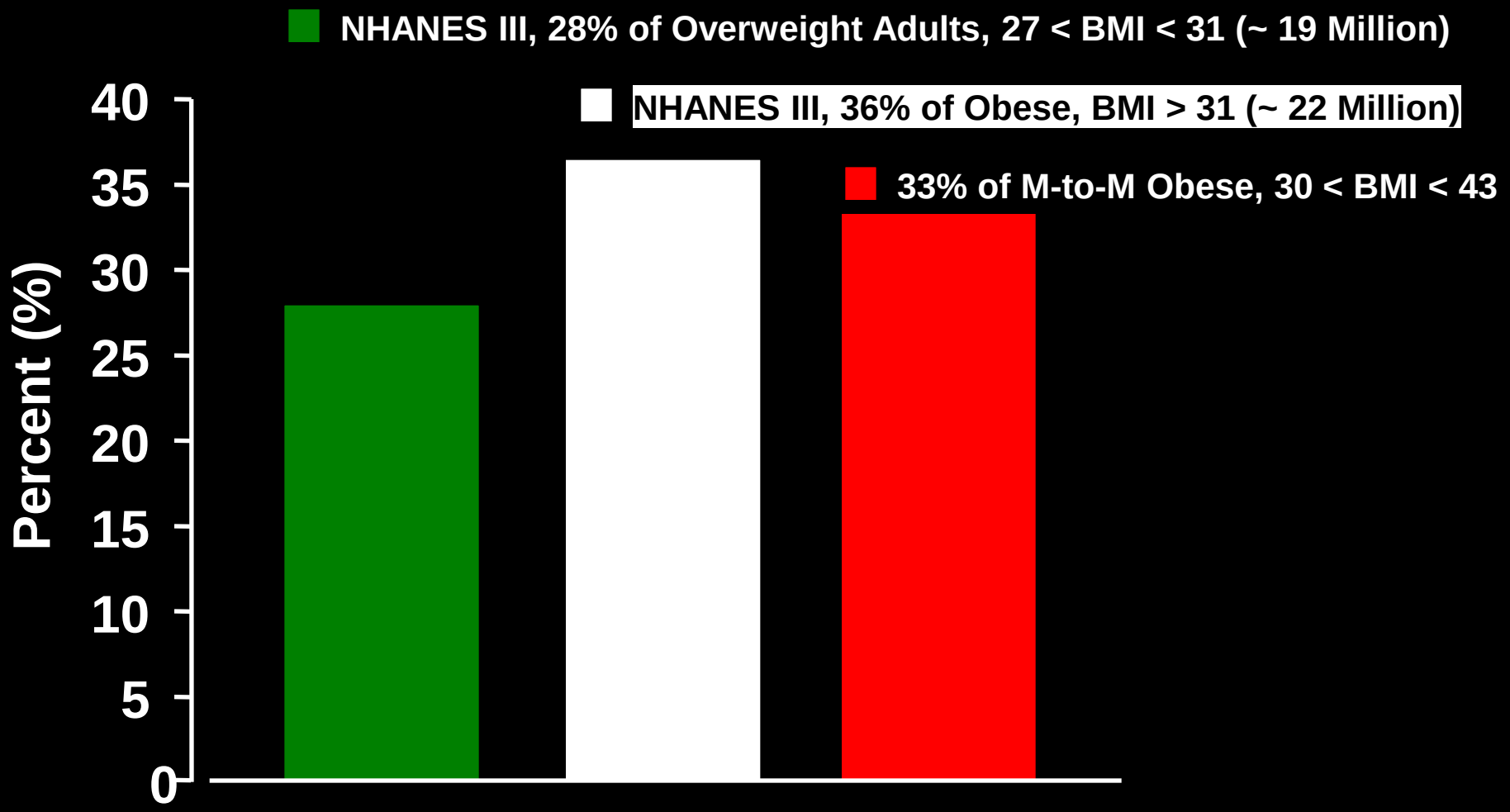
Bariatric surgery: effect on the lungs

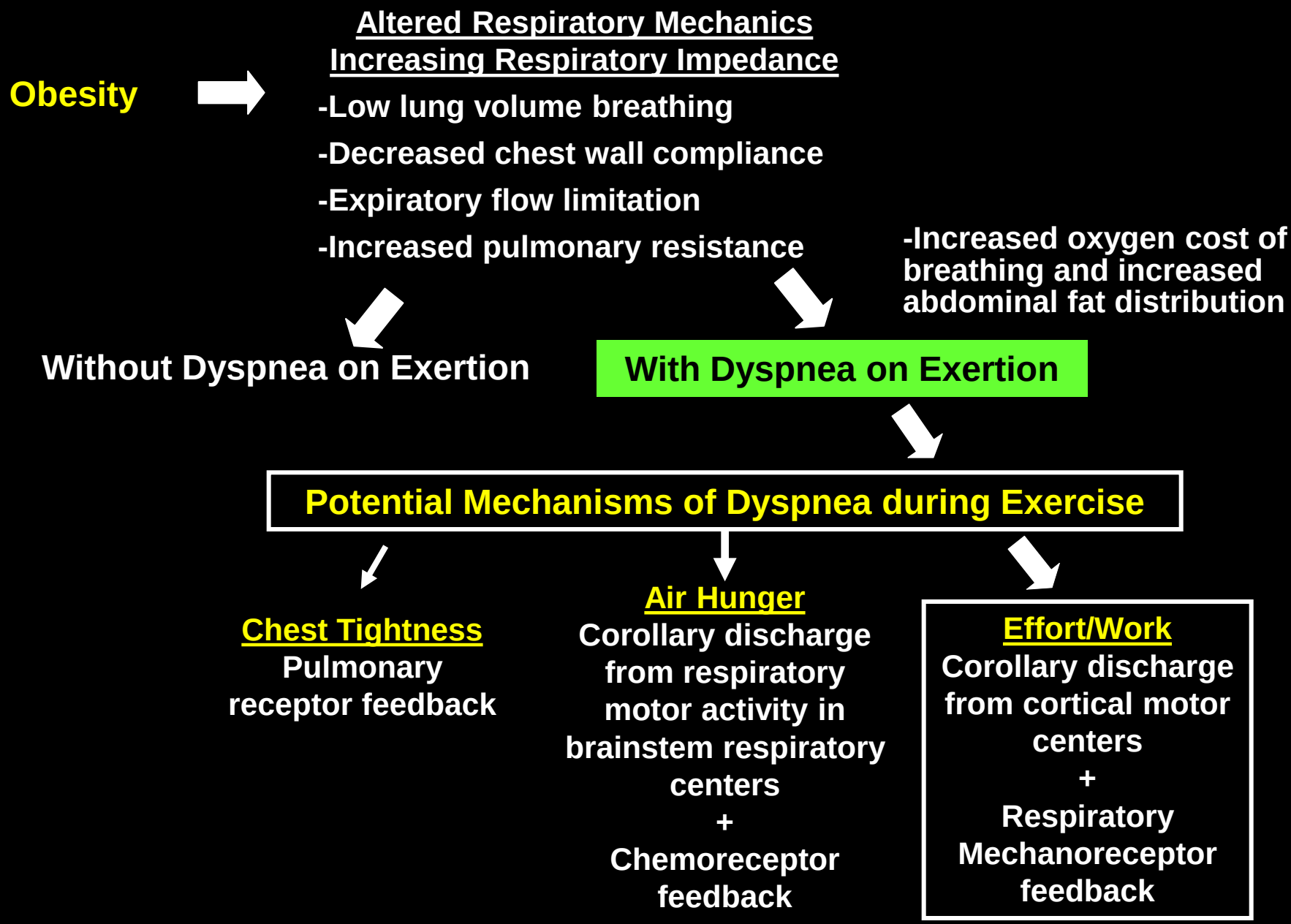
Prof. Gaetano Caramori MD, PhD, FERS,
Royal Society of Medicine Overseas Fellow,
Member of the New York Academy of Sciences, USA
Pulmonology
Department of Medicine and Surgery
University of Parma, Italy
gaetano.caramori@unipr.it

**“One cannot think well, love well, sleep well, if one has not dined well.”
Virginia Woolf**

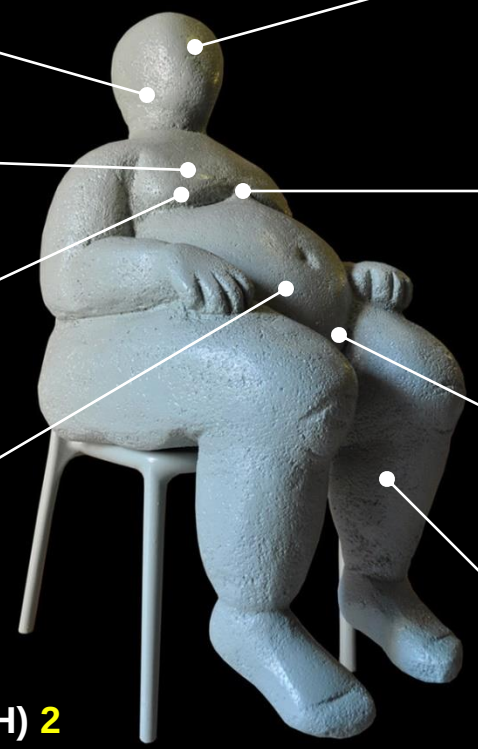
Prevalence of Breathlessness with Exertion in Overweight & Obese Individuals



