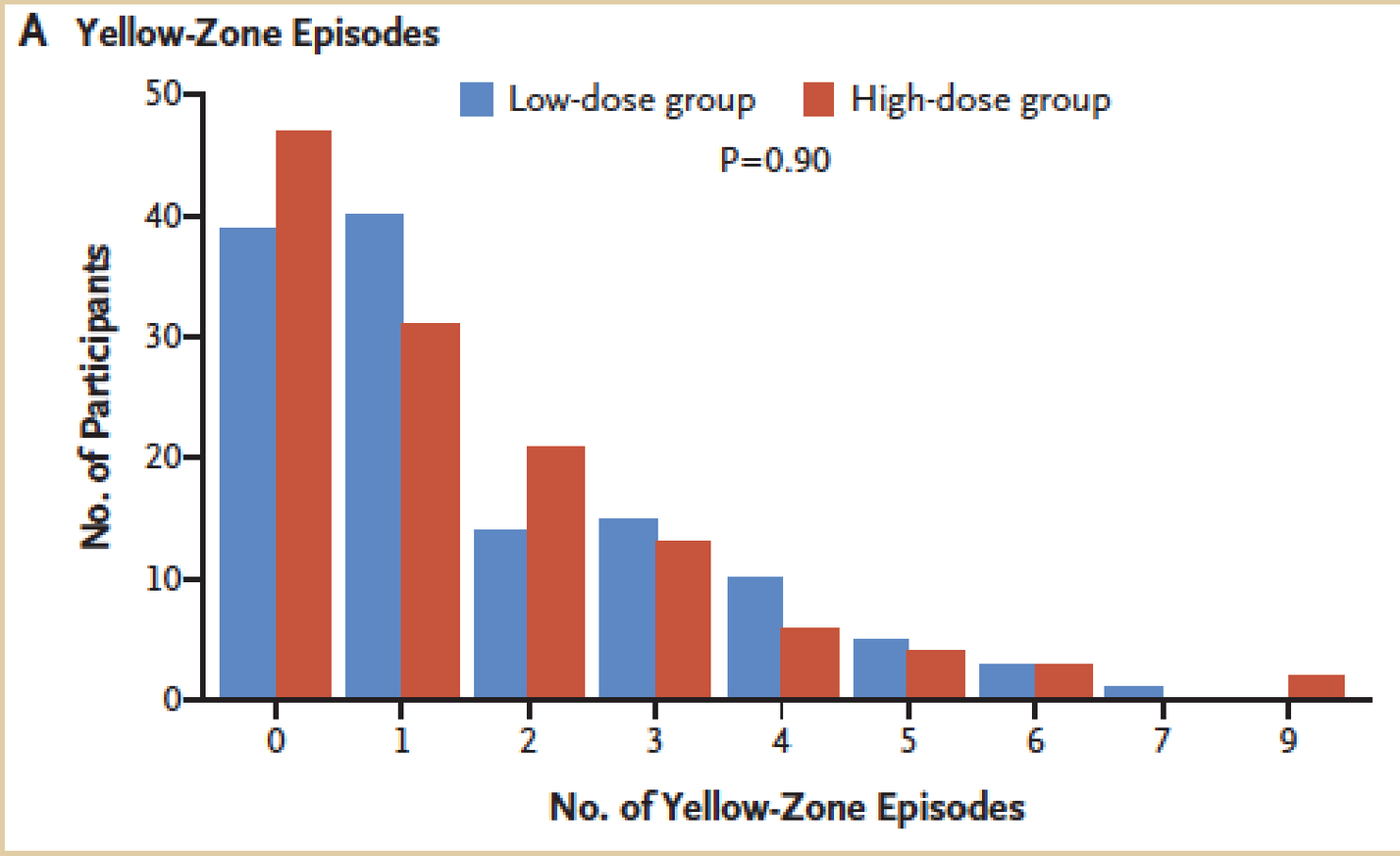
1. Primary outcome:

