70 ANNI DI
REUMATOLOGIA
ALLE MOLINETTE

RELAZIONE TRA BMI, ATTIVITÀ DI MALATTIA ED EFFICACIA TERAPEUTICA NEI REUMATISMI INFIAMMATORI

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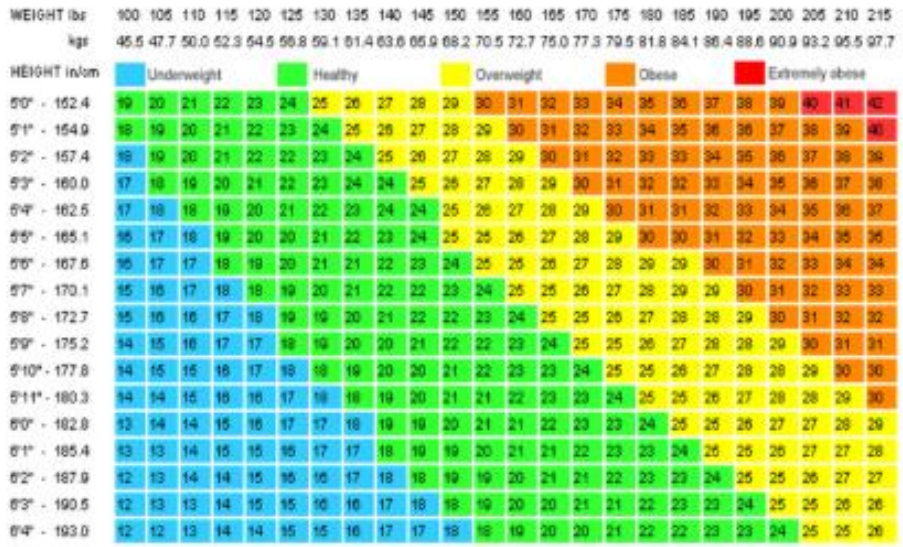
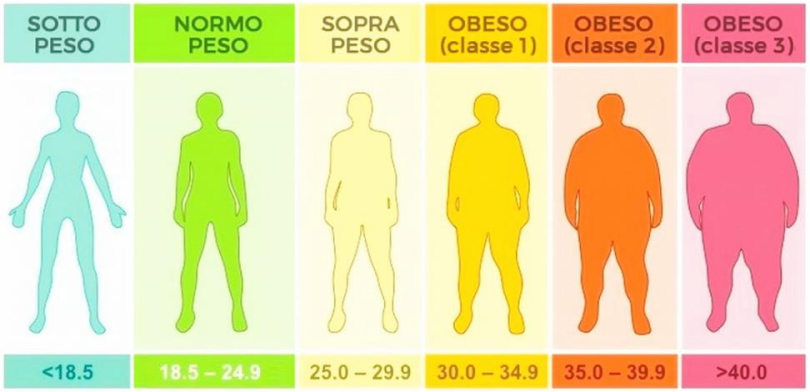
AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

BMI Chart





BMI (old): Kg / H²

BMI (new): (Kg x 1.3)/H$^{2.5}$

Your weight: 56 kgs ◉ lbs ○ (Convert from stones to pounds here)

Your height: 163 cms ◉ inches ○

Calculate BMI

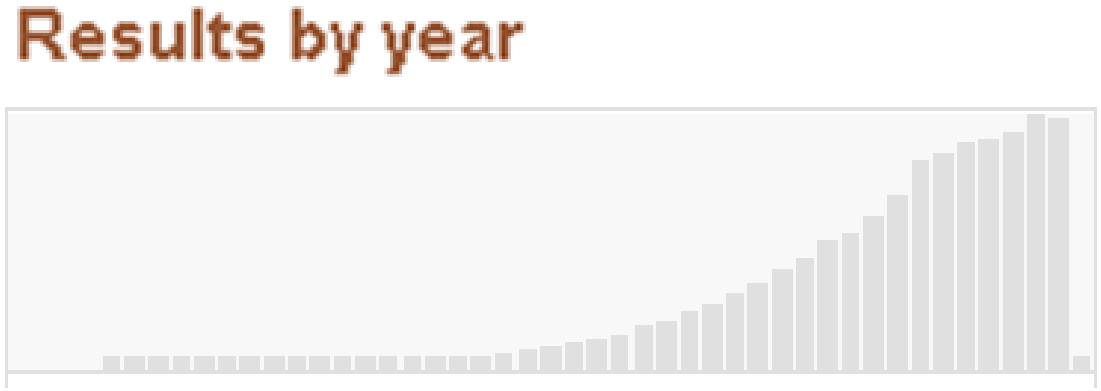
Your standard BMI is 21.08 a reading which classifies you as healthy.

Your new BMI is 21.46 a reading which classifies you as healthy.

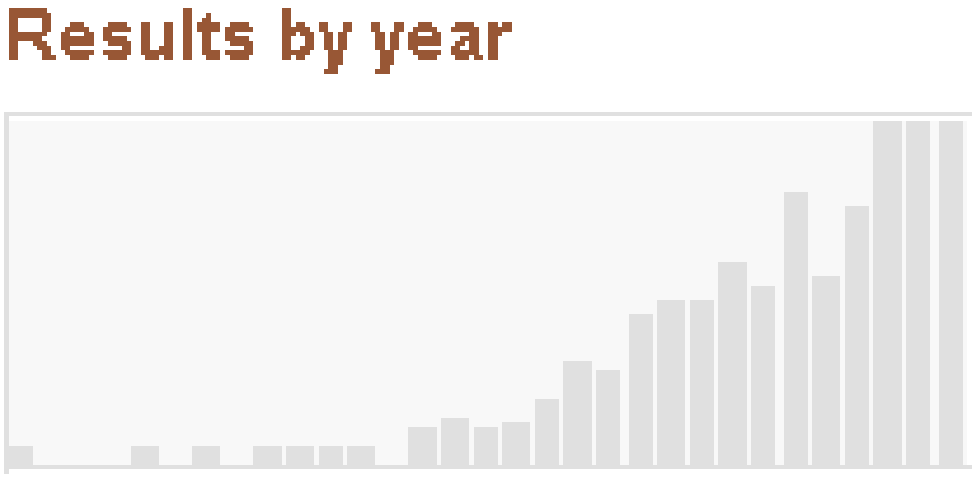
Your new BMI healthy range is 48.27 to 65.23 kgs

Reset

BMI < 18.50	**Underweight**
BMI < 16.00	Severe Thinness
BMI 16.00 - 16.99	Moderate Thinness
BMI 17.00 - 18.49	Mild Thinness
BMI 18.50 - 24.99	**Normal Weight**
BMI 18.50 - 22.99	Lower Range
BMI 23.00 - 24.99	Upper Range
BMI 25.00 - 29.99	**Overweight / Pre-Obese**
BMI 25.00 - 27.49	Lower Range
BMI 27.50 - 29.99	Upper Range
BMI ≥ 30	**Obese**
BMI 30.00 - 34.99	Obese Class I
BMI 35.00 - 39.99	Obese Class II
BMI ≥ 40.00	Obese Class III