Sin, et al, Arch Intern Med 1996


Obesity
Altered Respiratory Mechanics
Increasing Respiratory Impedance
-Low lung volume breathing
-Decreased chest wall compliance
-Expiratory flow limitation
-Increased pulmonary resistance
-Increased oxygen cost of breathing and increased abdominal fat distribution
Without Dyspnea on Exertion
With Dyspnea on Exertion
Potential Mechanisms of Dyspnea during Exercise
Chest Tightness
Pulmonary receptor feedback
Air Hunger
Corollary discharge from respiratory motor activity in brainstem respiratory centers
+
Chemoreceptor feedback
Effort/Work
Corollary discharge from cortical motor centers
+
Respiratory Mechanoreceptor feedback

Major complications of overweight and obesity, and approximate relative risks at BMI>27-30



Hirsutism 2
Sweating ↑

Hypoventilation ↑
Sleep apnoea ↑
Breathlessness 3.5
Lung Cancer 1.1
VTE ↑
Perioperativecomplications ↑
Asthma?

Breast cancer 1.3
Gallstones 2.7
Cancer of colon 1.5
Cancer of pancreas 1.6
Kidney disease ↑

Non-alcoholic steatohepatosis (NASH) 2
Diabetes mellitus 10
Dyslipidemia 1.5
Hyperinsulinaemia ↑ ↑

Stroke 1.6
Low mood, poor self-esteem ↑

Hypertension 2.9
Coronary heart disease 2.5
Thromboembolism 1.5
Heart failure 1.5

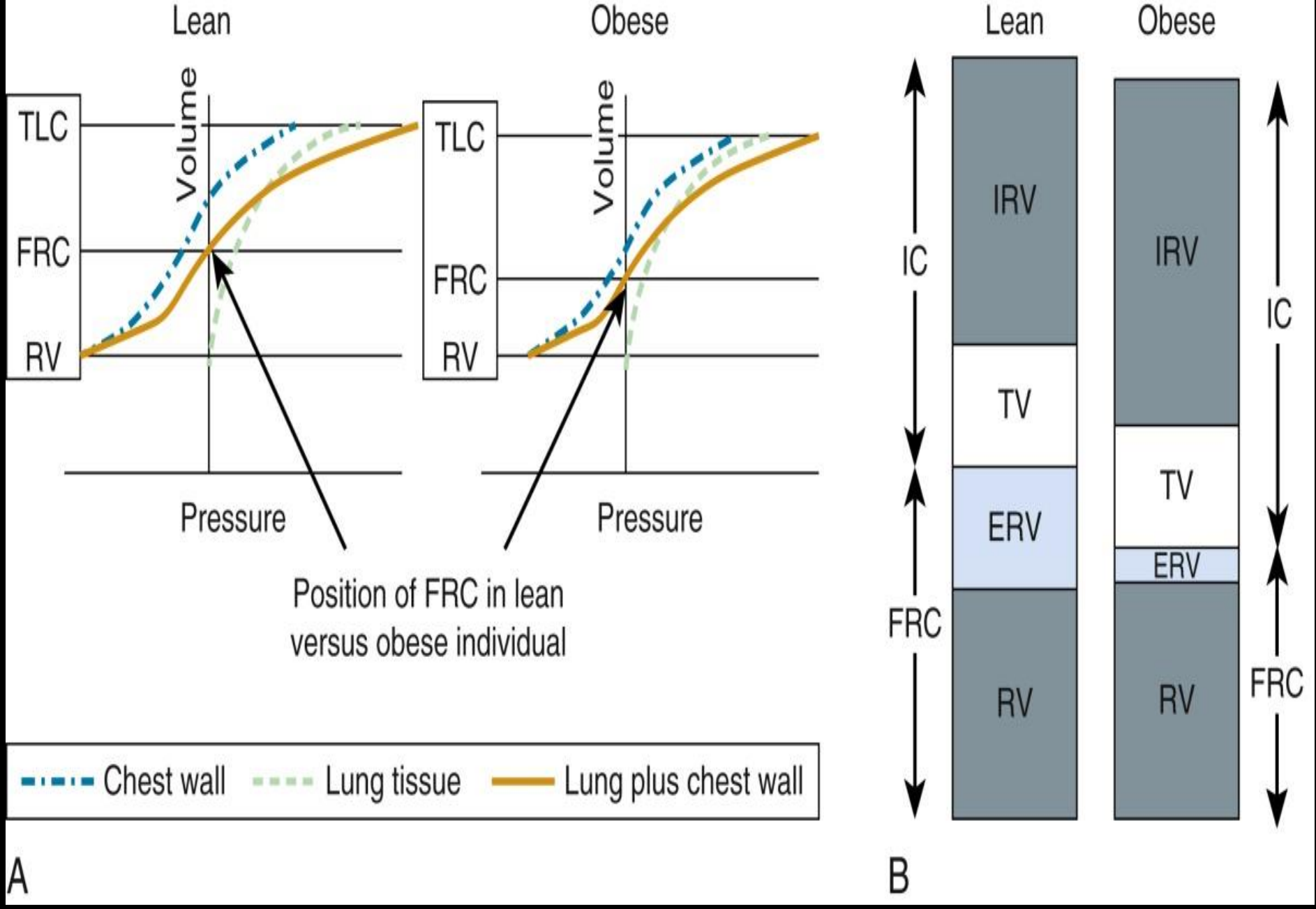
Infertility ↑
Pregnancy problems 2
Cancer of uterus 4.6
Menorrhagia 1.8

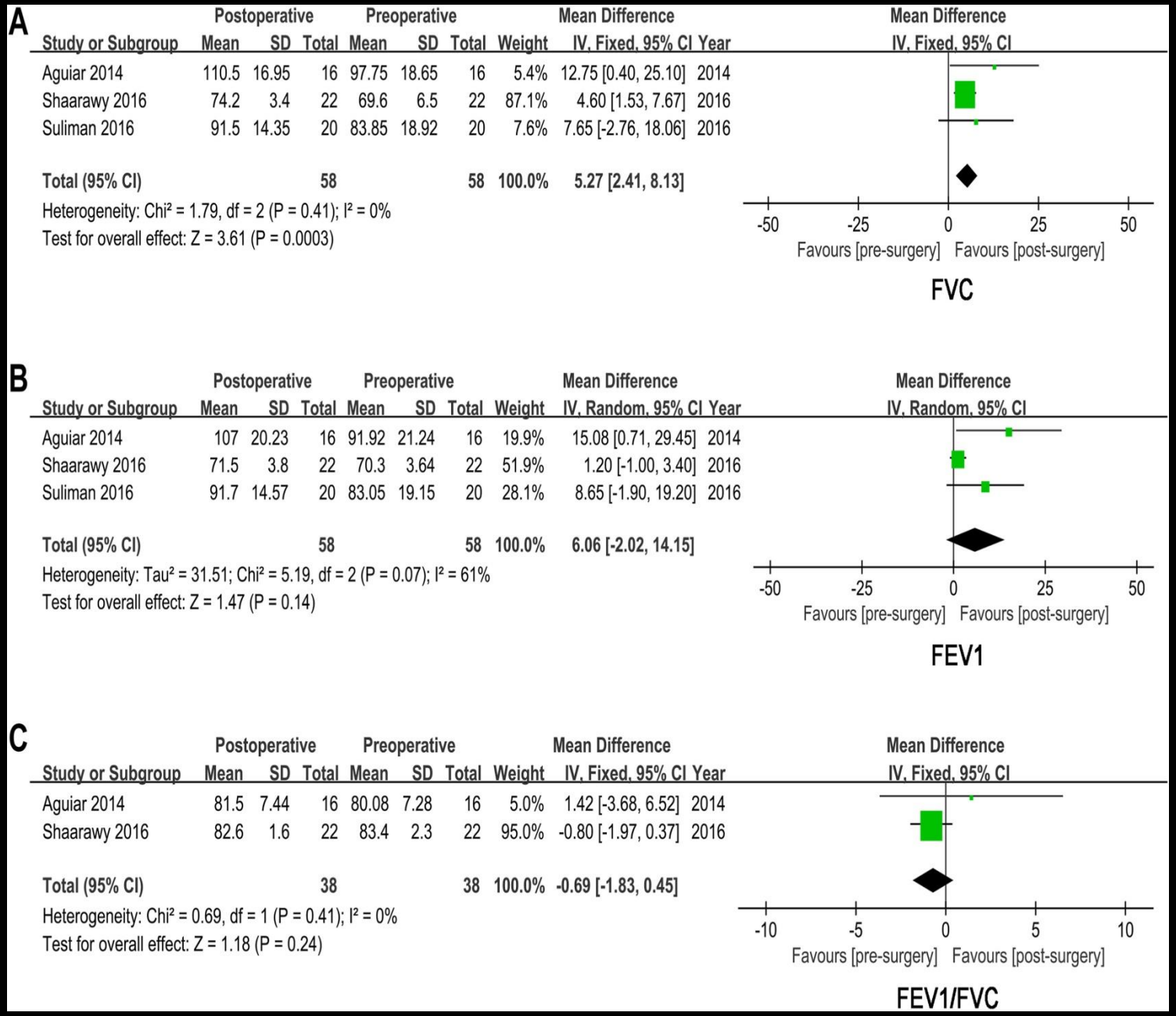
Osteoarthritis 2
Gout 3
Varicose veins ↑