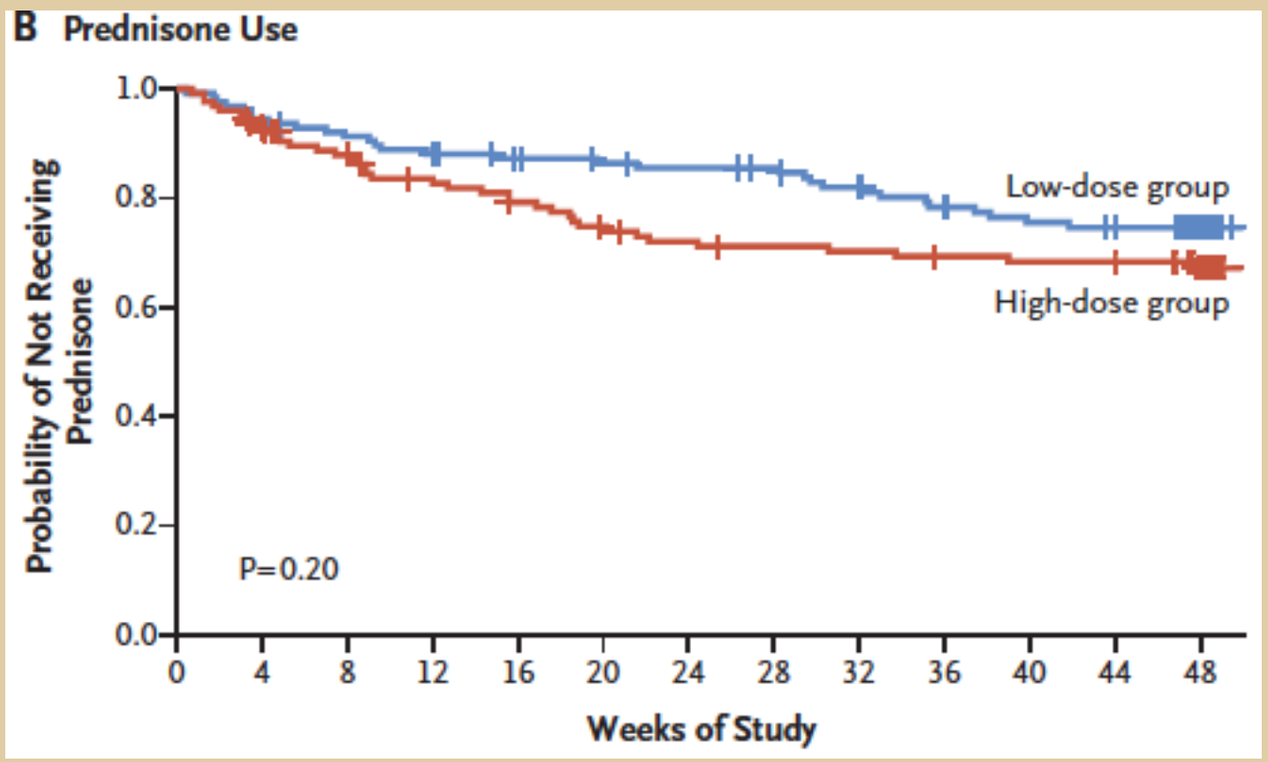
    - Rate of severe asthma exacerbations treated with systemic glucocorticoids