BMI 1978-2019



RA - BMI 1989-2019

Percentuali per Regione

Indicatore: Sovrappeso ▾ ◉ Dati standardizzati ○ Dati grezzi

Dati standardizzati

Sovrappeso per regione di residenza

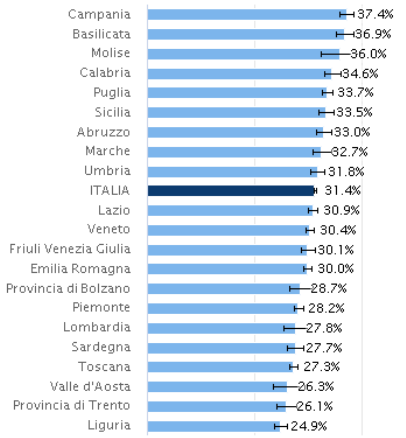
Passi 2015-2018

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

Sorveglianza Passi

Sovrappeso per regione di residenza

Passi 2015-2018



Sorveglianza Passi

☑ Mostra valori

Percentuali per Regione

Indicatore: Obesi ▾ ◉ Dati standardizzati ○ Dati grezzi

Dati standardizzati

Obesi per regione di residenza

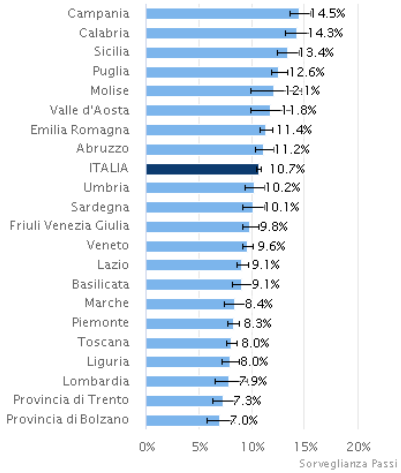
Passi 2015-2018

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

Sorveglianza Passi

Obesi per regione di residenza

Passi 2015-2018



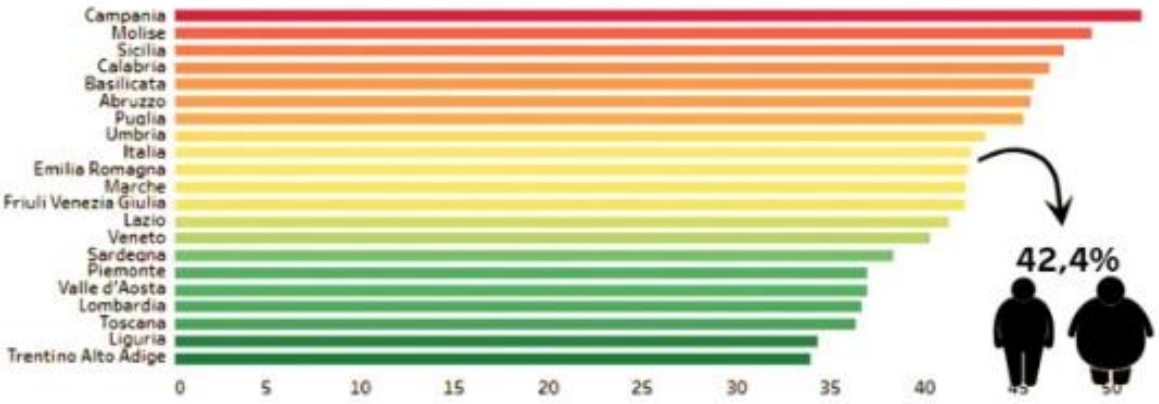
Sorveglianza Passi

☑ Mostra valori

SOVRAPPESO **OBESI**

Medie Nazionali

31,7% **10,7%**



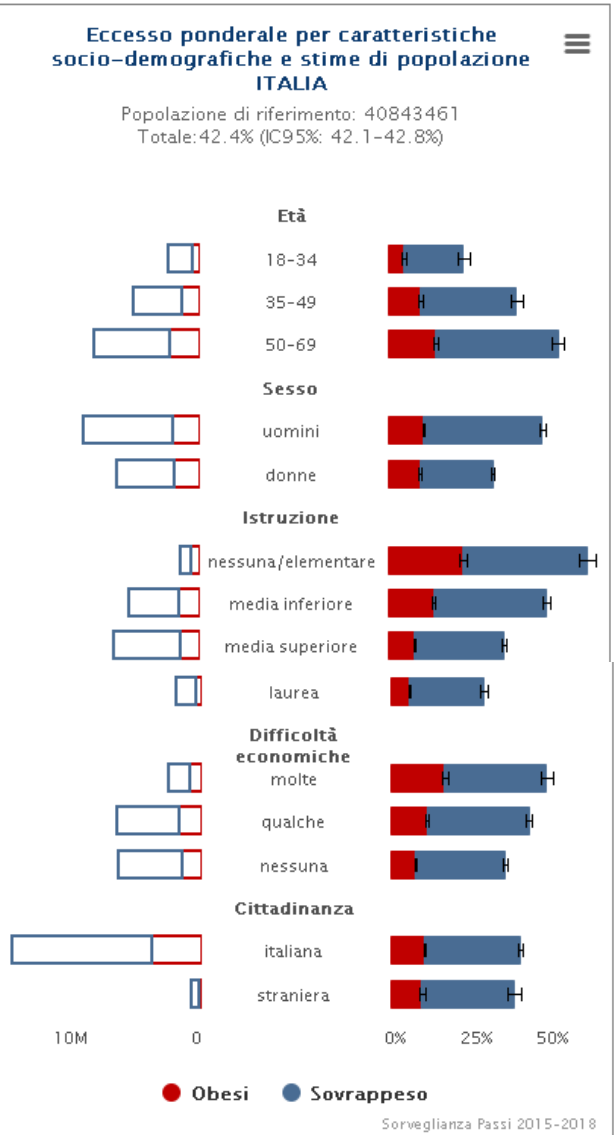
42,4%

EpiCentro **Il portale dell'epidemiologia per la sanità pubblica**
a cura dell'Istituto superiore di sanità

Eccesso ponderale

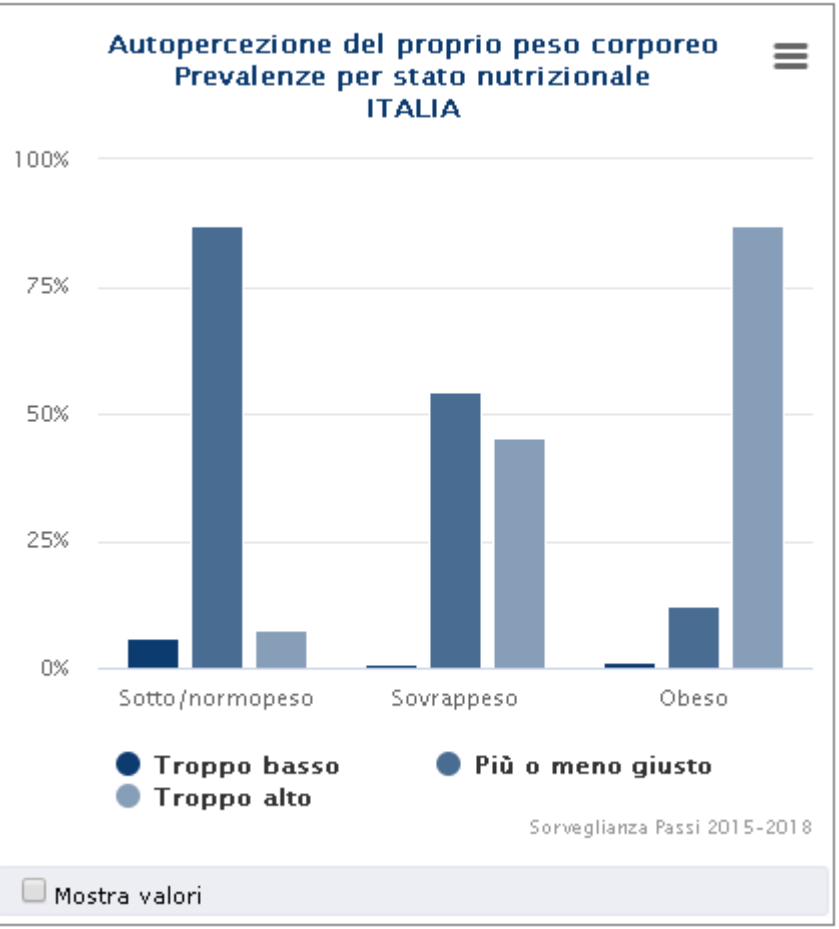
Obesi		ITALIA n = 132158		
		%	IC95% inf	IC95% sup
Età	18-34	5.1	4.5	5.9
	35-49	10.5	9.7	11.4
	50-69	15.7	14.8	16.5
Sesso	uomini	11.4	11.1	11.8
	donne	10.3	10.0	10.6
Istruzione	nessuna / elementare	24.5	23.2	25.9
	media inferiore	14.9	14.5	15.4
	media superiore	8.5	8.2	8.8
	laurea	6.0	5.6	6.4
Difficoltà economiche	molte	17.7	16.9	18.6
	qualche	11.8	11.4	12.1
	nessuna	8.1	7.9	8.4
Cittadinanza	italiana	10.9	10.7	11.1
	straniera	10.2	9.4	11.1

Sovrappeso		ITALIA n = 132158		
		%	IC95% inf	IC95% sup
Età	18-34	19.5	18.4	20.7
	35-49	31.5	30.4	32.7
	50-69	40.2	39.1	41.4
Sesso	uomini	39.3	38.8	39.8
	donne	24.0	23.6	24.4
Istruzione	nessuna / elementare	41.1	39.6	42.6
	media inferiore	37.1	36.4	37.7
	media superiore	29.6	29.2	30.1
	laurea	24.6	23.9	25.3
Difficoltà economiche	molte	33.5	32.6	34.5
	qualche	33.6	33.0	34.1
	nessuna	29.4	28.9	29.8
Cittadinanza	italiana	31.6	31.3	32.0
	straniera	30.4	29.1	31.7



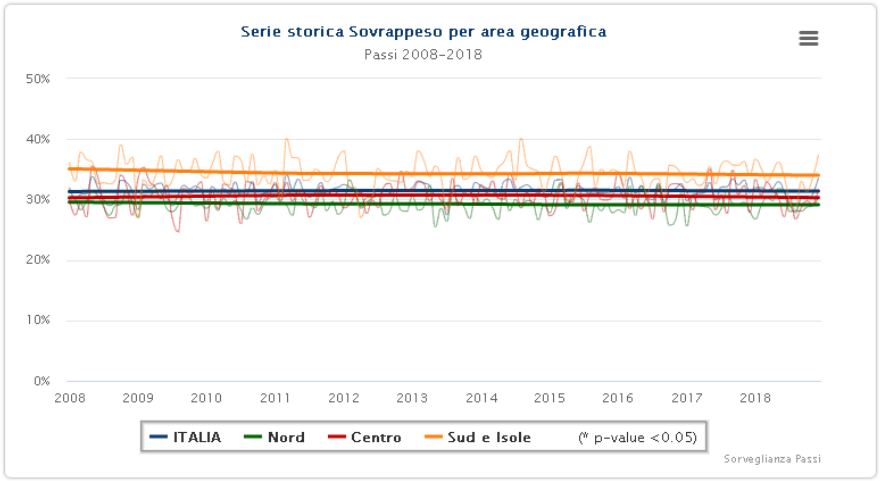
Autopercezione del proprio peso corporeo