Navarra G and Caramori G 2024

Bariatric surgery: effect on the lungs

- **Bariatric surgery: effect on lung function**
- **Bariatric surgery: effect on asthma and COPD**
- **Bariatric surgery: effect on OSA**
- **Key messages and future perspectives**


Lean
Obese
TLC
FRC
RV
Volume
Pressure
Position of FRC in lean
versus obese individual
Chest wall
Lung tissue
Lung plus chest wall
A
Lean
Obese
IC
FRC
IRV
TV
ERV
RV
B

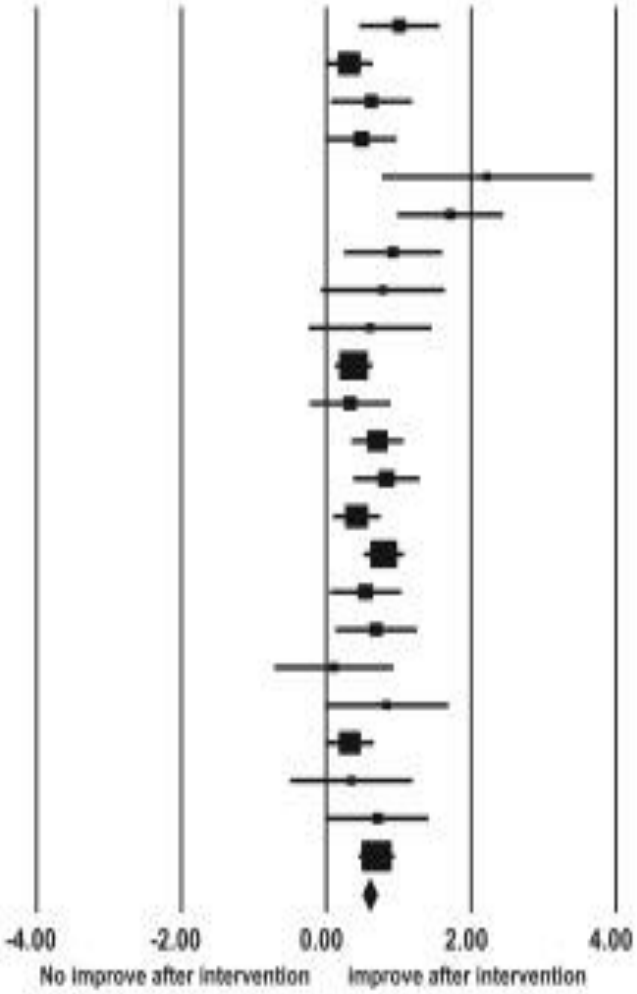

A
Postoperative
Preoperative
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI Year
IV, Fixed, 95% CI
Aguiar 2014 110.5 16.95 16 97.75 18.65 16 5.4% 12.75 [0.40, 25.10] 2014
Shaarawy 2016 74.2 3.4 22 69.6 6.5 22 87.1% 4.60 [1.53, 7.67] 2016
Suliman 2016 91.5 14.35 20 83.85 18.92 20 7.6% 7.65 [-2.76, 18.06] 2016
Total (95% CI) 58 58 100.0% 5.27 [2.41, 8.13]
Heterogeneity: Chi² = 1.79, df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 3.61 (P = 0.0003)
-50 -25 0 25 50
Favours [pre-surgery] Favours [post-surgery]
FVC
B
Postoperative
Preoperative
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
Aguiar 2014 107 20.23 16 91.92 21.24 16 19.9% 15.08 [0.71, 29.45] 2014
Shaarawy 2016 71.5 3.8 22 70.3 3.64 22 51.9% 1.20 [-1.00, 3.40] 2016
Suliman 2016 91.7 14.57 20 83.05 19.15 20 28.1% 8.65 [-1.90, 19.20] 2016
Total (95% CI) 58 58 100.0% 6.06 [-2.02, 14.15]
Heterogeneity: Tau² = 31.51; Chi² = 5.19, df = 2 (P = 0.07); I² = 61%
Test for overall effect: Z = 1.47 (P = 0.14)
-50 -25 0 25 50
Favours [pre-surgery] Favours [post-surgery]
FEV1
C
Postoperative
Preoperative
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI Year
IV, Fixed, 95% CI
Aguiar 2014 81.5 7.44 16 80.08 7.28 16 5.0% 1.42 [-3.68, 6.52] 2014
Shaarawy 2016 82.6 1.6 22 83.4 2.3 22 95.0% -0.80 [-1.97, 0.37] 2016
Total (95% CI) 38 38 100.0% -0.69 [-1.83, 0.45]
Heterogeneity: Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 1.18 (P = 0.24)
-10 -5 0 5 10
Favours [pre-surgery] Favours [post-surgery]
FEV1/FVC

Overall dynamic lung volumes meta-analysis (Random Effects model)

Study name		Std diff in means	Variance	Lower limit	Upper limit
Cervantes. AD et.al	Combined	1.010	0.081	0.454	1.567
De Souza SA. et.al	Combined	0.318	0.028	-0.008	0.644
Dixon AE. et.al	Combined	0.626	0.083	0.060	1.191
Lombardi C. et.al	Combined	0.488	0.062	-0.001	0.976
Lumachi F. et.al	Combined	2.223	0.553	0.766	3.681
Marti-Valeri C. et.al	Combined	1.714	0.141	0.977	2.450
Rivas E. et.al	Combined	0.924	0.121	0.242	1.606
Sideleva O. et.al	Combined	0.780	0.192	-0.078	1.639
Sebbane M. et.al	Combined	0.606	0.189	-0.247	1.459
Wei YF. et.al	Combined	0.379	0.018	0.114	0.643
Weiner P. et.al	Combined	0.330	0.062	-0.230	0.891
Arismendi E. et.al	Combined	0.708	0.035	0.342	1.073
Santana AN. et.al	Combined	0.833	0.055	0.372	1.294
Crapo R. et.al	Combined	0.421	0.029	0.089	0.752
Nguyen NT. et.al	Combined	0.795	0.020	0.515	1.074
Thomas PS. et.al	Combined	0.544	0.063	0.050	1.038
Barbalho-Moulim MC et.al	Combined	0.691	0.083	0.126	1.256
Al-Alwan A. et.al	Combined	0.107	0.177	-0.719	0.932
Boulet LP. et.al	Combined	0.833	0.192	-0.025	1.691
Gabrielsen AM. et.al	Combined	0.325	0.029	-0.011	0.661
Maniscalco M. et.al	Combined	0.347	0.187	-0.501	1.195
Van Huisstede A. et.al	Combined	0.713	0.128	0.012	1.413
Hewitt S. et.al	Combined	0.696	0.016	0.444	0.948
		0.595	0.002	0.502	0.687

