Undiagnosed COPD and Asthma in the Population (UCAP) Study:

Shawn Aaron

The Ottawa Hospital Research Institute

Disclosures- Shawn Aaron

- Canadian Advisory Boards: GSK, AZ, Sanofi, Methapharm, Valeo.
- These studies were sponsored by The Canadian Institutes of Health Research (CIHR).
- There was no industry involvement or sponsorship for this study.

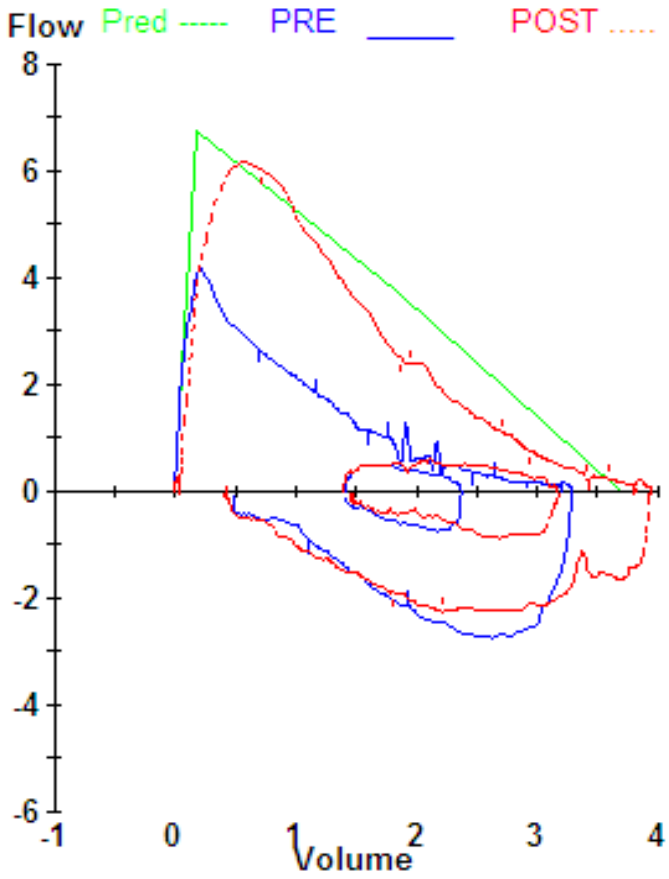
The Patient Who Inspired the Study:

- 26 year old male, civil servant, non-smoker.
- Referred to my clinic for 'chronic cough and frequent lung infections'.
- HPI: Cough with sputum X 1 year. Much worse when he gets a respiratory infection. Has had 4 chest infections in the past year. Each time treated with antibiotics.

Patient #1:

- Used to play hockey, had to quit because “I’m out of shape, too short of breath”.
- Has seen GP 4 times. Has had 3 CXR’s- all unremarkable. Has had 4 courses of antibiotics. Last time was given a Ventolin puffer as well.
- Has never had spirometry.

			Pre-Bronchodilator			Post-Bronchodilator			
Gender	Male								
Age	26 yr	**Spirometry**	Best	LLN	%Pred	Best	%Pred	Change	%Chg
Height	164 cm	FVC (L)	**3.30**	3.11	85%	**3.95**	102%	650 mL	20%
Weight	55 kg	FEV_1 (L)	**1.80**	2.67	54%	**2.76**	83%	960 mL	53%
Race	Caucasian	FEV_1/FVC	**0.55**	0.74		**0.70**			



The Bottom Line:

- This patient clearly has asthma.
- He has chronic respiratory symptoms plus variable expiratory airflow limitation.
- Despite symptoms lasting one year, he has not been diagnosed until now.

- The clinical problem: There are a lot of people living with chronic respiratory symptoms who have undiagnosed asthma or COPD!

The Clinical Problem:

- Up to 70% of individuals with asthma or COPD remain undiagnosed in the community.

- The 2007-2012 US National Health and Nutritional Examination Survey found obstructive lung disease in 13% of randomly selected American adults, however 71% had never been diagnosed with lung disease.

Martinez CH, Annals ATS 2015

The **UCAP** Study (**U**ndiagnosed **C**OPD and **A**sthma in the **P**opulation) Three Research Questions:

1) Can we find adults with undiagnosed asthma or COPD in the community?

2) Are they sick?

3) Can we treat them early to improve health outcomes?

Screening vs. case-finding

- Screening involves testing large numbers of apparently healthy people to detect unrecognized disease (ex. stool occult blood testing to detect colon CA).

- In contrast, case-finding evaluates subgroups of people at increased risk of having a disease (such as those with unexplained symptoms), to make a diagnosis earlier than would otherwise occur.

Can we find them?

Both asthma and COPD present with:

1) Similar respiratory symptoms -dyspnea, cough, wheeze, and/or chest tightness.

2) Both share expiratory airflow obstruction as a common physiologic impairment.

3) Both can be detected by the same diagnostic test (spirometry).

4) Both are highly prevalent in adults.

So, it makes sense to conduct **case finding** to simultaneously discover **symptomatic** individuals with undiagnosed cases of either disease.