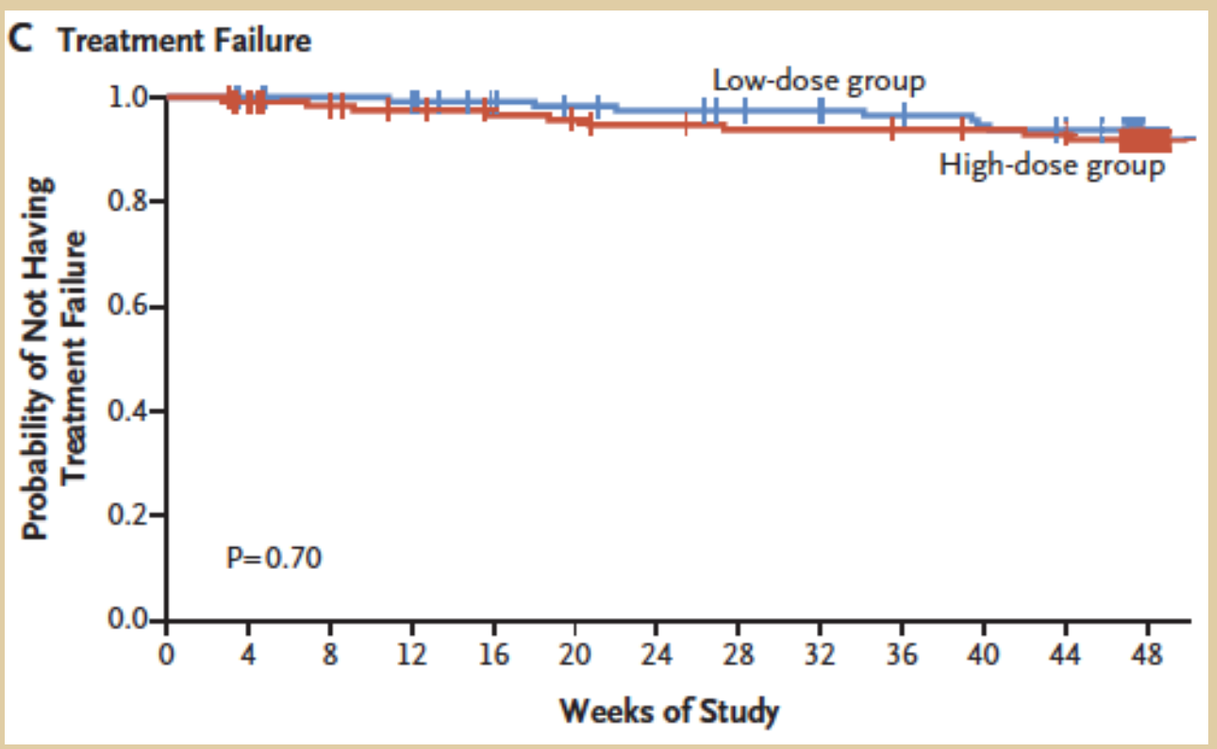
2. Secondary outcomes:

    - Time to 1st asthma exacerbation
    - Treatment failure
    - Unscheduled ED/WIC visits
    - Hospitalization
    - Total steroid exposure
    - Linear growth

Results


A Yellow-Zone Episodes
Low-dose group
High-dose group
P=0.90
No. of Participants
50
40
30
20
10
0
0 1 2 3 4 5 6 7 9
No. of Yellow-Zone Episodes


B Prednisone Use
Probability of Not Receiving Prednisone
1.0
0.8
0.6
0.4
0.2
0.0
Low-dose group
High-dose group
P=0.20
0 4 8 12 16 20 24 28 32 36 40 44 48
Weeks of Study


C Treatment Failure
Probability of Not Having Treatment Failure
1.0
0.8
0.6
0.4
0.2
0.0
Low-dose group
High-dose group
P=0.70
0 4 8 12 16 20 24 28 32 36 40 44 48
Weeks of Study

Results

- Similar number of yellow-zone episodes in treatment and control groups
- No difference in rates of severe exacerbations requiring oral corticosteroids
- No difference in time to first exacerbation needing steroids
- No difference in ER visits, treatment failure or hospitalizations

Results

- Compared with the control group, the treatment group had a: 14% greater exposure to inhaled glucocorticoids AND

  0.23cm/yr slower growth rate

Shouldn't you guys be trying to find medications that *increase* your height?...

Outcomes

Table 2. Outcomes.*

Outcomes	Low-Dose Group (N = 127)	High-Dose Group (N = 127)	Treatment Effect (95% CI)†	P Value
Primary outcome				
No. of exacerbations per year (95% CI)	0.37 (0.25 to 0.55)	0.48 (0.33 to 0.70)	1.3 (0.8 to 2.1)	0.30
Secondary outcomes				
No. of emergency department or urgent care visits per year (95% CI)	0.47 (0.31 to 0.72)	0.64 (0.42 to 0.96)	1.3 (0.8 to 2.4)	0.30
No. of hospitalizations	0	4	—	0.12
Equivalent of hydrocortisone exposure — g/yr (95% CI)				
Fluticasone only	10.6 (10.4 to 10.9)	12.2 (11.9 to 12.4)	1.14 (1.10 to 1.19)	
Fluticasone and prednisone	11.1 (10.6 to 11.4)	12.8 (12.4 to 13.2)	1.16 (1.10 to 1.22)	
Growth — cm/yr (95% CI)				
Mean	5.65 (5.48 to 5.81)	5.43 (5.26 to 5.60)	–0.23 (–0.47 to 0.01)	0.06
Effect per 7-day exposure to high-dose regimen				
Overall	—	–0.07 (–0.17 to 0.03)	–0.07 (–0.17 to 0.03)	0.20
According to age group‡				
5–7 yr	—	–0.12 (–0.22 to –0.02)	–0.12 (–0.22 to –0.02)	0.02
8–11 yr	—	0.02 (–0.21 to 0.26)	0.02 (–0.21 to 0.26)	0.80

Take Home Message

- In children 5 – 11 year old with asthma on low-dose ICS, increasing ICS by 5x for 7 days did NOT have any better outcomes than standard practice
- Greater exposure to ICS
- Small but significant effect on growth velocity

Will this article change your practice?