	ITALIA n = 132158		
	Troppo basso	**Più o meno giusto**	**Troppo alto**
Sotto/normopeso	5.8	86.9	7.3
Sovrappeso	0.7	54.2	45.1
Obeso	1.0	12.1	87.0



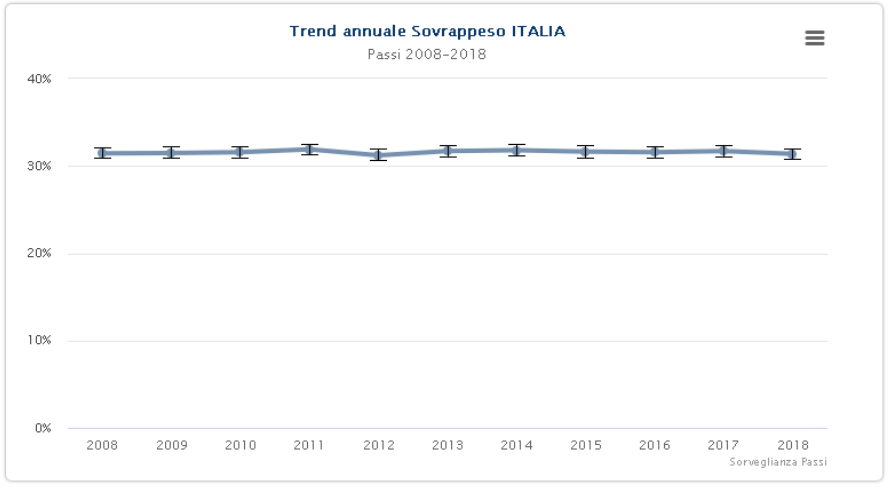
Analisi delle serie storiche

Indicatore: Sovrappeso ▾ ○ Serie storica ○ Trend annuale



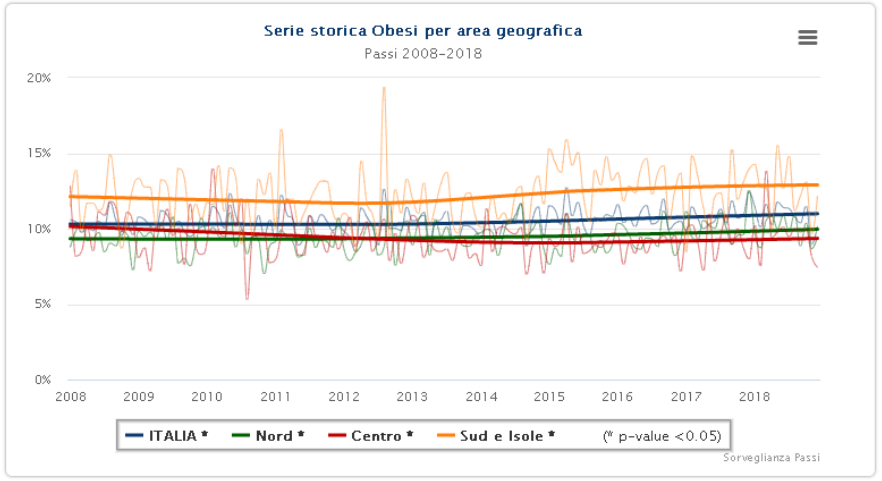
Analisi delle serie storiche

Indicatore: Sovrappeso ▾ ○ Serie storica ◉ Trend annuale



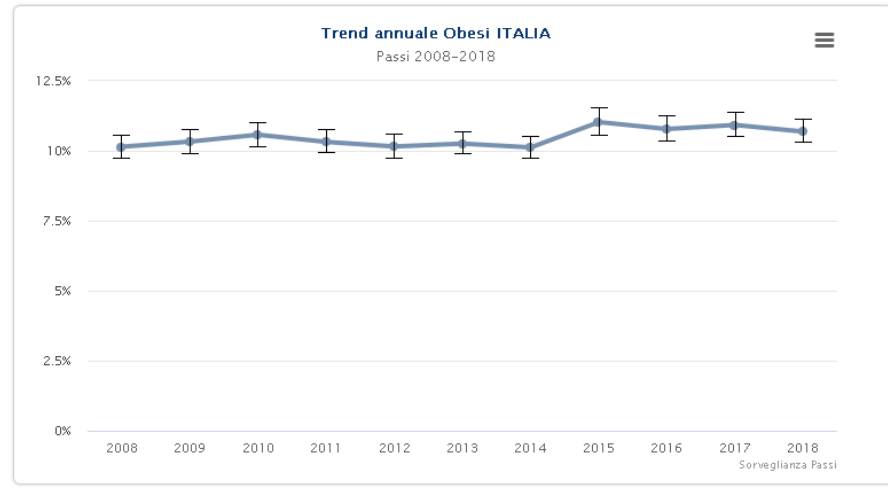
Analisi delle serie storiche

Indicatore: Obesi ▾ ○ Serie storica ○ Trend annuale



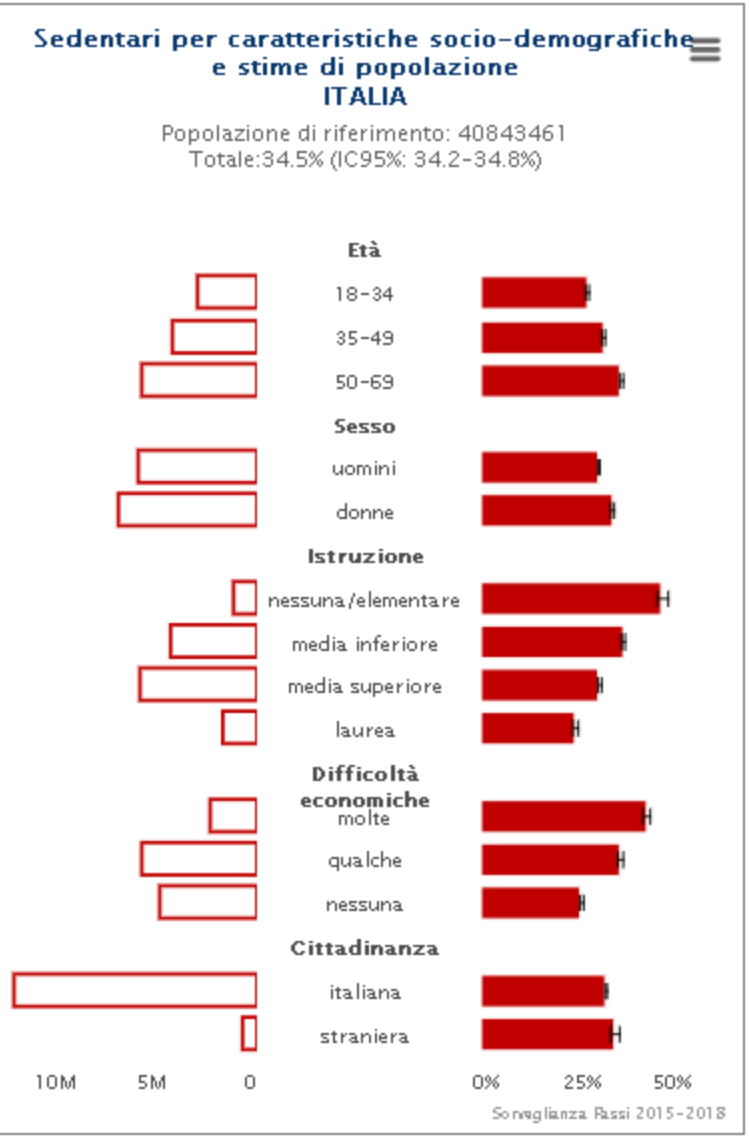
Analisi delle serie storiche

Indicatore: Obesi ▾ ○ Serie storica ◉ Trend annuale



Sedentari

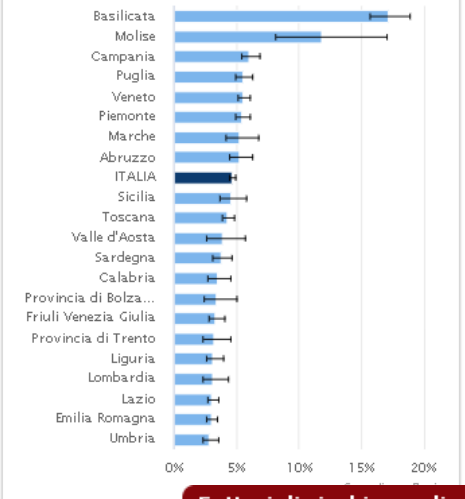
		ITALIA n = 129342		
		%	IC95% inf	IC95% sup
Età	18-34	29.3	28.7	29.9
	35-49	33.8	33.2	34.3
	50-69	38.6	38.1	39.1
Sesso	uomini	32.5	32.1	33.0
	donne	36.4	35.9	36.8
Istruzione	nessuna / elementare	50.2	48.7	51.8
	media inferiore	39.3	38.7	40.0
	media superiore	32.6	32.2	33.1
	laurea	26.0	25.3	26.8
Difficoltà economiche	molte	46.0	45.0	47.0
	qualche	38.6	38.0	39.1
	nessuna	27.7	27.2	28.1
Cittadinanza	italiana	34.4	34.1	34.7
	straniera	37.1	35.7	38.5