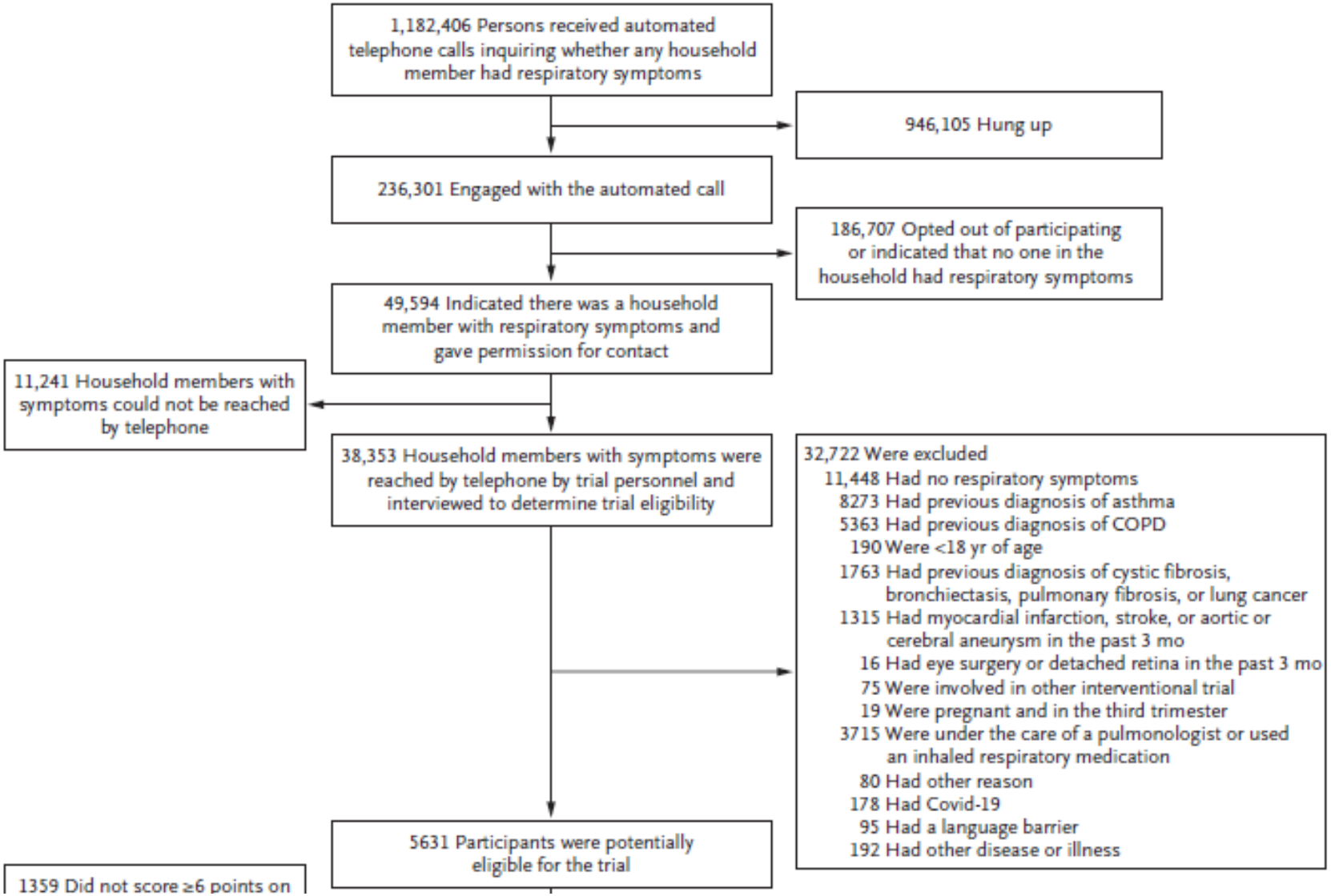
Problem #1: How should we try to find people with undiagnosed asthma or COPD?

- We want a representative, 'random sample' of adults from the population who are suffering from undiagnosed respiratory symptoms.
- Case-finding in doctor's waiting rooms may not be ideal, since some of these people may be seeing their MD that day for their respiratory symptoms, and they may be mere minutes from diagnosis.