Statistics for each study

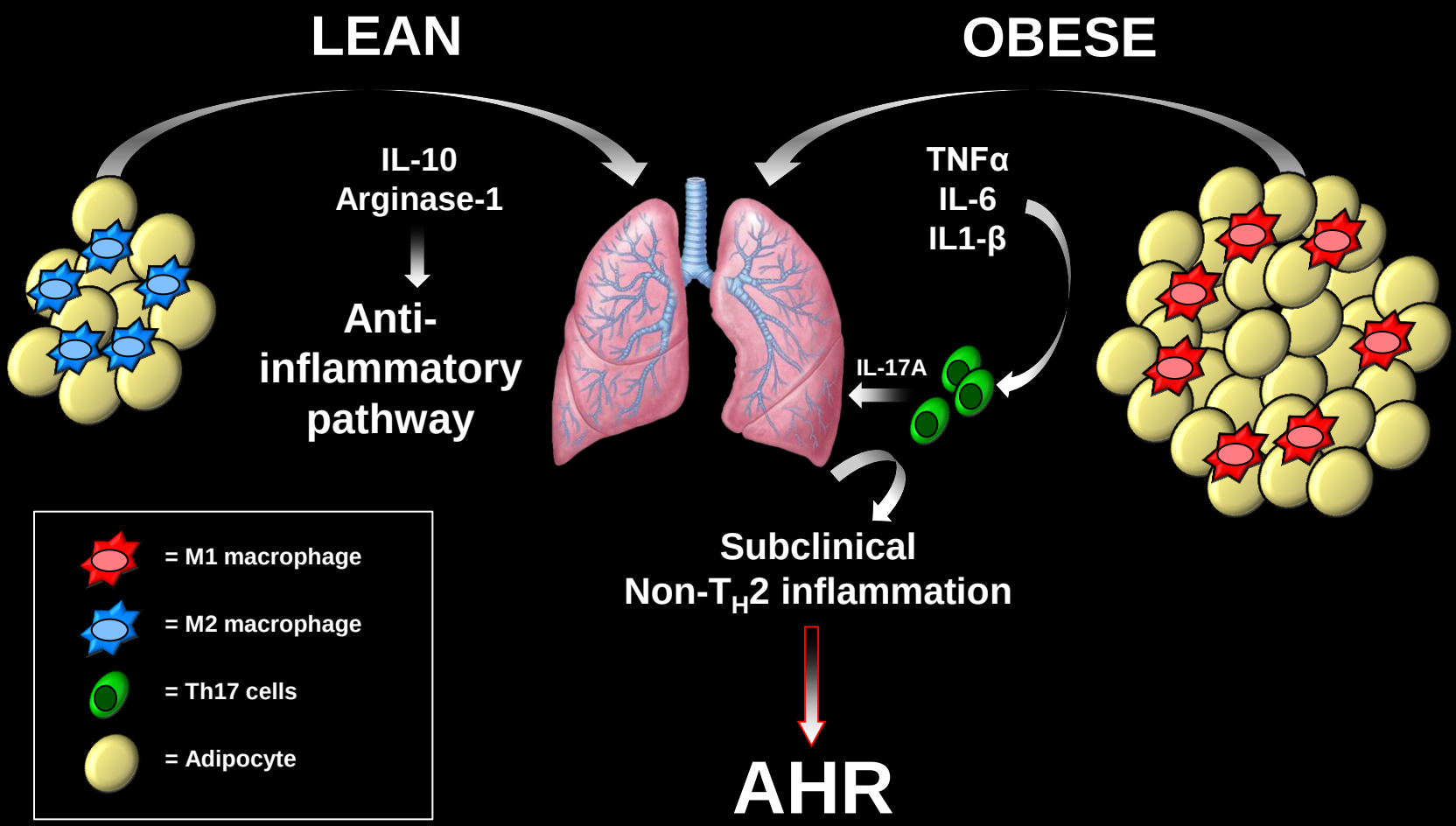
Std diff in means and 95% CI



Bariatric surgery: effect on the lungs

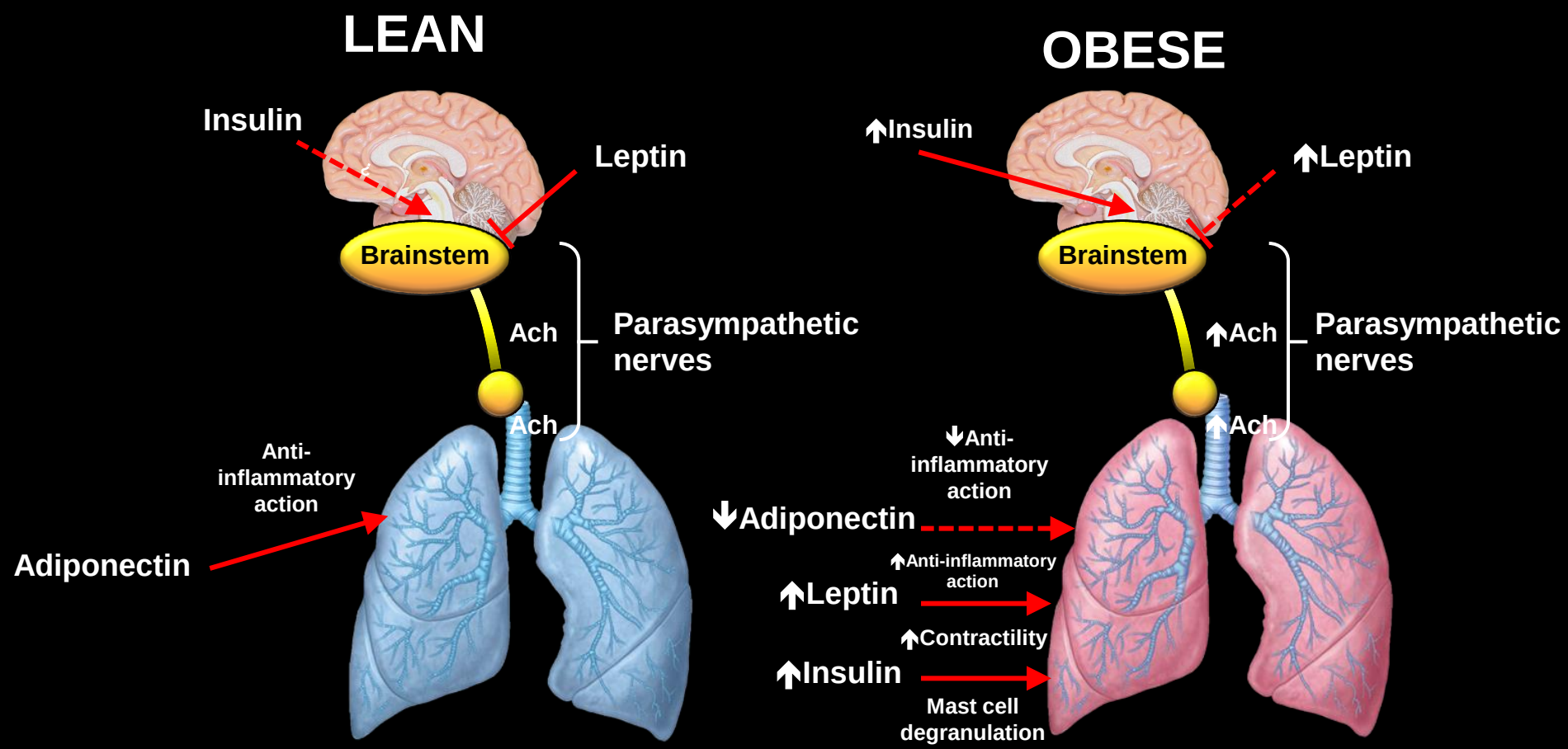
- Bariatric surgery: effect on lung function
- Bariatric surgery: effect on asthma and COPD
- Bariatric surgery: effect on OSA
- Key messages and future perspectives

Subclinical lung inflammation in obese mice



Caramori G 2024, adapted from Leiria LOS et al. Metabol Clin Exp 2014;64:172-181.

Hormonal regulation of airway responsiveness under physiological and obesity conditions in the mice



Caramori G 2024, adapted from Leiria LOS et al. Metabol Clin Exp 2014;64:172-181.

Does body mass index influence responsiveness to inhaled corticosteroids in persistent asthma?

Although the relationship between asthma and obesity has been extensively explored, the effect of body mass index (BMI) on the dose-response relationship to inhaled corticosteroids (ICS) has received little attention.

To assess the dose-response of inhaled budesonide on outcome measures of asthma between overweight and normal weight patients with persistent asthma.

72 patients with mild to moderate persistent asthma from a post hoc analysis of previously reported trial data were divided into 2 groups: overweight, BMI 25 kg/m2 or higher; normal weight, BMI less than 25 kg/m2.

Each group received 4 weeks' treatment with inhaled (hydrofluoroalkane) budesonide 200 µg/day then 800 µg/day with ICS washout pretreatment. Outcome measures forced expiratory volume in 1 second (FEV(1)), fractional exhaled nitric oxide (FeNO), methacholine PC20, total daily asthma symptom score, and overnight urinary cortisol/creatinine ratio were performed at baseline and after each dose.

Significantly greater improvements were seen in the normal weight group for both FeNO and symptom responses at 0 to 200 µg and 0 to 800 µg ICS doses (as change from baseline), compared with the overweight group:

FeNO 0 to 200 µg, p=0.002; 0 to 800 µg, p=0.045.

symptoms 0 to 200 µg, p=0.002; 0 to 800 µg, p=0.013.

A trend also was seen toward attenuated cortisol suppression in overweight subjects at 0 to 800 µg (p=0.06), but no significant difference was seen at either dose in FEV1 and methacholine PC20 between weight groups.