Percentuali per Regione

Indicatore: Calcolo rischio cardiovascolare ▾ (●) Dati standardizzati ( ) Dati grezzi

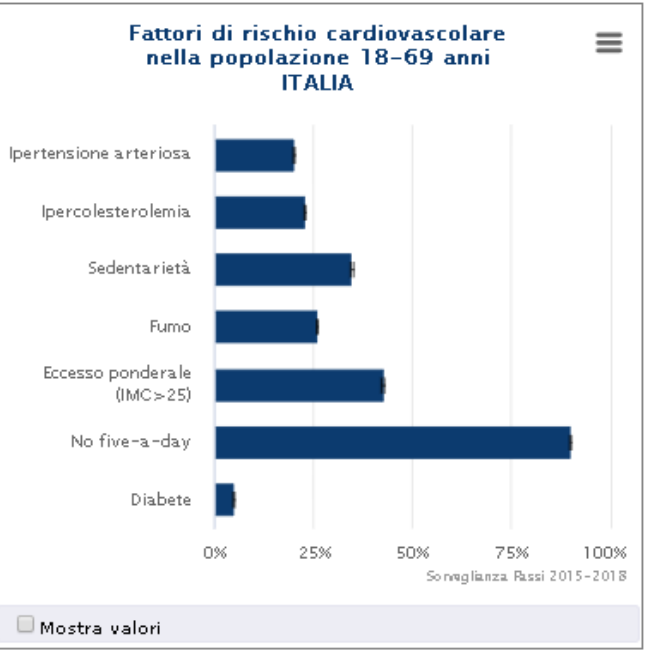
Dati standardizzati



Calcolo rischio cardiovascolare: su tutte le persone =35 anni, senz

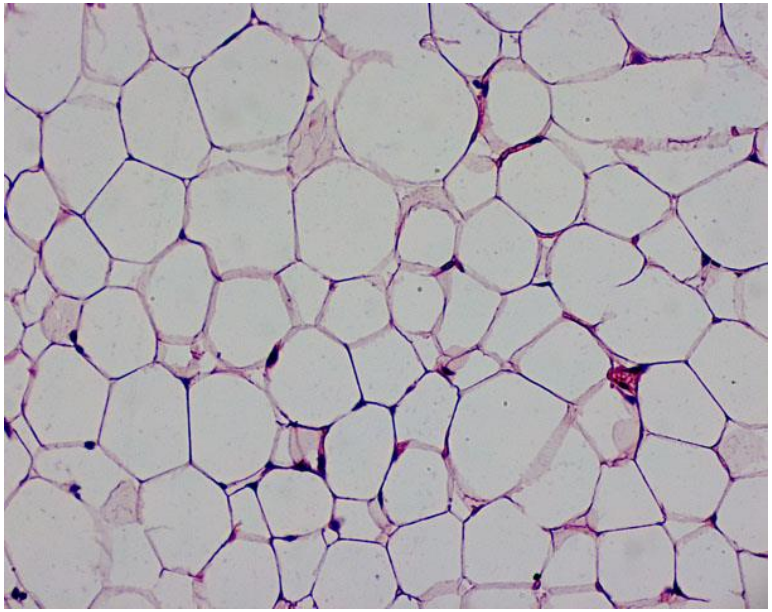
Fattori di rischio cardiovascolare nella popolazione 18-69 anni

	ITALIA		
	%	IC95% inf	IC95% sup
Ipertensione arteriosa	19.9	19.6	20.2
Ipercolesterolemia	22.6	22.3	23.0
Sedentarietà	34.5	34.2	34.8
Fumo	25.7	25.4	26.0
Eccesso ponderale (IMC>25)	42.4	42.1	42.8
Meno di 5 porzioni di frutta e verdura al giorno	90.0	89.8	90.2
Diabete	4.8	4.6	4.9



TESSUTO ADIPOSO E OBESITÀ NEI REUMATISMI INFIAMMATORI

- Risposta infiammatoria sistemica cronica di basso grado
- FRCV e a comorbidità metaboliche



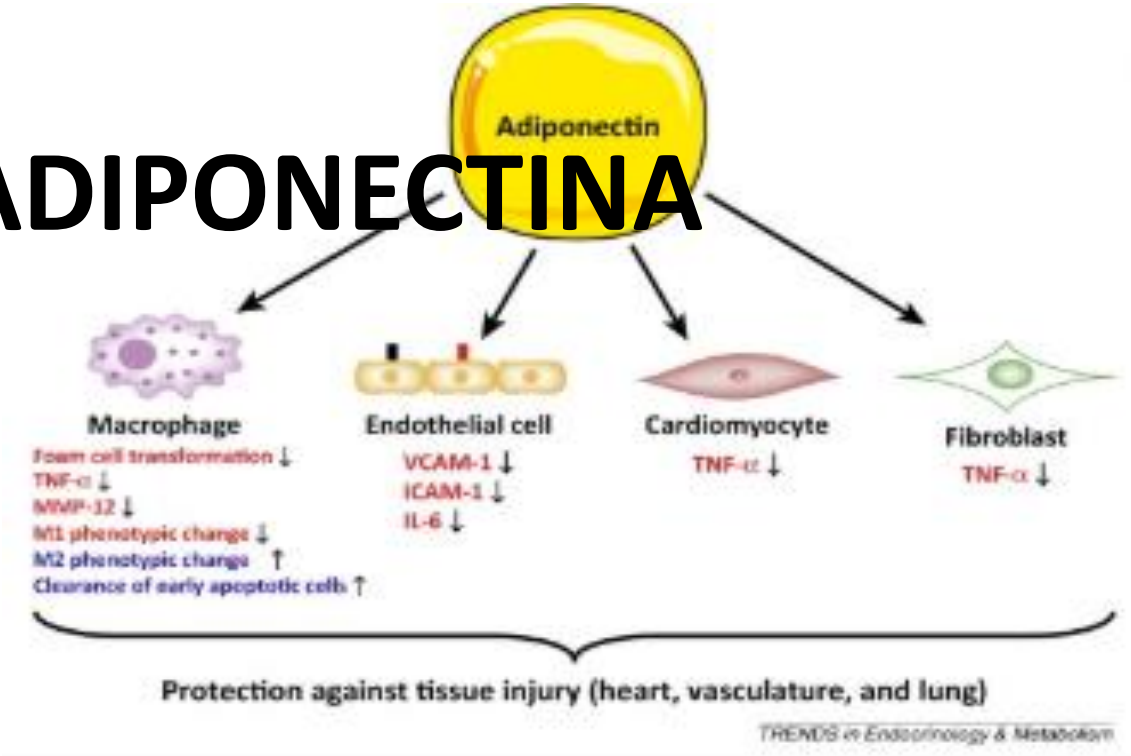
Engin et al. Adv Exp Med Biol. 2017, Lupoli et al.Arthritis Res Ther. 2016

ADIPOCHINE OBESITÀ-CORRELATE

- Funzione regolatoria: insulino-sensibilità, permeabilità vascolare e immunomodulazione
- Tessuto adiposo, leucociti, condrociti e sinoviociti
- ↑adipochine pro-infiammatorie in obesità

Gomez et al. Nat. Rev. Rheumatol. 2011, Kerekes et al. Nat. Rev. Rheumatol. 2014, Fasshauer et al. Trends Pharmacol Sci. 2015

ADIPONECTINA



- Relazione inversa con BMI

- Effetto anti-infiammatorio su endotelio e fagocitosi: inibisce signaling di TNF-α,NF-kB e INF-γ
- Stimola produzione di citochine anti-infiammatorie: IL-10 e IL 1-RA
- Regola insulino-resistenza e protegge da aterosclerosi

Wolf et al. Biochem. Biophys. Res. 2004

ADIPONECTINA

- Effetto pro-infiammatorio in AR (isoforma HMW)
- IL-6, VEGF e MMP-1/13 nei fibroblasti sinoviali, condrociti, cell. endoteliali, linfociti
- Aumentata in liquido sinoviale in AR
- Livelli plasmatici correlano con s-PCR
- Associazione con progressione danno radiografico