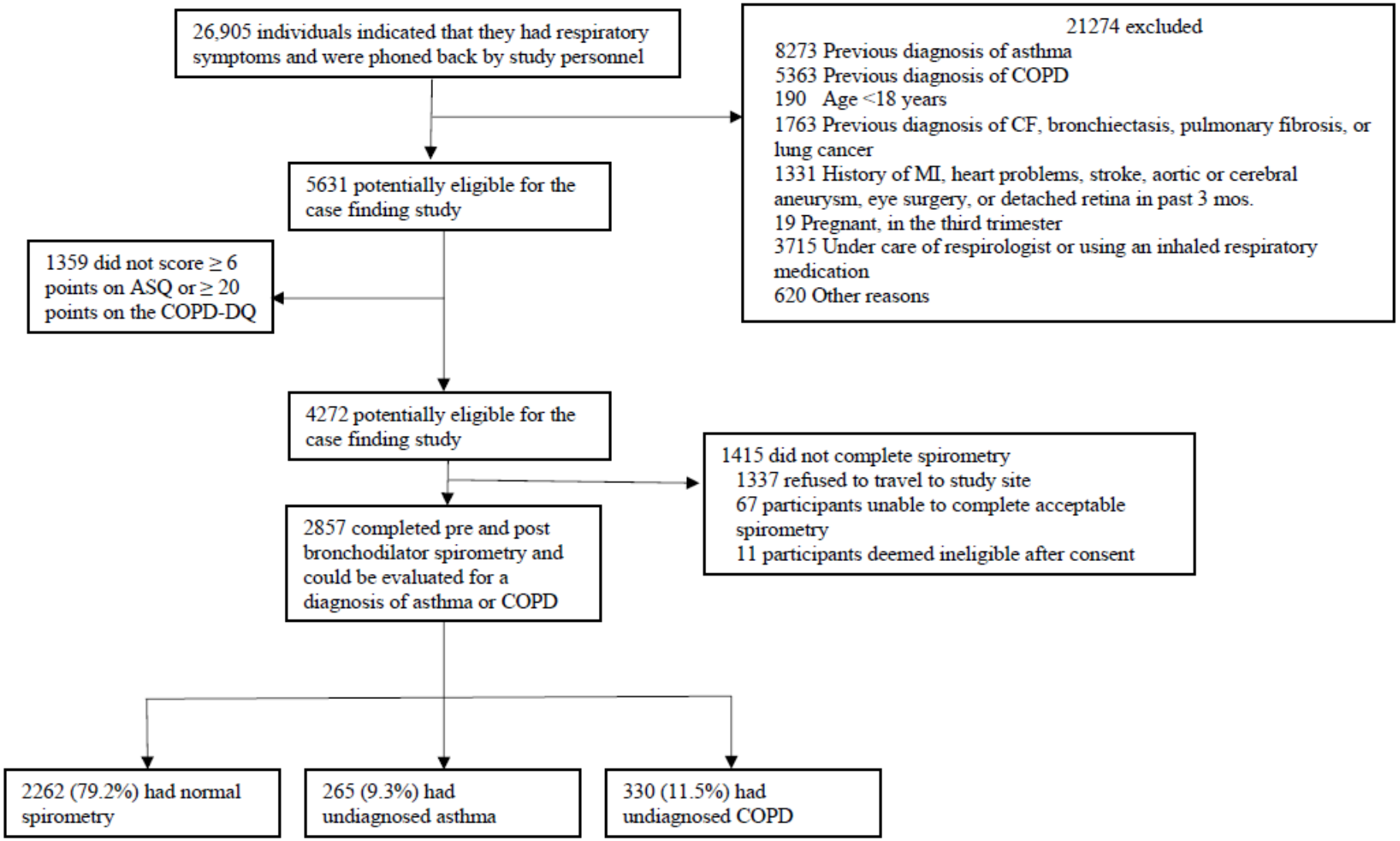
How did we find them in the UCAP study?

- We decided on a population-based strategy- we organized random-digit dialing of cellphones and landlines in 17 sites across Canada.
- We made over 1.1 million automated calls to find people with undiagnosed respiratory symptoms.
- Most people (~946,000) hung up.
- But ~50,000 indicated there was someone in the household suffering from respiratory symptoms.

Random-digit dialing



Case finding - 595 of 2857 symptomatic adults (21%) who underwent spirometry had undiagnosed asthma or COPD



The **UCAP** Study (**U**ndiagnosed **C**OPD and **A**sthma in the **P**opulation) Four Research Questions:

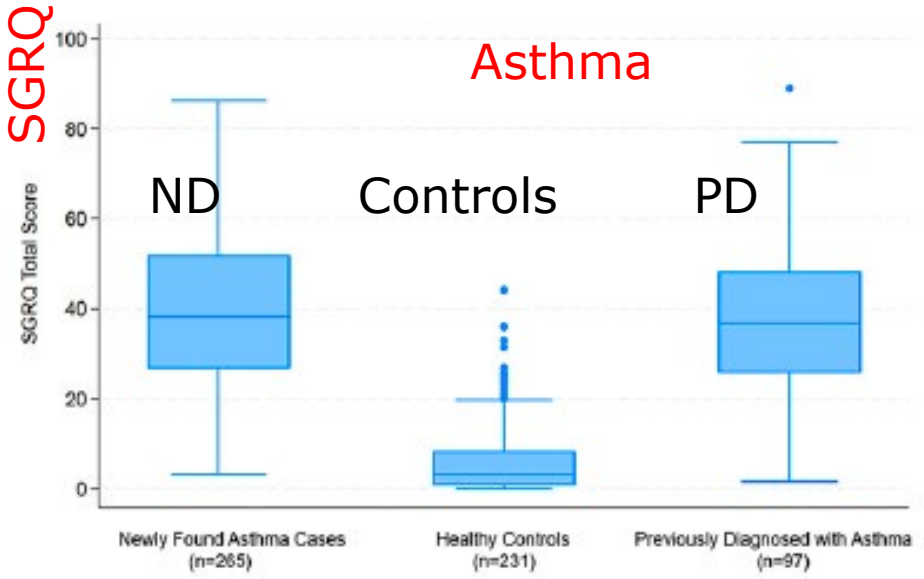
1) Can we find adults with undiagnosed asthma or COPD in the community? YES, we had to make a lot of automated calls, but we found these people, and 21% who underwent testing with spirometry had undiagnosed asthma or COPD.