1. Yes
2. No
3. Children don’t get asthma
4. Will think about it

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Sleep and Adolescent Behaviours

During a routine follow up with a teen girl and her mom, how often do you discuss sleep?

1. Sometimes
2. Only if the topic gets brought up by family/patient
3. At every visit
4. Never…I was taught not to poke bears…

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RESEARCH LETTER

Dose-Dependent Associations Between Sleep Duration and Unsafe Behaviors Among US High School Students

JAMA Paediatrics; 2018;172(12)

(not really an article….)

Short report of original research focused on particular topic

Sleep during adolescence

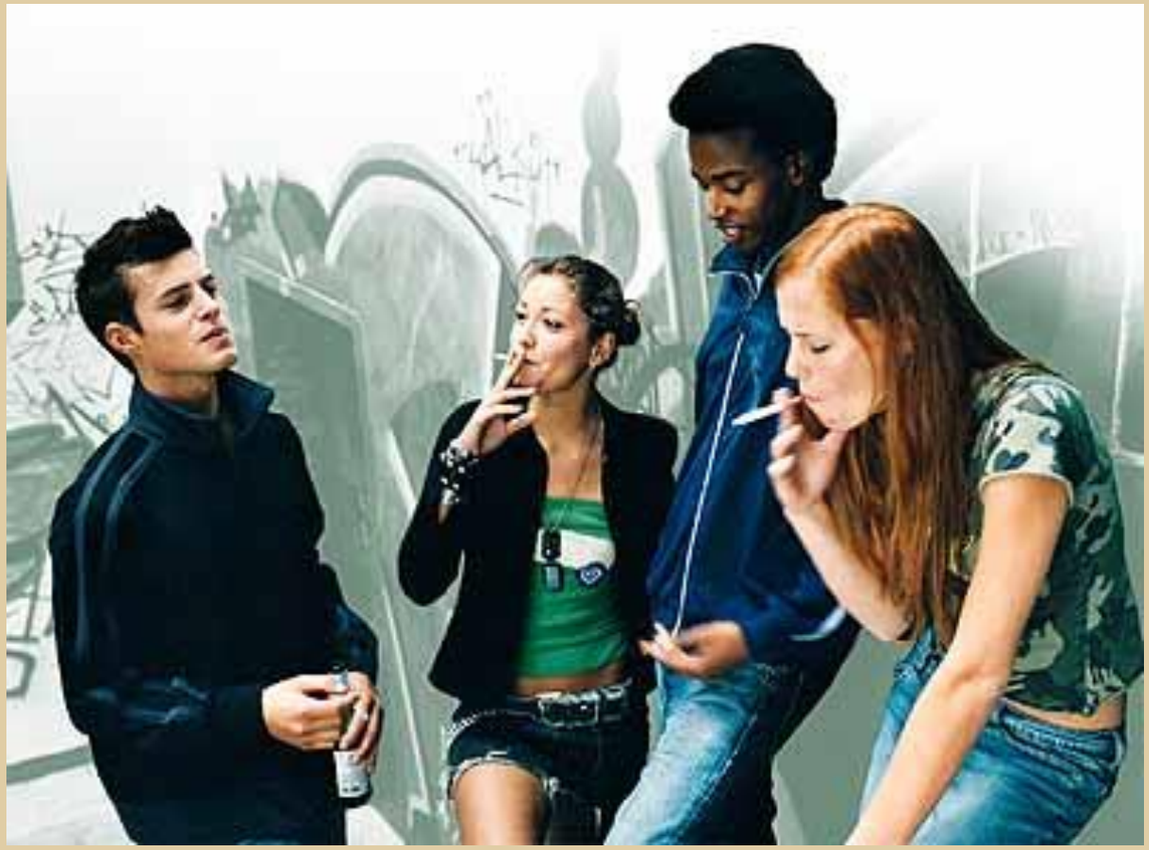
- Natural shift in circadian rhythm - ie. making it difficult to fall asleep until later
- **8-10 hrs/night** is recommended
- Stage of cognitive maturation - sleep supports brain development and physical growth