Liu et al. Int Immunopharmacol. 2015, Cao et al. Autoimmunity 2016

LEPTINA

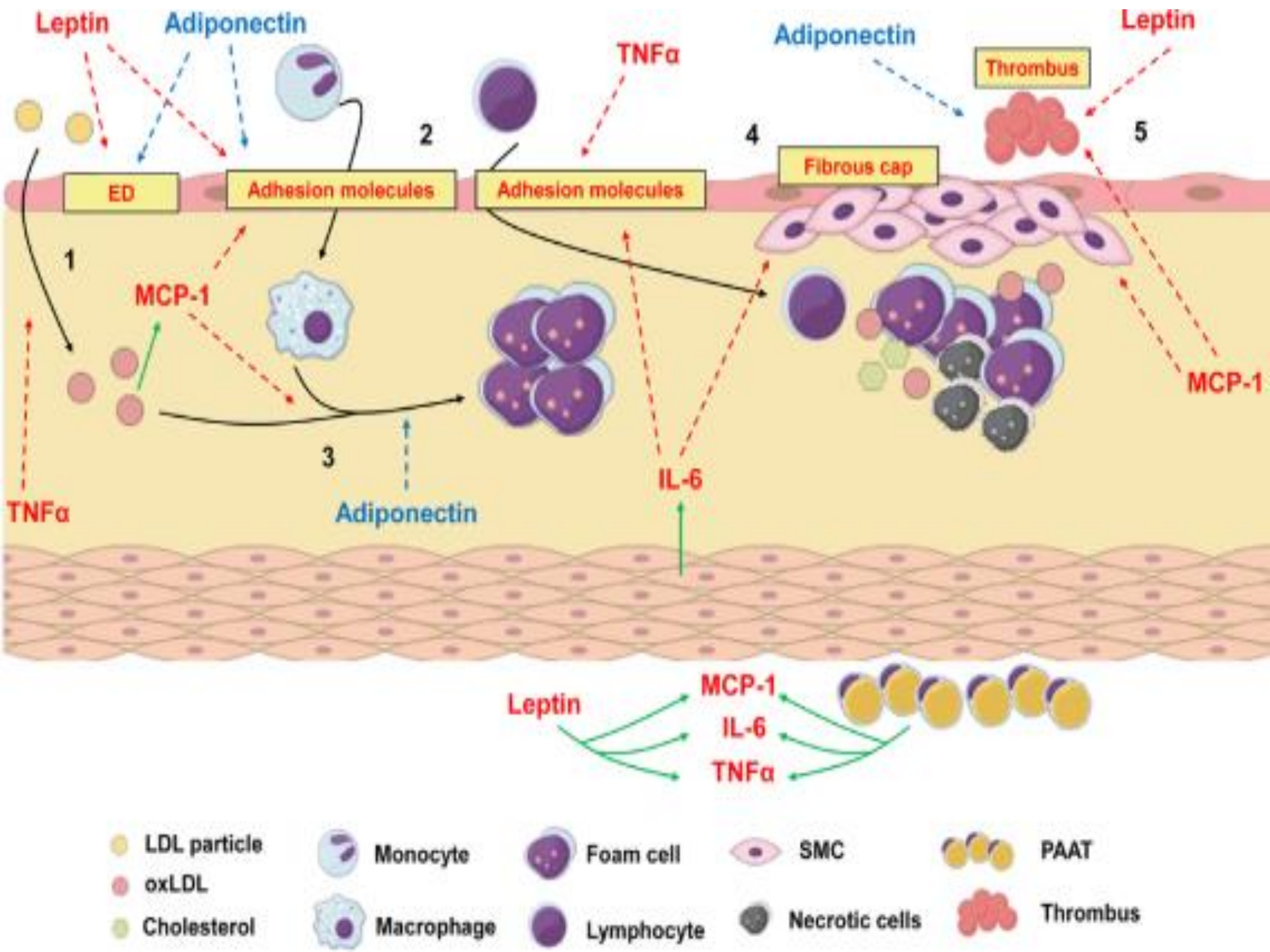
- Controlla appetito e spesa energetica
- Livelli sierici correlano con massa adiposa

- Effetti immunologici: ↑Th1, ↓Th2

  ↑TNF-α, IL-6, IL-12, IL-2RA e recettore della transferrina a livello sinoviale ed endoteliale

- Up-regulation in pazienti con AR erosiva
  Associazione con durata di malattia e DAS-28

Lee et al. Z Rheumatol 2016, Tousirot et al. Life Sci. 2015


Leptin
Adiponectin
TNFα
Adiponectin
Thrombus
Leptin
2
4
5
ED
Adhesion molecules
Adhesion molecules
Fibrous cap
1
MCP-1
MCP-1
3
IL-6
TNFα
Adiponectin
Leptin
MCP-1
IL-6
TNFα
LDL particle
oxLDL
Cholesterol
Monocyte
Macrophage
Foam cell
Lymphocyte
SMC
Necrotic cells
PAAT
Thrombus

RESISTINA

- Tessuto adiposo e macrofagi attivati (IL-1, IL-6, TNF-α, LPS)
- Insulino-resistenza
- Funzione endoteliale (↑ICAM-1)
- Livelli sinoviali ↑ in AR

M^{ac}Donald et al. Int J Mol Sci. 2019, Fatel et al.Adv. Rheumatol 2018

VISFATINA
(Pre B-cell colony enhancing factor)

- Leucociti→Tessuto adiposo viscerale
- Fibroblasti e macrofagi→↑IL-6, IL-8, MMP-1/3 e TNF-α
- Livelli sierici e sinoviali associati con s-FR, attività di malattia e progressione radiografica

Carrión et al. Int J Mol Sci. 2019, Lee YH et al. Int J Rheum Dis. 2018

CHEMERINA

- Adipociti, liquido sinoviale, endotelio sinoviale in AR

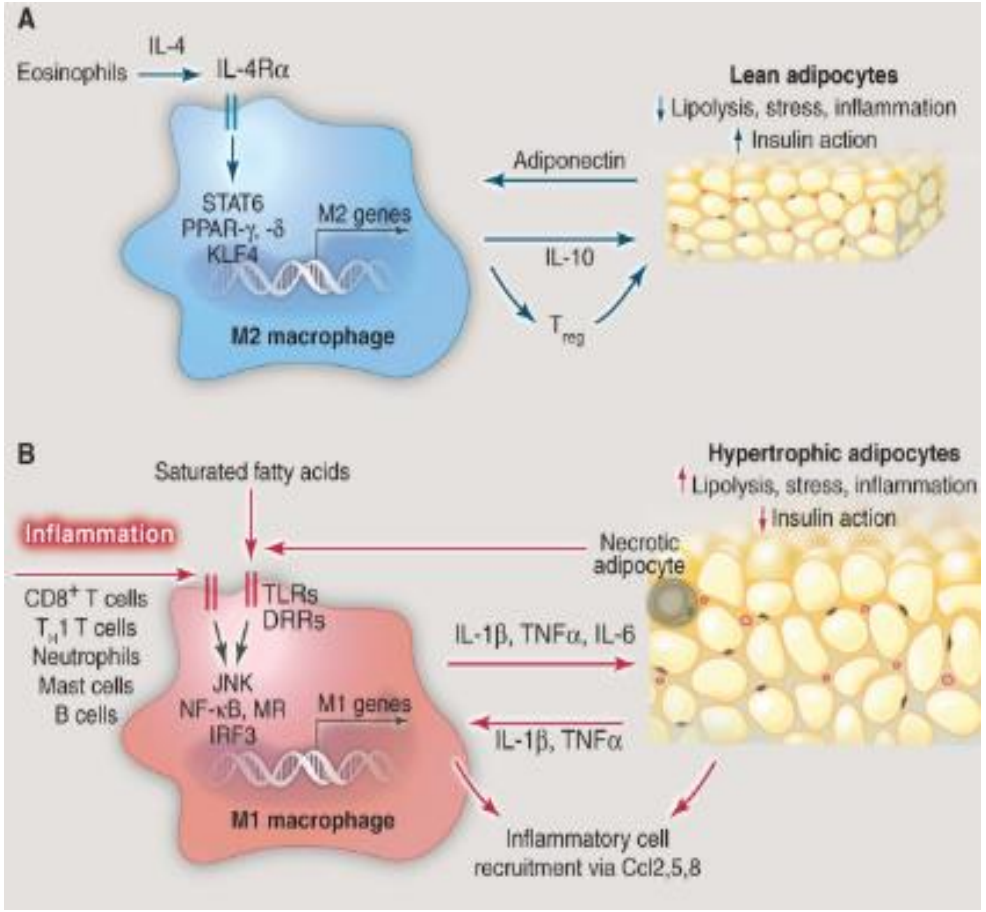
- Attività infiammatoria stimolata da TNF-α e INF-γ→ produzione sinoviale di IL-6, CCL2 e MMP-3

- Marker di attivazione endoteliale, angiogenesi e aterosclerosi in AR

Tolusso et al. Expert Rev Clin Immunol. 2016

PATOGENESI IMMUNO-MEDIATA IN OBESITÀ E REUMATISMI INFIAMMATORI

- Neutrofili: ↑IL-8* articolare in topi early collagen-induced arthritis (CIA) obesi
- Macrofagi: ↑infiltrazione tissutale (M1) in obesità
- Linfociti T: ↑ nel grasso viscerale degli obesi→differenziazione TH-17 patogenica (IL-1, IL-6, IL-23)



Kim et al. Ann. Rheum. Dis. 2016, Lee et al. Arch. Pharm. Res. 2013, Endo et al. Mol. Life Sci. 2017

THE LANCET, October 18, 1873.