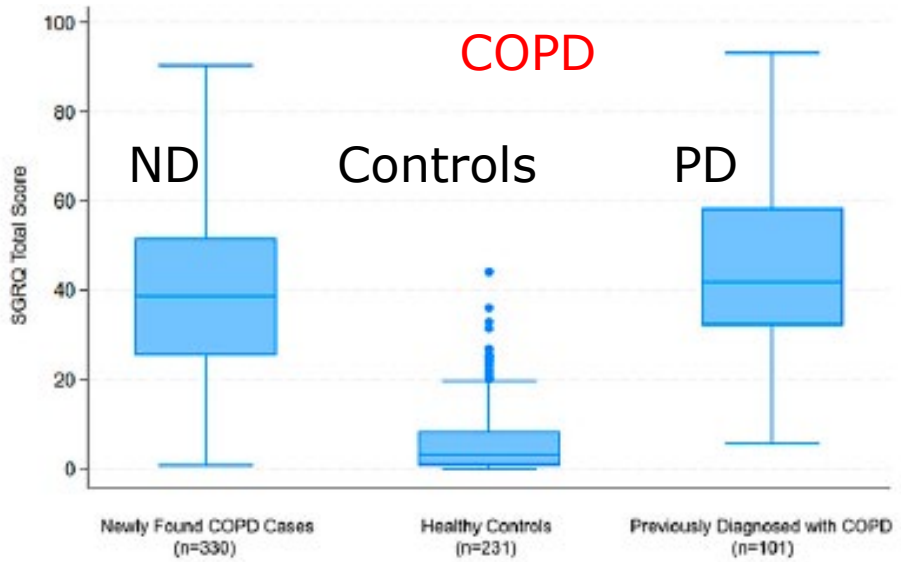
Are people with undiagnosed asthma or COPD sick?

- We compared 595 individuals who we found with undiagnosed asthma or COPD against 231 age and sex-matched controls recruited via identical random-digit dialing.
- We also compared these 595 individuals against 198 symptomatic individuals with previous physician-diagnosed asthma or COPD, again recruited identically.

Are they sick?

- Adults with undiagnosed COPD or asthma have worse disease-specific quality of life (SGRQ total scores) compared to healthy age and sex-matched controls.

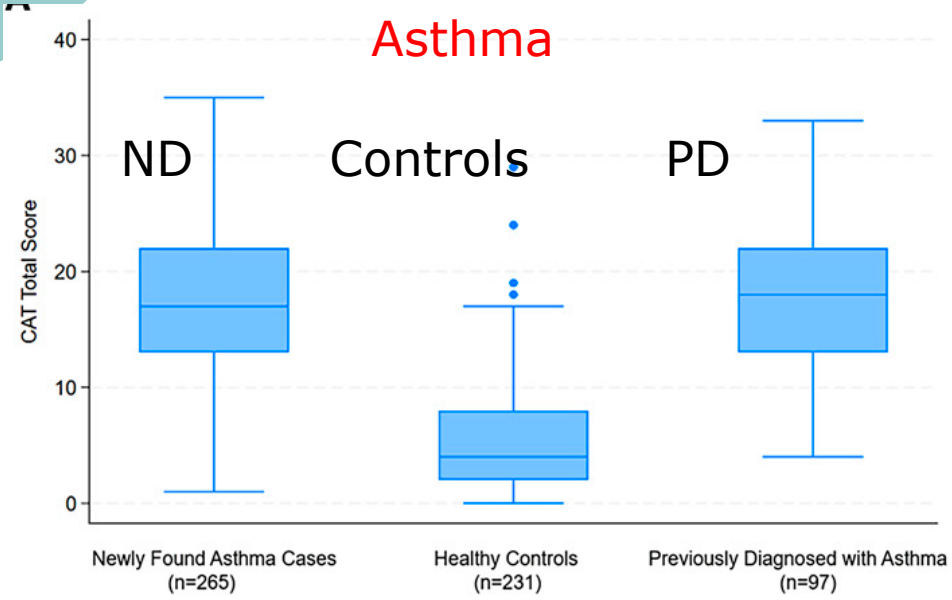


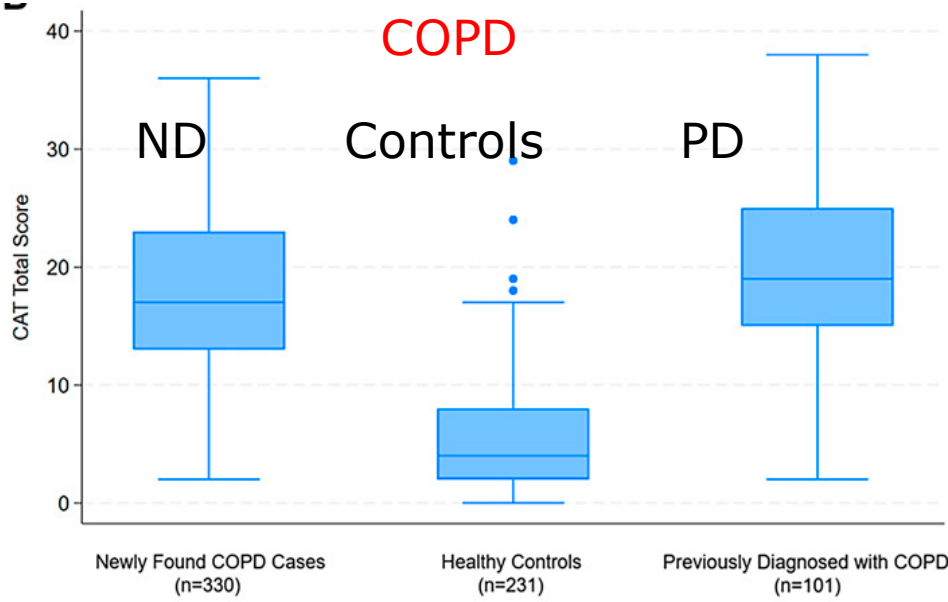


Gerstein et al, AmJRCCM 2023

Are they sick?