Attenuated cortisol suppression in the overweight group may be the clue to this difference, alluding to reduced peripheral lung deposition or absorption of budesonide in overweight patients with asthma.

Anderson WJ, Lipworth BJ.

Ann Allergy Asthma Immunol 2012; 108:237-242.

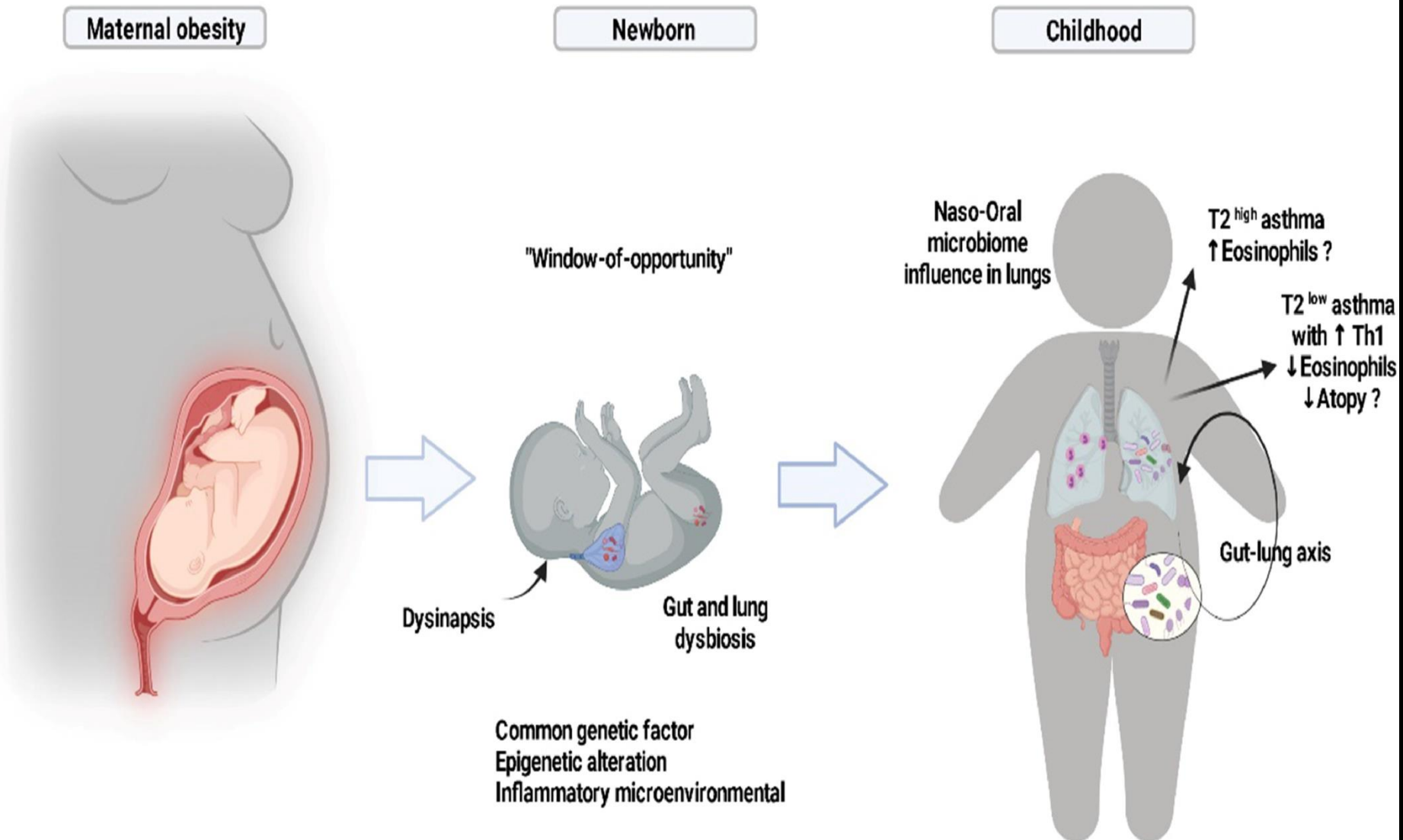
Bariatric surgery: effect on asthma control

Weight loss can reduce the impact of obesity on asthma and improve patient outcomes by diverse mechanisms including modulating airway inflammation, reducing oxidative stress, and improving lung function. Multiple lifestyle, nonpharmacological, pharmacological, and surgical interventions are effective at reducing weight in the general population. Fewer have been studied specifically in the context of patients with asthma. However, increasingly effective pharmacologic options for weight loss highlight the need for allergists and pulmonologists to understand the range of approaches that may directly or indirectly yield clinical benefits in asthma management. Weight loss interventions often require multidisciplinary support to create strategies that can realistically achieve a patient's personalized asthma and weight goals. This includes minimizing the adverse weight effects of glucocorticoids, which remain a mainstay of asthma management.

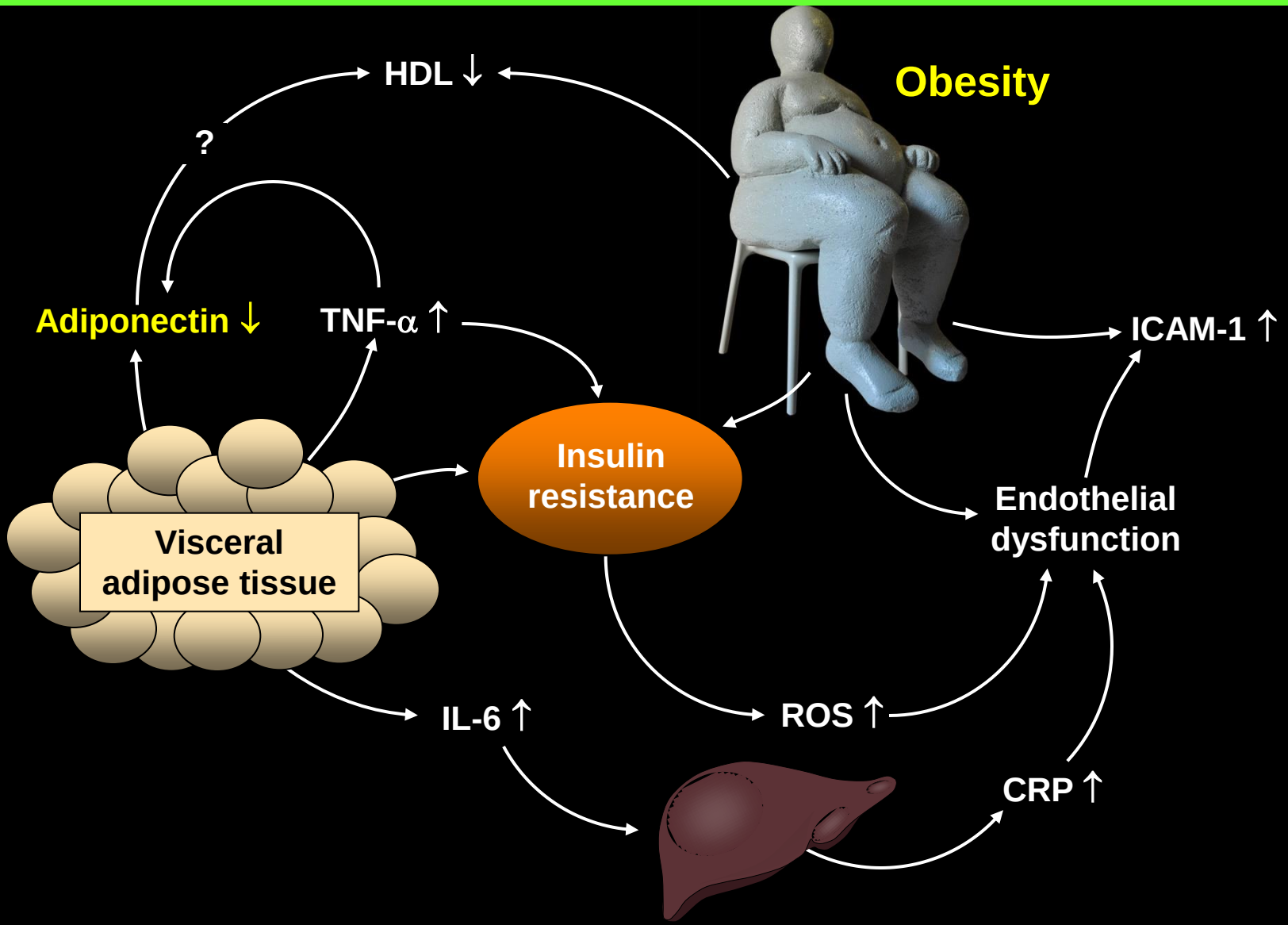
Future studies are needed to elucidate mechanisms of action of specific weight loss interventions on short-term and long-term asthma outcomes.