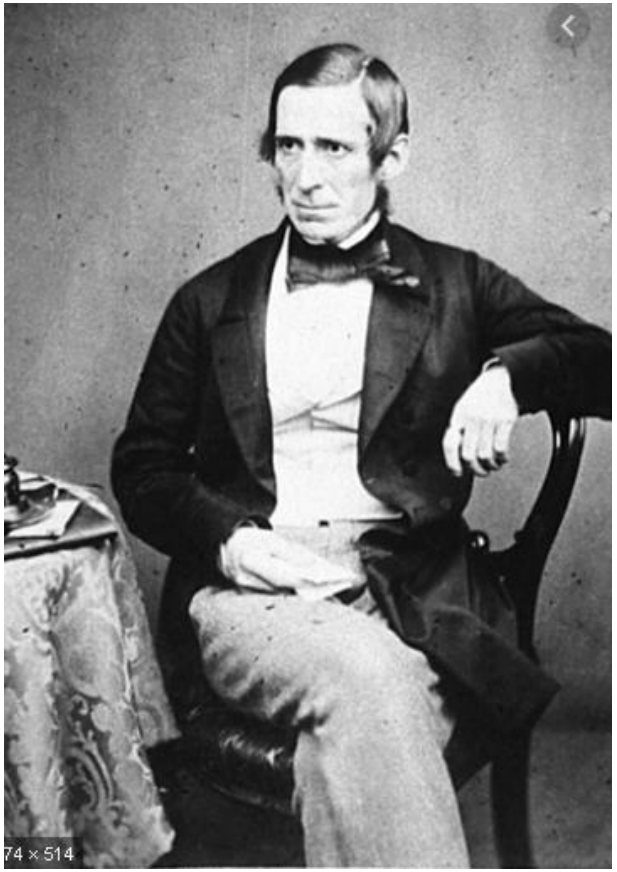
ON THE

NERVOUS MIMICRY OF ORGANIC DISEASES,

Delivered at St. Bartholomew's Hospital,

By Sir JAMES PAGET, Bart., F.R.S.,

CONSULTING SURGEON TO THE HOSPITAL.



Annals of the Rheumatic Diseases 1997;**56**:326–329

Prevalence of low body mass in rheumatoid arthritis: association with the acute phase response

R Munro, H Capell

1/8 sottopeso vs 1/20

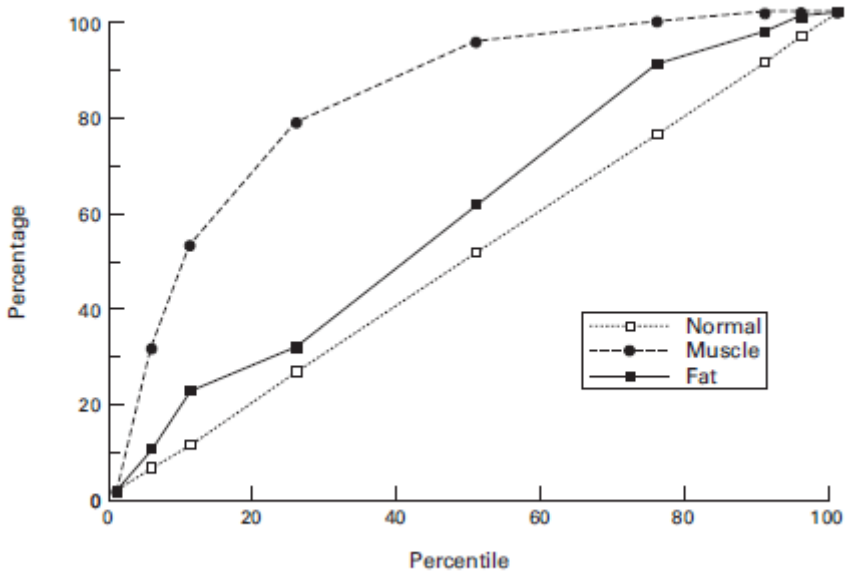


Figure 2 *Arm muscle and fat area percentiles versus normal controls.*

***Results*—13% of the RA group fell into the lowest 5th centile for BMI for the general population. The loss of body mass was greater for lean tissue than fat, with over 50% of the RA group falling into the lowest 10th centile of a reference population for the upper arm muscle area. Female patients who lost greater than 15% of their initial weight had higher health assessment questionnaire (HAQ) results than the rest of the group (p=0.020). In female patients there was a significant correlation between reduced fat free mass and the acute phase response (ESR p=0.016 and CRP p=0.003)**

***Conclusions*—There is an increased prevalence of low body mass, greatest for lean tissue, in the RA population. In the female group there was an inverse relation between the acute phase response and fat free mass. Female patients with RA who lose a significant amount of weight are more disabled as assessed by HAQ.**

J Rheumatol. 1992 Oct;19(10):1505-10.

Rheumatoid cachexia: depletion of lean body mass in rheumatoid arthritis. Possible association with tumor necrosis factor.

Roubenoff R[1], Roubenoff RA, Ward LM, Holland SM, Hellmann DB.

RESULTS: When compared to United States population norms, 16 of the subjects (67%) were cachectic. In regression models, lean body mass (LBM) was inversely associated with the number of swollen joints ($p < 0.025$). Elevated TNF-alpha was found in 3 of 5 flaring patients vs 0 of 18 patients with less active disease ($p = 0.001$). These 3 were all cachectic, while the 2 flaring patients without detectable TNF had normal LBM ($p < 0.03$). Among the whole group, there was a trend toward increasing disability with decreased LBM after adjusting for joint pain and disease duration ($p < 0.07$).

J Clin Invest. 1994 Jun;93(6):2379-86.

Rheumatoid cachexia: cytokine-driven hypermetabolism accompanying reduced body cell mass in chronic inflammation.

Roubenoff R[1], Roubenoff RA, Cannon JG, Kehayias JJ, Zhuang H, Dawson-Hughes B, Dinarello CA, Rosenberg IH.

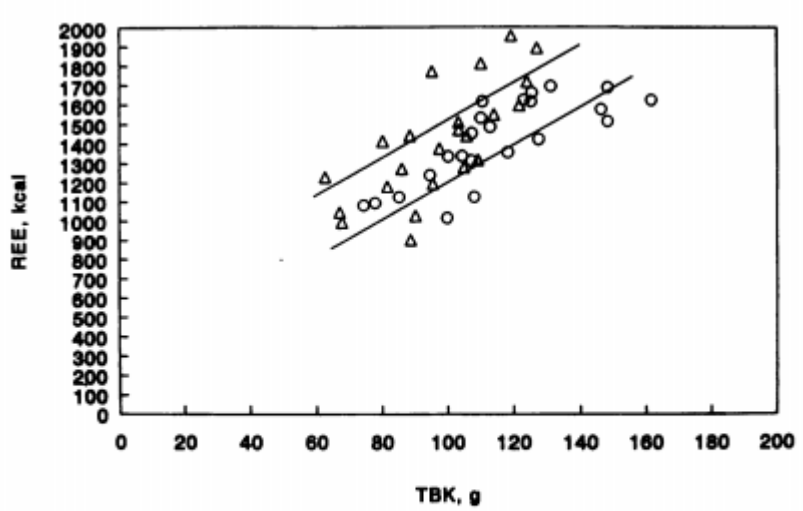


Figure 3. REE (kilocalories per day) vs BCM based on TBK (grams) for subjects with RA (*open triangles*) and controls (*open circles*). Difference between the two groups is significant ($P < 0.008$, analysis of covariance).

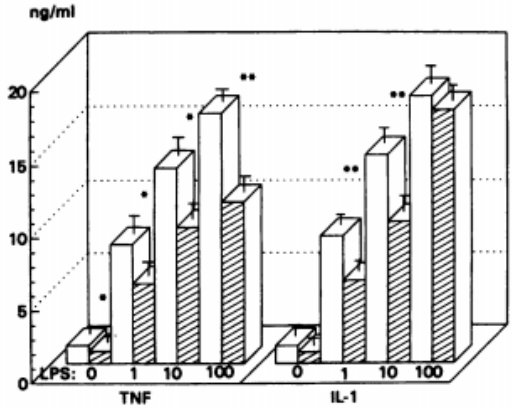


Figure 2. Production of TNF-α (*left*) and IL-1β (*right*) in subjects with RA (*open bars*) and in controls (*hatched bars*) with increasing concentration of LPS (nanograms per milliliter). Significant differences between RA and control cells were seen for TNF at all four levels of stimulation and for IL-1 at 1 and 10 ng LPS only. $*P < 0.05$; $**P < 0.01$.

Joint Bone Spine. 2001 Oct;68(5):403-9.

Nutritional status in patients with rheumatoid arthritis.

Gómez-Vaquero C[1], Nolla JM, Fiter J, Ramon JM, Concustell R, Valverde J, Roig-Escofet D.