- Adults with undiagnosed COPD or asthma have worse symptoms and health status (total CAT score) compared to healthy age and sex-matched controls.





Gerstein et al, AmJRCCM 2023

Are they sick?

- Adults with undiagnosed COPD have significant work impairment compared to healthy controls.

WPAI	Undiagnosed COPD Cases ($n = 330$)	Healthy Control Subjects ($n = 231$)	Previously Diagnosed Control Subjects ($n = 101$)	Pairwise Comparison *P* Values: Undiagnosed Cases vs. Healthy Control Subjects	Pairwise Comparison *P* Values: Undiagnosed Cases vs. Previously Diagnosed Control Subjects
Are you currently employed (working for pay)?	108 (33%)	101 (44%)	23 (23%)	0.01	0.06
During the past 7 d, how many hours did you miss from work because of your health problems?					
Zero missed hours	93 (86%)	99 (98%)	22 (96%)	0.002	0.30
During the past 7 d, how much did your health problems affect your productivity while you were working?					
(Likert 0–10 scale)	1.92 (2.25)	0.10 (0.44)	1.65 (1.82)	<0.001	0.48
During the past 7 d, how much did your health problems affect your ability to do your regular daily activities, other than work at a job?					
(Likert 0–10 scale)	2.54 (2.29)	0.15 (0.46)	1.87 (2.34)	<0.001	0.10

The **UCAP** Study (**U**ndiagnosed **C**OPD and **A**sthma in the **P**opulation) Four Research Questions:

1) Can we find adults with undiagnosed asthma or COPD in the community? YES

2) Are they sick? YES

3) Can we treat them early to improve health outcomes?

OK, so how should we design the trial?

- Remember, our objective is to show that early diagnosis of previously undiagnosed symptomatic asthma or COPD, and subsequent treatment, improves health outcomes.
- Can we randomize an intervention group to early diagnosis and treatment of asthma or COPD, and a control group to nothing?

Rethinking clinical trials:

The most scientifically rigorous trial design would keep the control group unaware of their diagnosis for 12 months.

- This would have allowed a comparison of outcomes between an intervention group who received a diagnosis and treatment and a control group who remained undiagnosed and largely untreated.
- This trial design would likely have maximized the between-group differences in health outcomes at one year between the two randomized groups.
- This also would have allowed us to observe the 'natural history' of undiagnosed, untreated asthma or COPD prospectively for one year.

Rethinking clinical trials:

The most scientifically rigorous trial design would keep the usual-care group unaware of their diagnosis for 12 months.

- However, because all the participants were symptomatic, this trial design would have been unethical.

- We designed the trial to be ethical and we accepted that we could not keep the participants' diagnoses from their PCP's or from the participants themselves.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

S.D. Aaron, K.L. Vandemheen, G.A. Whitmore, C. Bergeron, L.-P. Boulet, A. Côté, R.A. McIvor, E. Penz, S.K. Field, C. Lemière, I. Mayers, M. Bhutani, T. Azher, M.D. Lougheed, S. Gupta, N. Ezer, C.J. Licskai, P. Hernandez, M. Ainslie, G.G. Alvarez, and S. Mulpuru, for the UCAP Investigators*

N Engl J Med 2024 Jun 13;390(22):2061-2073

Can we treat them early to improve health outcomes?

The UCAP Randomized, Controlled Clinical Trial

The Participants:

508 adults with previously undiagnosed asthma or COPD discovered using pre and post bronchodilator spirometry.

At the time of randomization, all participants in both randomized groups were given a copy of their interpreted spirometry report with their diagnosis. This information was also sent directly to the participants' PCP.

Randomization 1:1

The Intervention Group:

Treatment was provided by a study pulmonologist and asthma/COPD educator who initiated guideline-based care.

- Patients were prescribed inhalers and taught how to use them.
- Many were given action plans, provided with smoking cessation pharmacotherapy, exercise and weight counselling, and pneumonia and flu vaccines.

The Control Group:

The control group received usual care provided by their primary-care practitioner.

Participants in both groups were advised to see their primary care practitioners or, alternatively, to visit an urgent care center or emergency department if they had respiratory symptoms warranting medical attention during the 12-month follow-up period.

The UCAP RCT:

Primary outcome:

The annual rate of patient-initiated healthcare utilization events for respiratory illness (outpatient or emergency department visits or hospitalizations for respiratory illness).

Secondary outcomes:

One-year changes in quality of life, symptoms, and lung function.

The UCAP RCT Results:

- 253 randomized to the intervention,
- 255 randomized to usual care.