Youth Risk Behaviour Surveillance System (YRBSS)

- Centers for Disease Control and Prevention
- Developed in 1990 to monitor health behaviours that contribute to the leading causes of death, disability and social problems among youth/adults in US
- Data collected from 1991-2017 - 4.4 million high school students
- Administered biannually, national sample of gr 9-12

- Data between February 2007 - May 2015 = 67 615 surveys
- Sleep duration on “average” school night:
  - > 8 or more hours
  - 7 hrs
  - 6 hrs
  - < 6 hrs

- Association between sleep duration and personal safety risk-taking behaviours of high school students



Outcomes

Alcohol

Risky sexual behaviours

Self-harm

Depressed mood

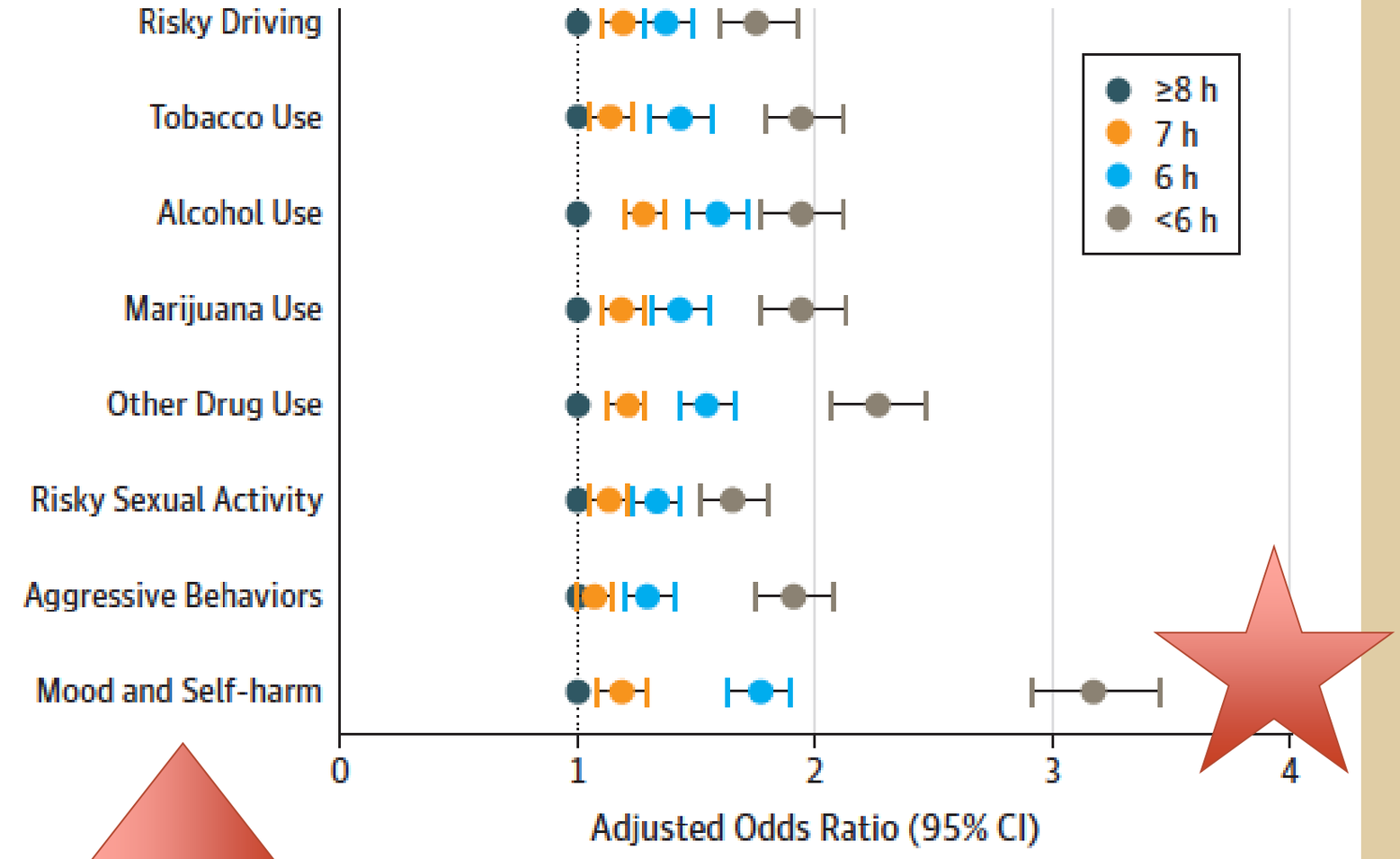
Tobacco

Risky driving

Marijuana

8 hours or more…

Figure. Adjusted Association Between Sleep Duration and Risk-Taking Behaviors



Estimate lds ratios are from weighted logistic regression models adjusted for age, sex, e/ethnicity, and year of survey.

Table. Prevalence of Each Risk-Taking Behavior in the Past 30 Days and Its Adjusted Association With Sleep Duration

Risk-Taking Behavior	Prevalence, % (No./Total No.) (N = 67 615)	Odds Ratio (95% CI)		
		7 Hours (20 266 [30.0%])[a]	6 Hours (14 900 [22.0%])[a]	<6 Hours (11 912 [17.6%])[a]
Risky driving	35.5 (24 001/67 550)	1.19 (1.12-1.26)	1.37 (1.29-1.46)	1.75 (1.61-1.91)[b]
Rarely or never wore a seat belt	8.2 (5469/67 061)	1.04 (0.93-1.18)	1.56 (1.39-1.75)	2.98 (2.65-3.34)[b]
Texted or emailed while driving (among drivers)	41.7 (6756/16 220)	1.30 (1.14-1.49)	1.32 (1.17-1.49)	1.29 (1.12-1.50)[b]
Rode with a driver who had been drinking alcohol	24.6 (16 601/67 401)	1.19 (1.12-1.26)	1.41 (1.31-1.51)	1.79 (1.66-1.93)[b]
Drove after drinking alcohol (among drivers)	8.8 (1409/15 987)	1.04 (0.84-1.30)	1.27 (1.03-1.56)	1.98 (1.62-2.42)[b]
Tobacco use	26.6 (17 953/67 463)	1.13 (1.06-1.21)	1.43 (1.32-1.55)	1.94 (1.80-2.10)[b]