Table 1 *Comparison of anthropometric measurements in RA patients and controls*

	RA patients (n=50)			*Controls (n=50)*			
	Mean	*SD*		*Mean*	*SD*		*p value*
Body-mass index (W/H²)*	22·7	3·6	(30%)	25·5	3·3	(4%)	<0·001
Triceps skinfold thickness (mm)							
female	15·7	6·6	(28%)	21·2	6·6	(4%)	<0·01
male	8·9	3·2		12·7	3·3		<0·001
Upper arm muscle circumference (cm)							
female	21·8	3·5	(14%)	22·0	2·0	(4%)	NS
male	23·6	2·7		26·0	2·4		<0·01

*W=weight in kg, H=height in m.
Values in parentheses indicate the percentage of patients with significant deficits. NS=not significant.

Table 2 *Comparison of biochemical indices of nutrition in RA patients and controls*

	RA patients (n=50)			*Controls (n=50)*			
	Mean	*SD*		*Mean*	*SD*		*p value*
Albumin (g/l)	39·3	4·1	(14%)	43·5	3·1	(—)	<0·001
Transferrin (g/l)	2·8	0·5	(18%)	3·3	0·6	(—)	<0·001
Zinc (μmol/l)	12·3	2·3	(8%)	13·5	2·2	(—)	<0·05
Retinol-binding protein (mg/l)	53·7	18·9	(26%)	68·2	13·9	(—)	<0·001
Thyroxine-binding prealbumin (g/l)	0·21	0·09	(24%)	0·27	0·07	(—)	<0·001
Folic acid (μg/l)	3·2	1·5	(20%)	3·8	1·6	(6%)	<0·05

Values in parentheses indicate the percentage of patients with measurements below the laboratory reference range.

Pz in classe funzionale IV

Table 3 *Comparison of age, disease duration, and indices of inflammation in malnourished patients (n=13) and the remaining rheumatoid patients (n=37)*

	RA patients (n=50)				
	Malnourished (n=13)		*Remainder (n=37)*		
	Mean	*SD*	*Mean*	*SD*	*p value*
Age (years)	59·7	10·9	59·4	12·4	NS
Disease duration (years)	9·9	8·7	6·7	7·5	NS
Disease activity					
ESR (mm/h)	63·2	25·1	34·4	16·4	<0·001
CRP (mg/l)	99·3	63·6	40·6	41·2	<0·01
α_1ACT (g/l)	1·96	0·77	1·30	0·73	<0·05

Annals of the Rheumatic Diseases, 1984, **43**, 386–390

Editorial

Rheumatoid cachexia: a complication of rheumatoid arthritis moves into the 21st century

Ronenn Roubenoff[1,2]

Loss of fat-free mass and higher fat mass are each associated with greater disability in RA [7], and low body weight (that is, both fat and fat-free tissue) in patients with RA is associated with threefold higher mortality [8]. Thus, rheumatoid cachexia may be an important contributor to increased morbidity and premature mortality in RA.

For example, the inflammatory cytokines tumor necrosis factor (TNF)-α and IL-1β are centrally involved in the pathogenesis of RA, but, in addition, these cytokines exert a powerful influence on whole-body protein and energy metabolism. Other sarcoactive molecules include IL-6, IFN-γ, transforming growth factor-β1, and MyoD

Harefuah. 2007 May;146(5):349-51, 406.

[Cachexia, malignancy and tumor necrosis factor alpha (TNF-alpha)].

Nussinovitch U[1], Shoenfeld Y.

It is believed that tumor necrosis factor alpha (TNFalpha) plays an essential rule in cachexia induction and propagation.

Blockade of tumour necrosis factor-α in rheumatoid arthritis: effects on components of rheumatoid cachexia

G. S. Metsios[1–3], A. Stavropoulos-Kalinoglou[1,2], K. M. J. Douglas[2], Y. Koutedakis[3], A. M. Nevill[1], V. F. Panoulas[2], M. Kita[2] and G. D. Kitas[1,2]

TABLE 2. Mean ± S.D. and differences in the studied body composition and disease-related variables between the three different times of assessment

	Baseline	Time-1 (2 weeks)	Time-2 (12 weeks)	*P*
Body composition assessment				
Weight (kg)	79.4 ± 15.6	80.4 ± 16.2	78.8 ± 16.6	>0.05
BMI (kg/m^2)	28.3 ± 3.7	28.6 ± 3.8	28.1 ± 4.1	>0.05
Total body fat (%)	38.8 ± 7.5	36.5 ± 6.9	36.0 ± 7.4	>0.05
Truncal fat (%)	35.9 ± 6.7	37.4 ± 6.3*	36.7 ± 6.4	0.036
FFM (kg)	50.9 ± 12.7	50.5 ± 12.4	51.1 ± 12.5	>0.05
RA-related assessments				
CRP (mg/l)	33.7 ± 34.4	17.7 ± 11.9	15.3 ± 18.9	>0.05
ESR (mm/1st h)	41.7 ± 25.6	22.1 ± 16.9**	18.3 ± 15.4**	0.002
HAQ	1.83 ± 0.3	1.54 ± 0.3**	1.41 ± 0.4**	<0.001
DAS28	5.66 ± 0.7	4.64 ± 0.6**	3.59 ± 0.7**	<0.001
TNF-α (pg/ml)	38.1 ± 41.1	22.2 ± 26.8	8.9 ± 10.2*	0.024

P = level of significance between times of assessment using repeated-measures ANOVA. Difference from baseline assessment: **$P < 0.001$ and *$P < 0.05$.

Dopo 12 settimane di terapia anti-TNF nessun cambiamento significativo nel RRE (dispendio energetico a riposo) o nella FFM (massa muscolare magra).

Rheumatology 2007;46:1824–1827

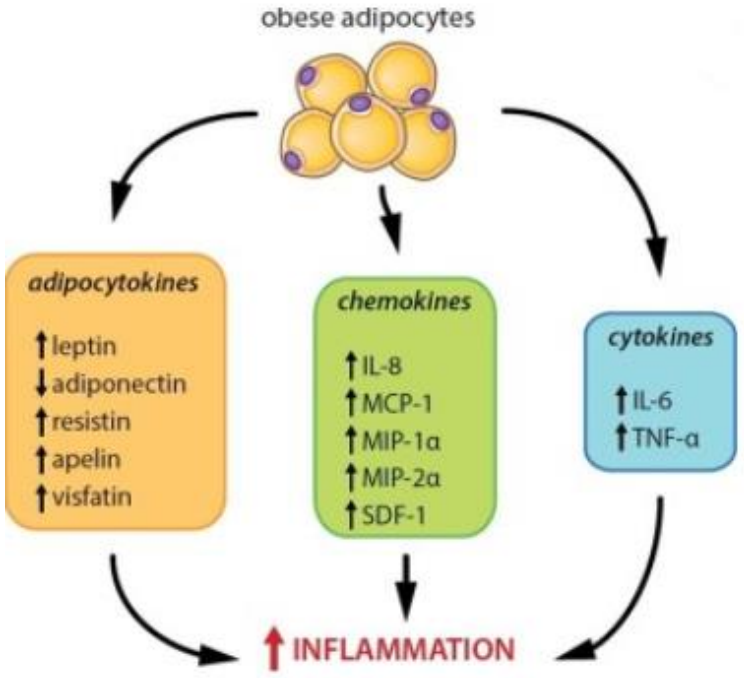
Autoimmun Rev. 2014 Sep;13(9):981-1000. doi: 10.1016/j.autrev.2014.07.001. Epub 2014 Aug 2.

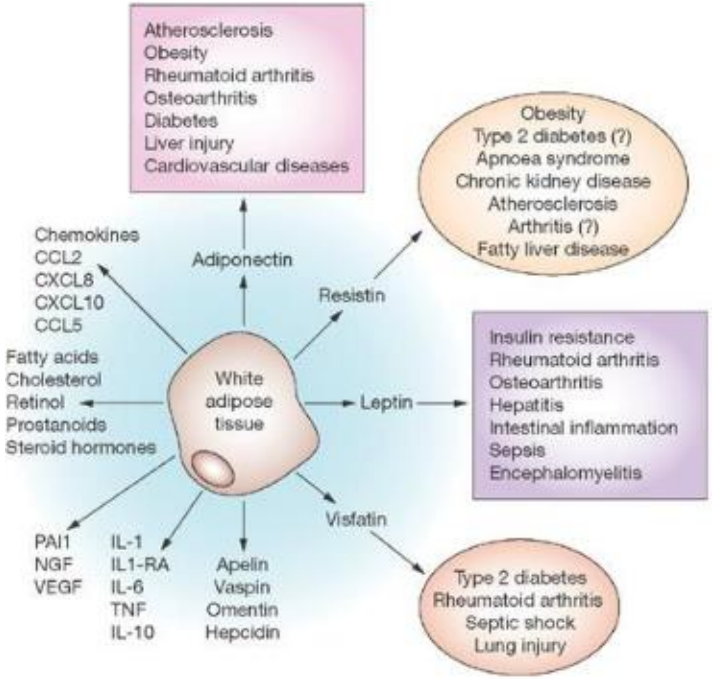
Obesity in autoimmune diseases: not a passive bystander.

Versini M[1], Jeandel PY[2], Rosenthal E[2], Shoenfeld Y[3].

relationship between obesity, adipokines - namely leptin, adiponectin, resistin, visfatin - and various immune-mediated conditions, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), multiple sclerosis (MS), type-1 diabetes (T1D), psoriasis and psoriatic arthritis (PsA), and thyroid autoimmunity (TAI), especially Hashimoto thyroiditis (HT). The strongest levels of evidence support an increased risk of RA (OR=1.2-3.4), MS (OR=2), psoriasis and PsA (OR=1.48-6.46) in obese subjects. A higher risk of IBD, T1D and TAI is also suggested.