- During the 12-month study period 92% randomized to the intervention arm and 60% randomized to the usual care arm were started on new medications for asthma or COPD.

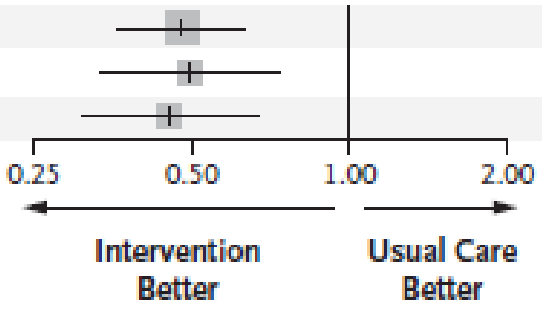
Treatment Received by Randomized Group:

Table 2. Respiratory Treatments Received during the 12-Month Trial Period.*

Treatment†	Intervention (N=253)	Usual Care (N=255)
	number (percent) of participants	
No respiratory treatments during the entire trial period	19 (7.5)	92 (36.1)
SABA only	15 (5.9)	35 (13.7)
LAMA	32 (12.6)	27 (10.6)
LABA	0	11 (4.3)
ICS	56 (22.1)	32 (12.5)
LTRA	1 (0.4)	2 (0.8)
LAMA + LABA	34 (13.4)	6 (2.4)
LABA + ICS	101 (39.9)	53 (20.8)
LAMA + LABA + ICS	29 (11.5)	9 (3.5)
Supplemental oxygen at home	3 (1.2)	1 (0.4)
Short-course systemic glucocorticoid	13 (5.1)	7 (2.7)

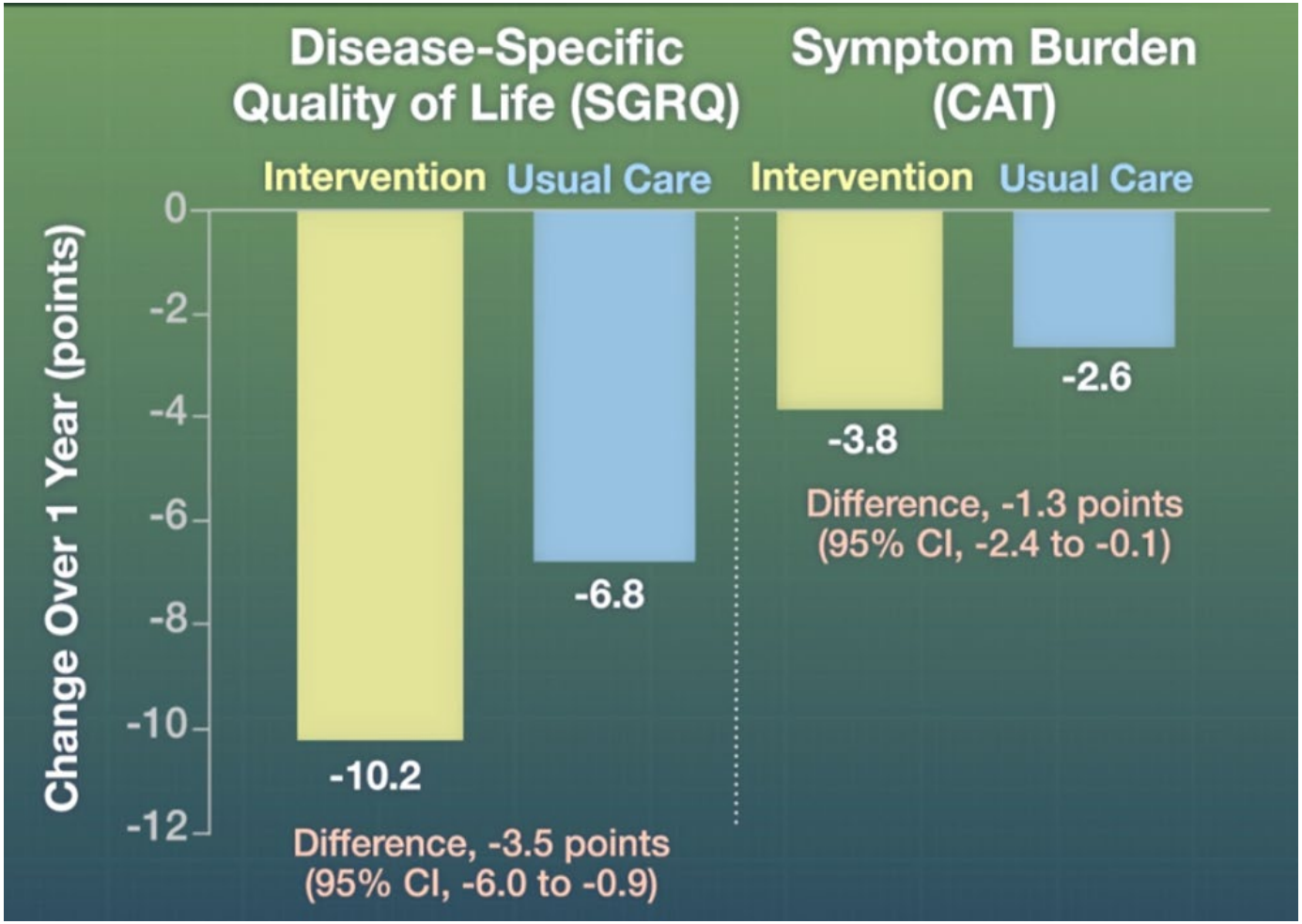
Primary Outcome: Treatment by a Pulmonologist/Educator Reduced HCU for Respiratory Illness