J Allergy Clin Immunol Pract 2024;12:840-847.

Bariatric surgery: effect on risk of asthma development



Metabolic syndrome contributes to systemic inflammation



Navarra G and Caramori G 2024, adapted from Van Gaal et al, Nature 2006

Adiponectin is Associated with Neutrophils to Lymphocyte Ratio in Patients with Chronic Obstructive Pulmonary Disease

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as valuable markers of the systemic inflammation in COPD.

Adiponectin (Acpr30) circulates in serum as complexes of different molecular weight (HMW, MMW, LMW) with multifaceted metabolic and anti-inflammatory properties.

Seventy stable COPD patients were enrolled.

Both NLR and PLR are associated with lower BMI.

Interestingly, total Acpr30 is negatively associated with NLR but not with PLR; after adjusting for age, BMI and FEV1,

Acpr30 was independently associated with NLR.

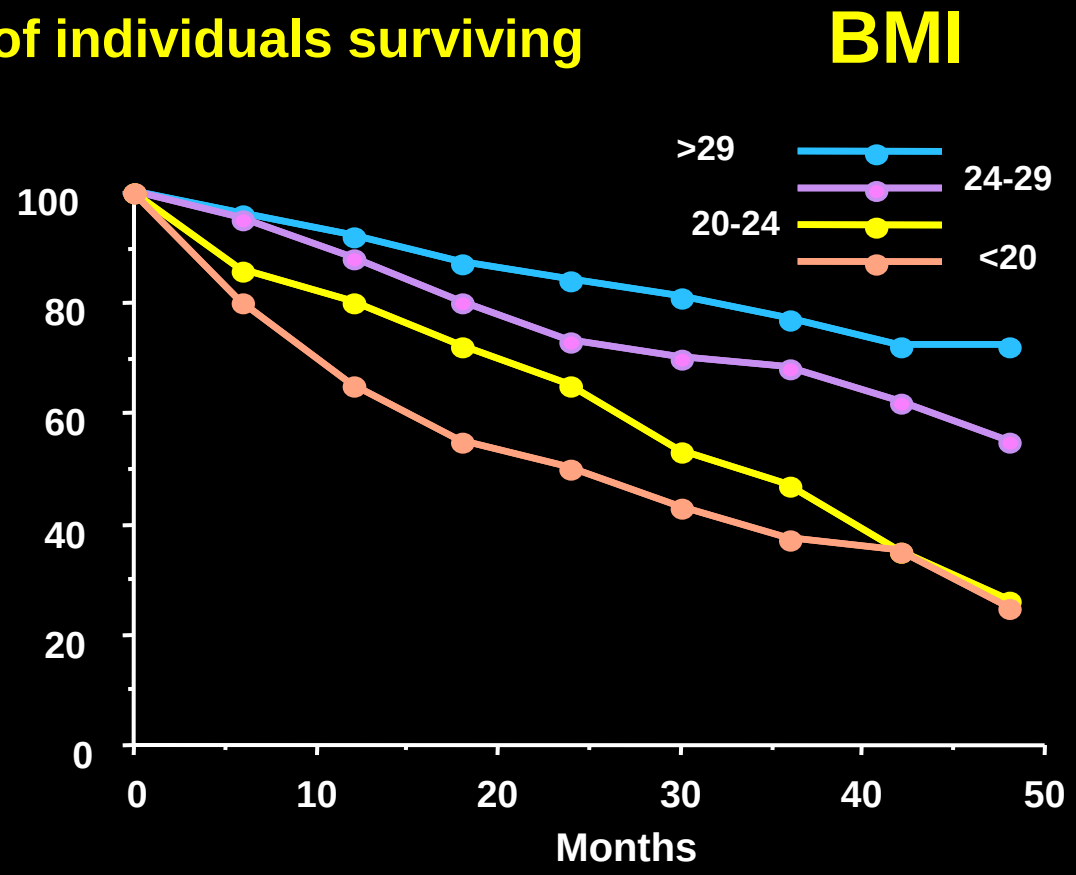
Conversely, HMW Acpr30 and HMW/Acpr30 ratio were positively correlated to NLR.

The association of Acpr30, HMW Acpr30 and HMW/totalAcpr30 ratio with NLR but not with PLR in COPD patients indicates that Acrp30 oligomerization could represent a biological mechanism interfering with systemic inflammation in COPD.

Perrotta F, Bianco A, Caramori G et al. COPD 2021;18:70-75

BODY MASS AND SURVIVAL IN COPD

- 400 consecutive COPD patients
- stable
- referred for rehabilitation
- no special dietary intervention
- body mass index



Schols et al. Am J Resp Crit Care Med 1998

Bariatric surgery: effect on COPD exacerbations

Using the population-based ED and inpatient sample in three US states (California, Florida, and Nebraska), we performed a self-controlled case series study of **481 adults (40-65 years of age) with COPD who were obese who underwent bariatric surgery.**

The primary outcome was an ED visit or hospitalization for acute exacerbation of COPD (AECOPD) from 2005 through 2011.

During the 13 to 24 months before bariatric surgery (ie, reference period), 28% of patients had an ED visit or hospitalization for AECOPD. In the subsequent 12-month pre-surgery period, the risk did not change significantly (31%), with an adjusted OR (aOR) of 1.16; p=0.29).

By contrast, during the first 12 months after bariatric surgery, the risk declined significantly (12%; aOR 0.35; p<0.001).

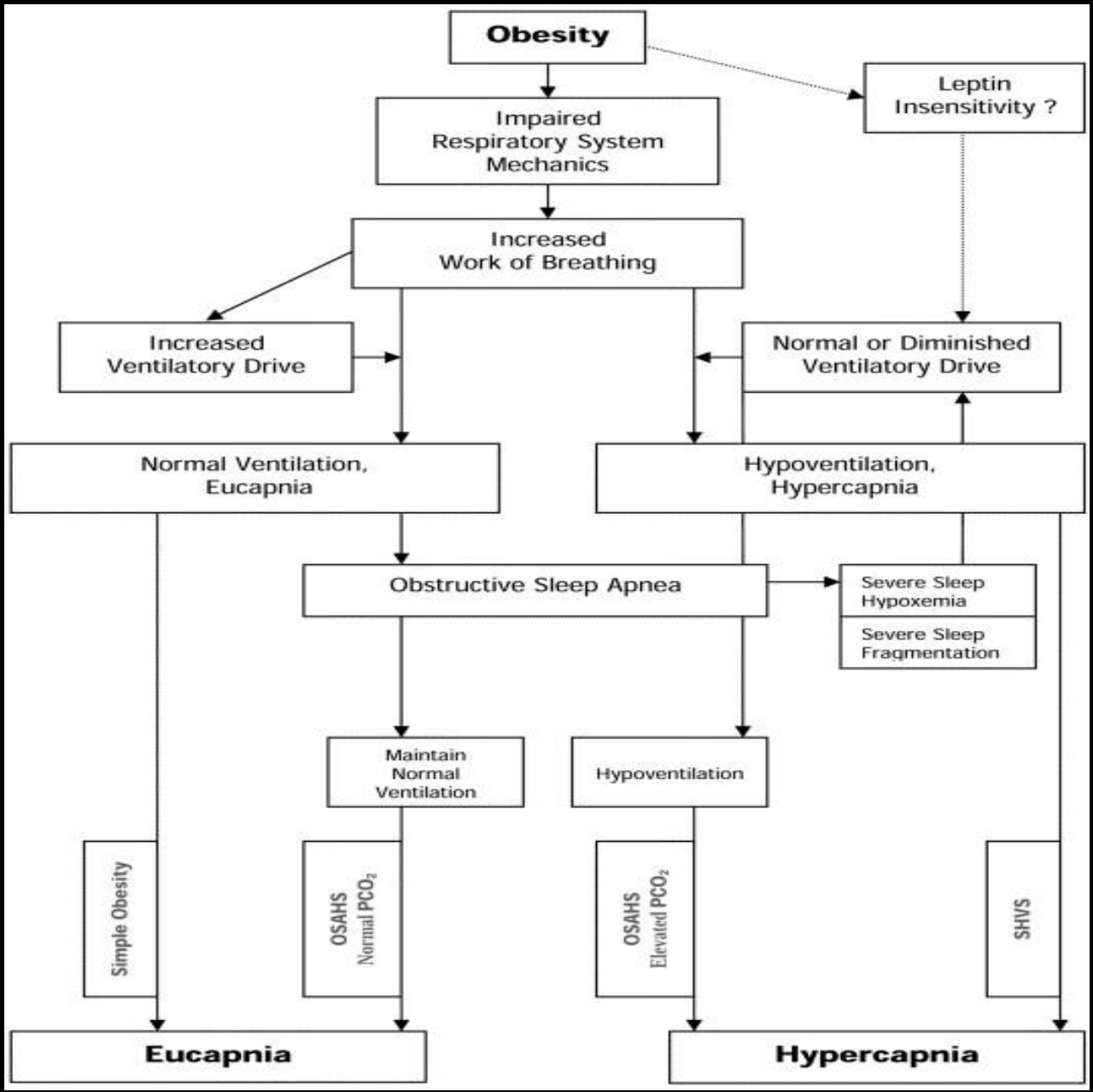
Likewise, in the subsequent period of 13 to 24 months after bariatric surgery, the risk remained significantly low (13%; aOR 0.39; p< 0.001).