Alcohol use	38.9 (24 261/62 291)	1.28 (1.21-1.35)	1.61 (1.50-1.74)	2.01 (1.84-2.19)[b]
Marijuana use	21.9 (14 571/66 610)	1.18 (1.11-1.27)	1.43 (1.33-1.54)	1.94 (1.78-2.11)[b]
Other drug use[c]	24.9 (16 420/65 977)	1.17 (1.10-1.25)	1.51 (1.41-1.62)	2.34 (2.16-2.52)[b]
Risky sexual activity	37.0 (23 805/64 309)	1.12 (1.06-1.19)	1.33 (1.25-1.41)	1.65 (1.53-1.78)[b]
Currently sexually active	33.4 (21 452/64 170)	1.11 (1.05-1.19)	1.30 (1.23-1.38)	1.59 (1.48-1.71)[b]
Sexually active, have used alcohol or drugs before sex	21.9 (4672/21 369)	1.04 (0.92-1.18)	1.17 (1.04-1.32)	1.91 (1.69-2.17)[b]
Sexually active, withdrawal method of birth control	5.1 (3191/63 029)	1.15 (1.00-1.33)	1.63 (1.44-1.85)	1.85 (1.61-2.14)[b]
Sexually active, no method of birth control	5.8 (3644/63 029)	1.04 (0.91-1.19)	1.31 (1.15-1.49)	1.94 (1.72-2.19)[b]
History of sexual intercourse with ≥4 persons[d]	13.9 (8930/64 083)	1.03 (0.95-1.11)	1.32 (1.21-1.45)	1.99 (1.81-2.20)[b]
Aggressive behaviors	36.1 (24 367/67 561)	1.06 (1.00-1.13)	1.29 (1.21-1.39)	1.91 (1.76-2.06)[b]
Carried a weapon	17.3 (11 370/65 909)	0.96 (0.89-1.04)	1.16 (1.06-1.26)	1.95 (1.77-2.14)[b]
Carried a gun	5.3 (3493/65 506)	0.79 (0.68-0.92)	1.03 (0.89-1.18)	1.73 (1.54-1.96)[b]
In physical fight	29.1 (19 220/66 158)	1.09 (1.03-1.16)	1.37 (1.28-1.46)	1.97 (1.81-2.15)[b]
Mood and self-harm	34.3 (23 106/67 419)	1.18 (1.09-1.27)	1.77 (1.65-1.88)	3.17 (2.92-3.44)[b]
Felt sad or hopeless	28.5 (19 150/67 274)	1.16 (1.07-1.25)	1.74 (1.62-1.86)	3.11 (2.87-3.37)[b]
Seriously considered suicide	15.9 (10 670/67 235)	1.15 (1.05-1.26)	1.73 (1.58-1.89)	3.12 (2.85-3.41)[b]
Made plan about how to attempt suicide	12.6 (8459/66 942)	1.10 (1.01-1.21)	1.63 (1.50-1.77)	3.17 (2.87-3.51)[b]
Attempted suicide	7.4 (4524/61 435)	0.98 (0.87-1.10)	1.48 (1.31-1.68)	3.39 (3.00-3.82)[b]
Attempted suicide and required treatment	2.3 (1367/60 462)	1.05 (0.85-1.30)	1.29 (1.05-1.58)	4.24 (3.53-5.10)[b]