Group	Intervention	Usual Care	Incidence Rate Ratio (95% CI)	P Value
	no. of participants/events per person-yr			
Overall	253/0.53	255/1.12	0.48 (0.36–0.63)	<0.001
Asthma subgroup	123/0.61	127/1.23	0.49 (0.33–0.73)	
COPD subgroup	130/0.46	128/1.01	0.46 (0.31–0.67)	

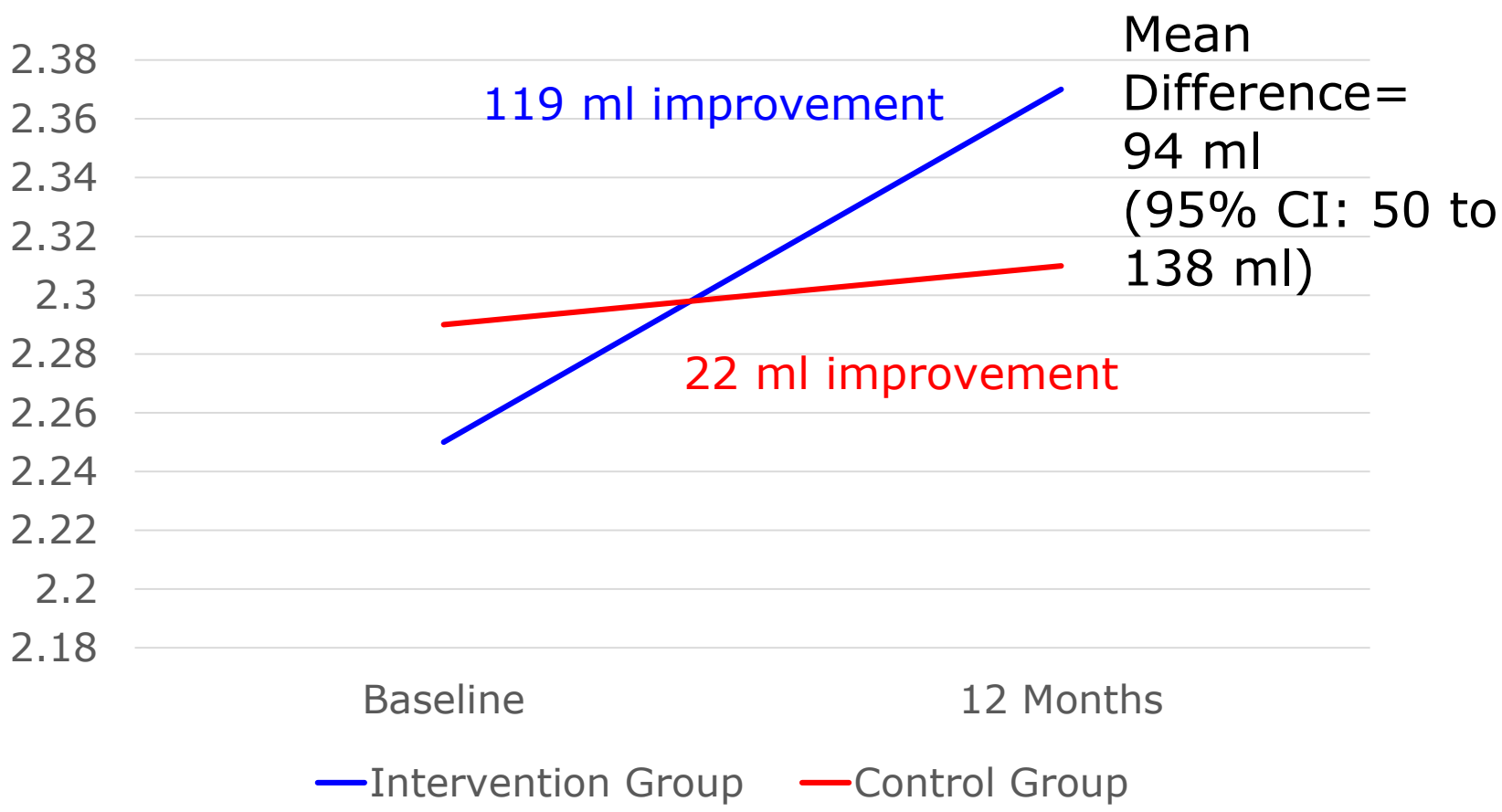


The annualized rate of healthcare utilization for respiratory illness was lower in the intervention group than in the usual care group (incidence rate ratio, 0.48; 95% confidence interval 0.36 to 0.63; P<0.001).