Chest 2018;153:611-617.

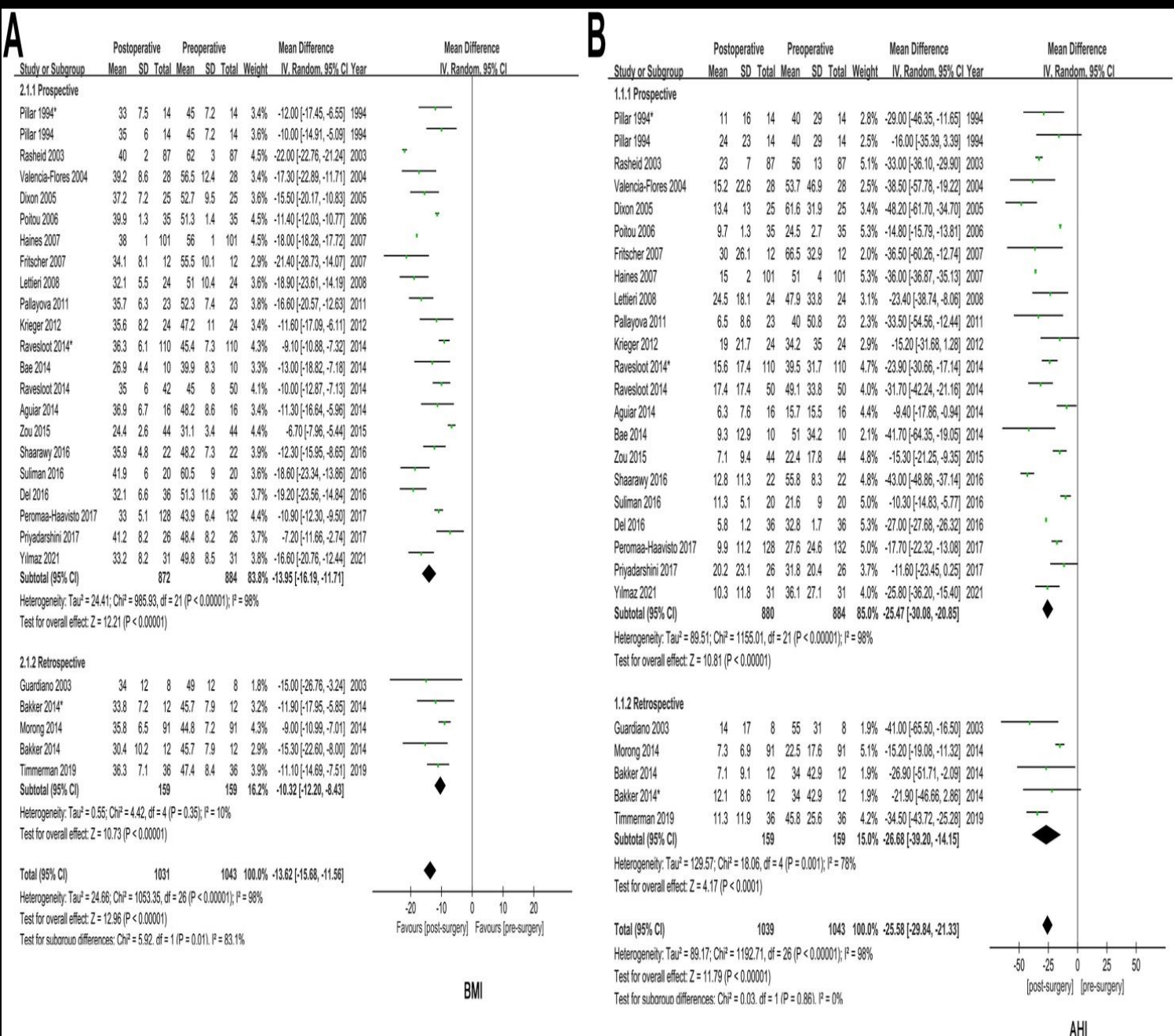
Bariatric surgery: effect on the lungs

- Bariatric surgery: effect on lung function
- Bariatric surgery: effect on asthma and COPD
- Bariatric surgery: effect on OSA

- Key messages and future perspectives



The prevalence of obstructive sleep apnea (OSA) among the bariatric surgery population is estimated to be 45-70%.



The forest plot for mean difference (95% CI) in (A) body mass index (BMI) and (B) apnea-hypopnea index (AHI) in meta-analysis of patients with obstructive sleep apnea before and after bariatric surgery.

Surg Obes Relat Dis 2023;19:1444-1457

The impact of bariatric surgery on obstructive sleep apnea:

Resolution of obstructive sleep apnea after bariatric surgery occurs in 66% of patients according to a systematic review (Sarkhosh K, et al.. Obes Surg. 2013;23:414– 423.)

Surgical patients had a mean pre-intervention BMI of 51 and achieved a significant 14 decrease in BMI, with a 29/h decrease in AHI. Non-surgical patients had a mean pre-intervention BMI of 38 and achieved a significant decrease in BMI of 3.1, with a decrease in AHI of 11/h. Heterogeneity was high across all outcomes according to another systematic review (Obes Surg 2015;25:1239-50

Data was analysed on all patients with OSA who underwent bariatric procedures [laparoscopic Roux-en-Y gastric bypass (LRYGB) and sleeve gastrectomy (LSG)] between June 2012 and September 2016 in our unit. 47 patients (26.7%) were diagnosed with OSA. Mean age was 48.5 years. 63.8% were female. 43 required nocturnal continuous positive airway pressure (CPAP) support. Procedures were LRYGB (n = 26) and LSG (n = 21). Mean excess weight loss was 56.1%. Mean start apnoea-hypopnoea index (AHI) on CPAP was 6.4 events/hr and end AHI was 1.4 events/h. 14 patients (32.6%) had complete OSA resolution and 12 (27.9%) showed improvement in pressure support requirements. We demonstrated that 55.3% of patients had resolution or improvement in OSA following bariatric surgery. However, there was a high rate of non-attendance of follow-up appointments. Future efforts will involve analysis of the reasons for this to ensure more robust monitoring.(BMC Res Notes 2018;11:385

Weight loss obtained by bariatric surgery is not always associated with full remission of OSA, suggesting that other confounding factors are present.

Relevant studies of more than 50 patients that assessed pre- and post-operative presence and severity of OSA detected by poly(somno)graphy (PG/PSG) in bariatric populations were collected.

Six retrospective and prospective studies were evaluated that included 1302 OSA patients, with a BMI range of 42.6 to 56 kg/m2, age range of 44.8 to 50.7 years, and percentage of women ranging from 45% to 91%.

The studies were very heterogeneous regarding type of bariatric surgery, diagnostic criteria for OSA and OSA remission, and delay of OSA reassessment. OSA remission was observed in 26% to 76% of patients at 11-12 months post-surgery. Loss to follow-up was high in all studies, leading to a potential underestimation of OSA remission. Based on this limited sample of bariatric patients, age, pre-operative OSA severity, proportion of weight loss, and type 2 diabetes (T2D) were identified as factors associated with OSA persistence but the results were inconsistent between studies regarding the impact of age and the magnitude of weight loss. Several other factors may potentially lead to OSA persistence in the bariatric surgery population, such as fat distribution, ethnicity, anatomical predisposition, pathophysiological traits, supine position, and REM-predominant hypopnea and apnea. **Further well-conducted multicentric prospective studies are needed to document the importance of these factors to achieve a better understanding of OSA persistence after bariatric surgery in obese patients.**

Nat Sci Sleep 2024:16:111-123.