[a] Participants reporting 8 hours or more of sleep (n = 20 538 [30.4%]) are the referent category for all comparisons.

[b] $P < .001$.

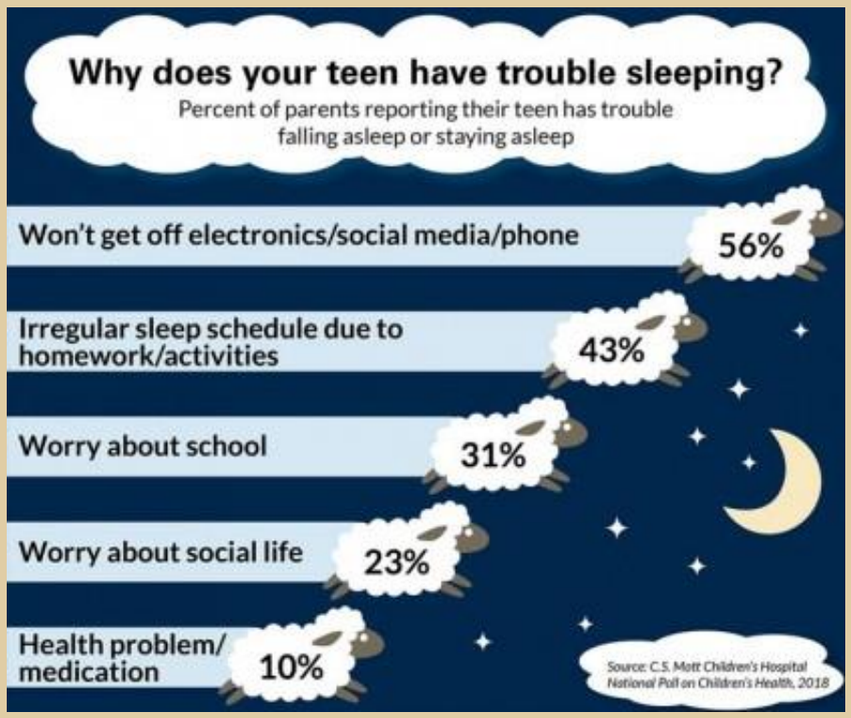
[c] Reported ever using cocaine, inhalants, heroin, methamphetamines, ecstasy, synthetic marijuana, steroids without a prescription, prescription drugs without a prescription, or injecting an illegal drug.

[d] Lifetime history.

- Significant increased odds of reported unsafe behaviours in teens with insufficient sleep
- Precursors to accidents and suicides which are leading causes of death among teens

Take home message

- Sleep deprivation may lead to increased risky behaviours in teens
- Importance of careful sleep history
- Opportunity for preventative counselling at visits



Will this article change your practice?

1. Yes, will talk about sleep more with teens

2. No - still won't poke the bear….

3. Will think about it

4. Teens scare me

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Thank you!

(for listening and enduring bad jokes…)