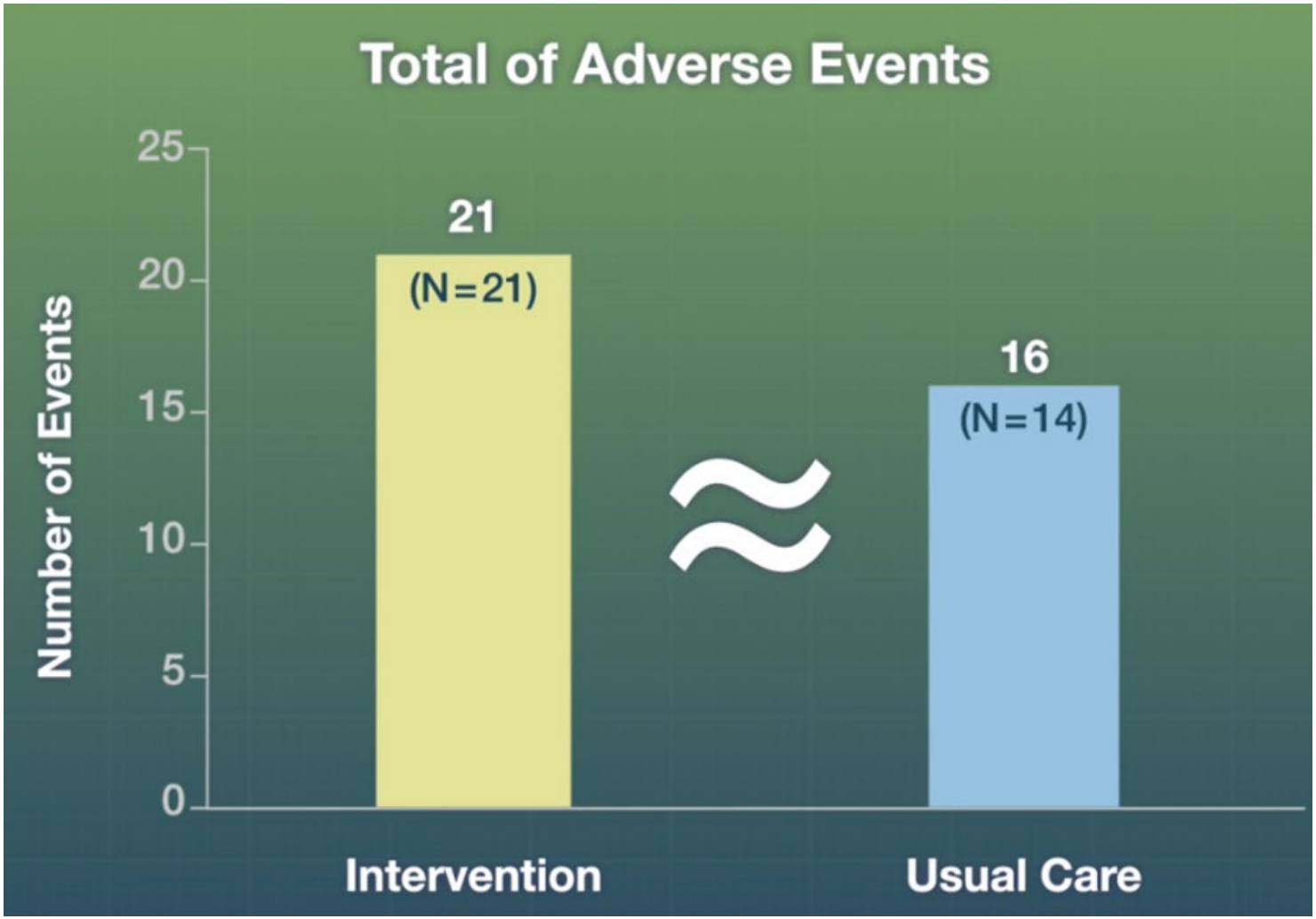
12 Month SGRQ and CAT Score Changes:



FEV_1 Change over 12 Months:



Adverse Events:



Conclusions:

1) We can find people with undiagnosed COPD or asthma in the community by targeting their symptoms using case-finding.

2) These people are undiagnosed, untreated and suffering.

3) Once we find them:

Guideline- directed treatment of undiagnosed COPD or asthma by a pulmonologist/educator improves healthcare utilization, symptoms, QOL and lung function more so than usual care.

Conclusions:

- "In the real world, not everyone can see a lung specialist"
- While the results favored a pulmonologist-based intervention, the one-year improvements in SGRQ and CAT scores in the control arm were >MCID.
- The good news is that our trial results suggest that if people with undiagnosed asthma or COPD get diagnosed and treated by any healthcare practitioner, their health will improve.

Acknowledgments:

Ottawa: Kathy Vandemheen, Dr. Sunita Mulpuru, Dr. Gonzalo Alvarez, Susan Deveau, Victoria Thompson

Montreal: Dr. G. Alex Whitmore, Dr. Catherine Lemiere, Dr. Nicole Ezer

Vancouver: Dr. Celine Bergeron

Quebec: Dr. Louis Philippe Boulet, Dr. Andreanne Cote

Hamilton: Dr. Andrew McIvor

Saskatoon: Dr. Erika Penz

Calgary: Dr. Stephen Field

Edmonton: Dr. Irvin Mayers, Dr. Mohit Bhutani

Halifax: Dr. Paul Hernandez

Winnipeg: Dr. Martha Ainslie

St. John's: Dr. Tanweer Azher

Toronto: Dr. Samir Gupta

London: Dr. Christopher Licskai

Kingston: Dr. Dianne Lougheed

Winnipeg: Dr. Martha Ainslie