Bariatric surgery: effect on the lungs

- Bariatric surgery: effect on lung function
- Bariatric surgery: effect on asthma and COPD
- Bariatric surgery: effect on OSA
- Key messages and future perspectives

Eccesso ponderale per regione di residenza

Passi 2013-2016

- peggiore del valore nazionale
- simile al valore nazionale
- migliore del valore nazionale

Sorveglianza Passi

KEY MESSAGES

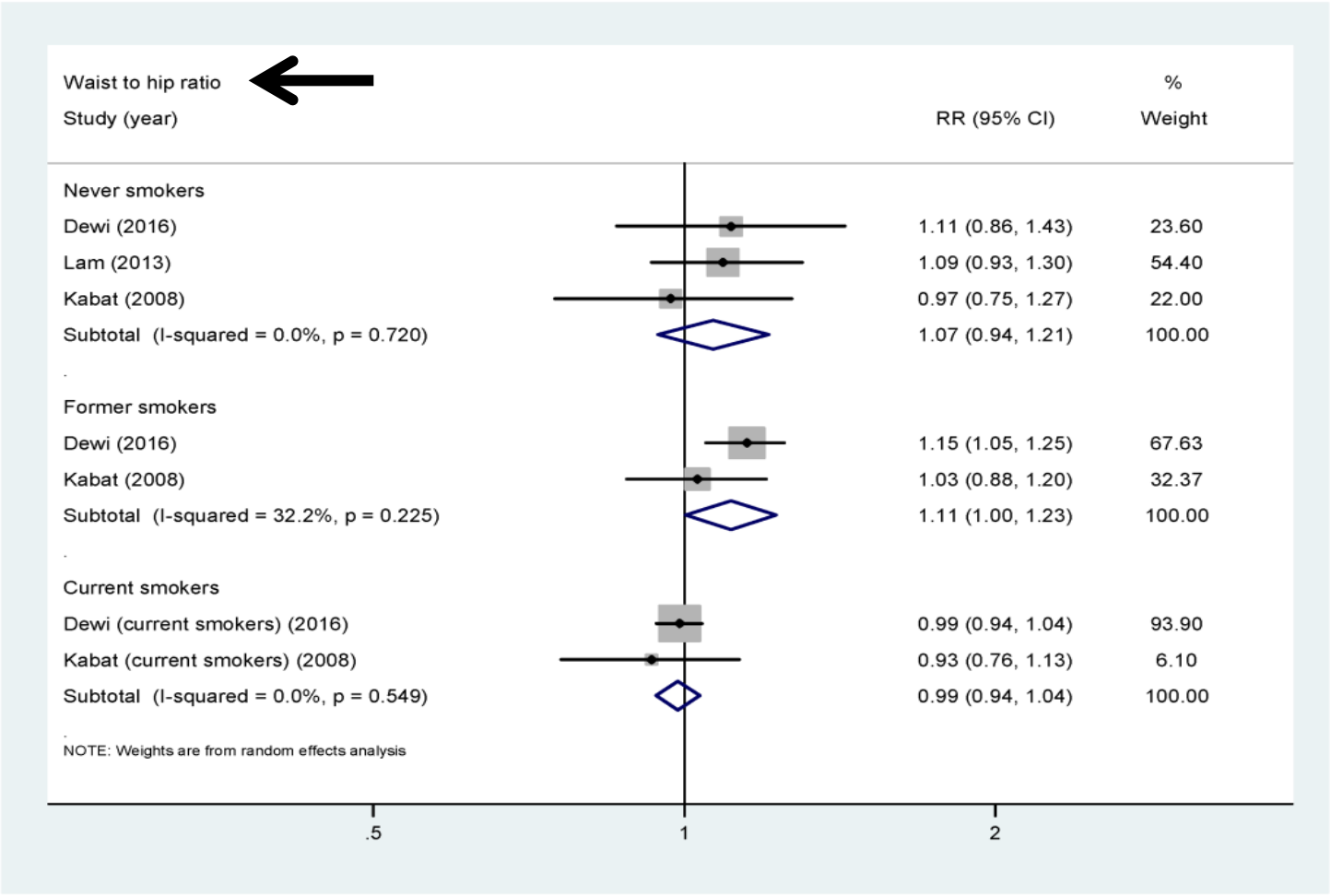
- Obesity is a growing epidemic in affluent countries and Sicily has one of the highest prevalence of obesity between the Italian regions
- Obesity increase changes the lung physiology and increase the risk for many pulmonary complications and lung function tests (including spirometry, blood gases analysis and polysomnography) and Pulmonary evaluation must be part of the routine clinical evaluation of these Patients
- The indication, according to current guidelines for lifestyle interventions and/or medical therapy and/or bariatric surgery on weight reduction is mandatory for all physicians.

FUTURE PERSPECTIVES

- The long-term efficacy of bariatric surgery in restoring the normal lung physiology, decreasing lung and systemic inflammation and decreasing the risk of respiratory complications is still unknown.

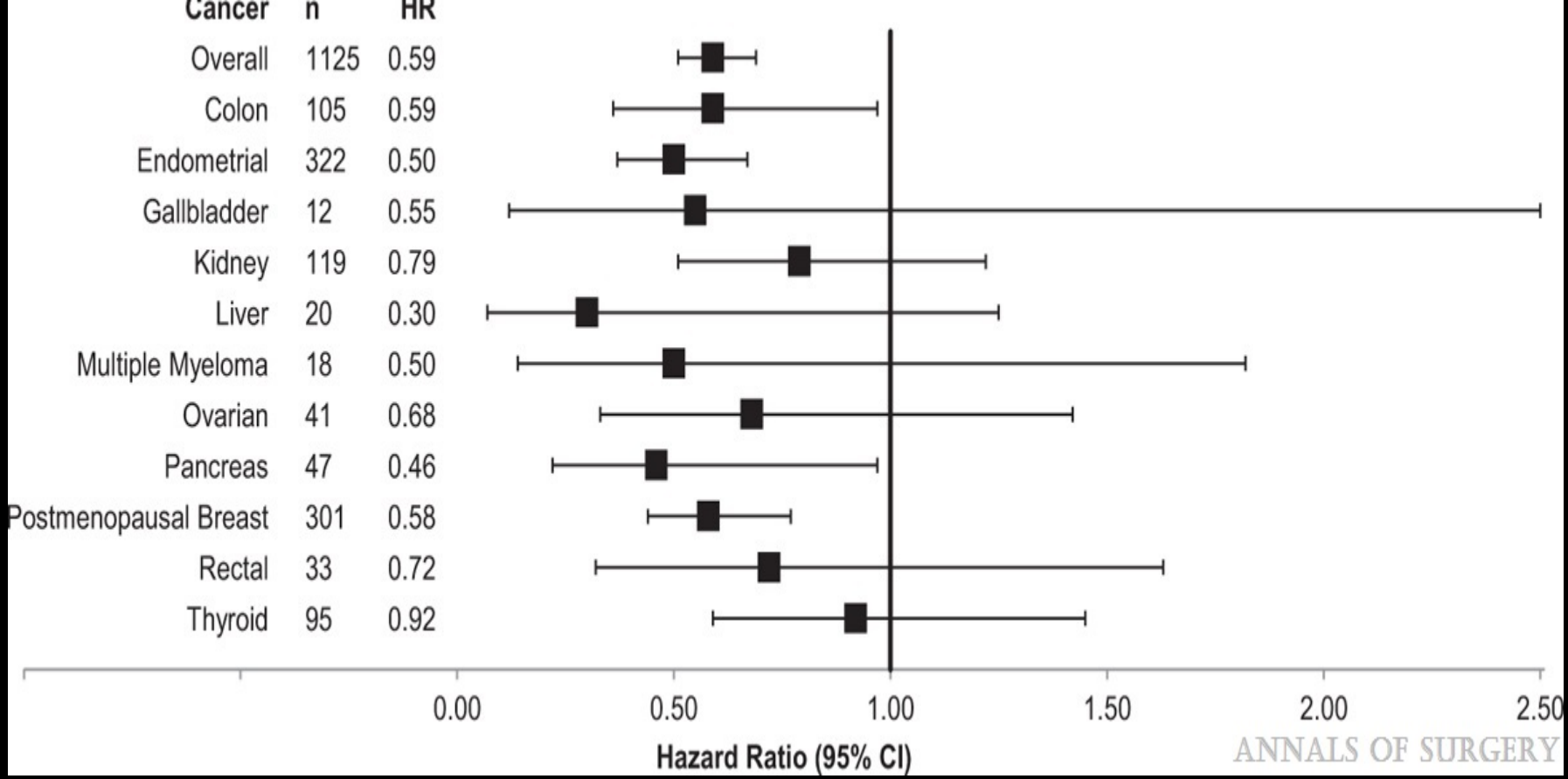
- The effect of bariatric surgery on the long-term risk of lung cancer of these Patients is an area of active research.

Obesity increases the risk of lung cancer in both never and former smokers



(B)

Nutrients 2016;8:810



We conducted a retrospective cohort study of patients undergoing bariatric surgery between 2005 and 2012 with follow-up through 2014 using data from a large integrated health insurance and care delivery systems with 5 study sites. The study included **22,198 subjects who had bariatric surgery and 66,427 nonsurgical subjects matched on sex, age, study site, body mass index, and Elixhauser comorbidity index.** Multivariable Cox proportional-hazards models were used to examine **incident cancer up to 10 years after bariatric surgery compared to the matched nonsurgical patients.**

Schauer DP et al. Ann Surg 2019;269:95-101

Marsala ICL, UK meeting 2015