Moreover, obesity worsens the course of RA, SLE, IBD, psoriasis and PsA, and impairs the treatment response of RA, IBD, psoriasis and PsA. Extensive clinical data and experimental models demonstrate the involvement of adipokines in the pathogenesis of these autoimmune diseases. Obesity appears to be a major environmental factor contributing to the onset and progression of autoimmune diseases.





Obesity in RA was found prevalent in 18–31% of patients, overall slightly higher than in the general population. An overweight condition has been noted in more than 60% of RA patients (74, 75).

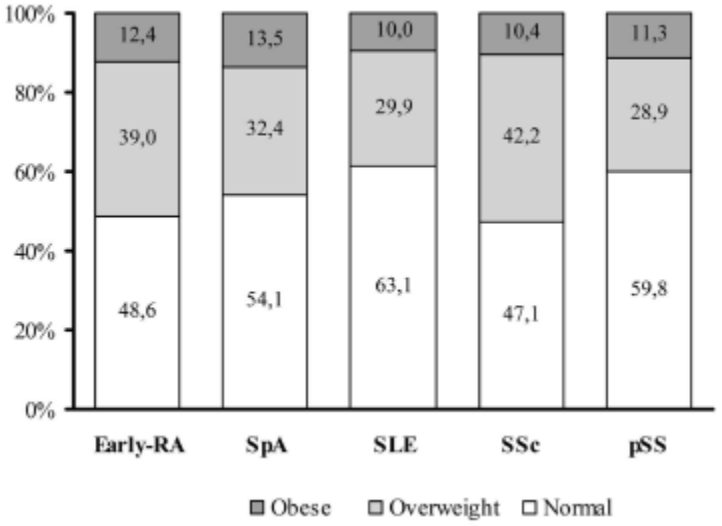


FIGURE 1 | Distribution of BMI categories among an Italian cohort of adult autoimmune disease patients. In our tertiary referral centre, the prevalence of overweight [defined according to the WHO International standards as a body mass index (BMI) of 25–29.9] or obesity (BMI ≥30) is similar between the different autoimmune disease categories. The graph summarized data from an early-rheumatoid arthritis (early-RA) cohort of patients ($N = 401$, 76.3% female, mean age: 54.6 ± 14.0 years, mean BMI of 25.3 ± 4.4 Kg/m^2), a Spondyloarthritis (SpA) cohort ($N = 220$, 30.6% female, mean age: 39.5 ± 11.8 years, mean BMI of 25.1 ± 4.4 Kg/m^2), a Systemic Lupus Erythematosus (SLE) cohort (506 patients, 90.3% female, mean age: 44.1 ± 14.8 years, mean BMI of 24.0 ± 4.6 Kg/m^2), a Systemic Sclerosis (SSc) cohort (442 patients, 88.2% female, mean age: 58.5 ± 14.2 years, mean BMI of 24.4 ± 4.8 Kg/m^2), and a primary Sjogren Syndrome (pSS) cohort (204 patients, 96.1% female, mean age: 56.4 ± 14.3 years, mean BMI of 24.3 ± 4.3 Kg/m^2) (10). Data are reported as percentage (%) of normal weight, overweight, and obesity in the different diseases.

Gremese et al. Front Immunol. 2014; 5: 576.

Body mass index distribution in rheumatoid arthritis: a collaborative analysis from three large German rheumatoid arthritis databases

i pz AR erano significativamente più obesi dei controlli

Table 2 Distribution of the body mass index (BMI) by sex and age groups (%)

Cohort	BMI (kg/m^2)	Females				Males			
		40– < 55	55– < 70	≥70	Total	40– < 55	55– < 70	≥70	Total
CAPEA	<18.5	1.0	1.0	2.9	1.4	0.9	0.8	0	0.6
	18.5 to <25	40.4	34.2	33.1	36.3	35.7	24.8	32.0	30.6
	25 to <30	32.7	34.6	42.5	35.8	43.8	52.0	45.0	47.2
	≥30	26.0	30.2	21.6	26.5	19.6	22.4	23.0	21.7
RABBIT	<18.5	2.6	1.7	2.0	2.1	0.5	0.7	0.5	0.6
	18.5 to <25	43.2	37.2	38.2	39.6	30.0	27.2	33.9	29.3
	25 to <30	29.8	35.3	36.8	33.6	45.5	46.7	49.9	46.8
	≥30	24.4	25.8	23	24.8	24	25.3	15.8	23.3
NDB	<18.5	2.0	1.2	2.4	1.8	1.0	0.3	0.7	0.6
	18.5 to <25	48.9	40.6	40.8	42.8	35.4	25.4	34.8	31.3
	25 to <30	26.0	34.3	36.5	33.0	43.9	49.8	48.4	47.8
	≥30	23.1	23.9	20.3	22.4	19.7	24.4	16.0	20.2
DEAS	<18.5	1.1	1.4	1.2	1.2	0.3	0.1	0.5	0.3
	18.5 to <25	54.9	43.4	36.7	45.7	34.4	26.9	28.6	29.8
	25 to <30	29.9	36.8	39.9	35.2	49.4	51.9	52.8	51.4
	≥30	14.1	18.4	22.2	17.9	15.9	21.1	18.2	18.5

Albrecht *et al. Arthritis Research & Therapy* (2016) 18:149
DOI 10.1186/s13075-016-1043-9

BMI & RA

- in presenza di fattori di rischio le donne obese hanno una più elevata probabilità di sviluppare AR

- in particolare se BMI>30 e sieronegative per ACPA

- nel gruppo obeso vi era minore probabilità di raggiungere una remissione, il mantenimento della remissione indipendentemente dall'uso di DMARDs, steroidi e bDMARDs

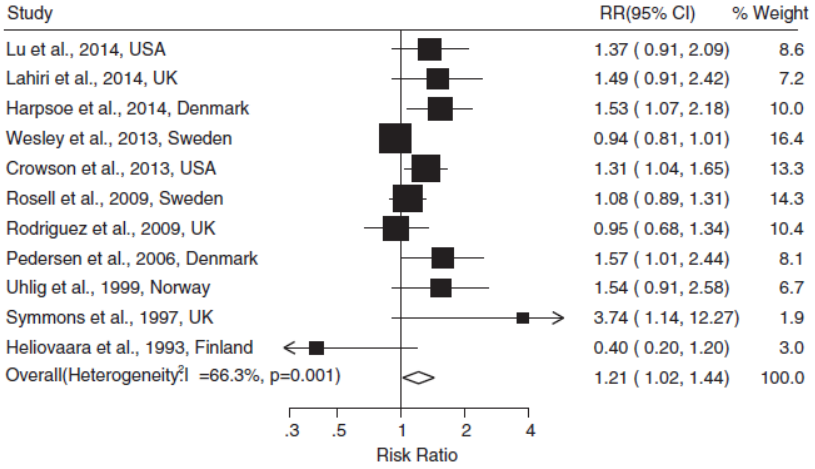


FIGURE 2. Adjusted relative risks of rheumatoid arthritis for obesity compared to normal weight.

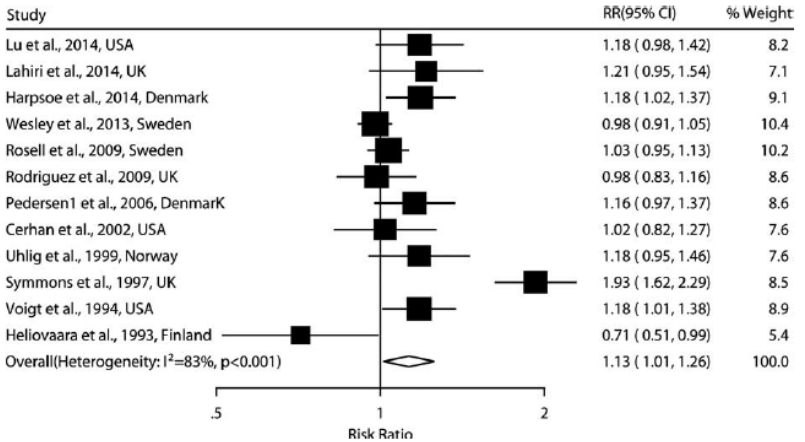


FIGURE 4. Adjusted relative risks of rheumatoid arthritis for every 5 kg/m² increase in body mass index.

BioMed Research International
Volume 2019, Article ID 3579081, 12 pages
https://doi.org/10.1155/2019/3579081

Association Between Body Mass Index and Anti–Citrullinated Protein Antibody–Positive and Anti–Citrullinated Protein Antibody–Negative Rheumatoid Arthritis: Results From a Population-Based Case–Control Study

Arthritis Care & Research
Vol. 65, No. 1, January 2013, pp 107–112
DOI 10.1002/acr.21749

- l'obesità è associata allo sviluppo di AR ACPA-negativa nelle donne
- associazione inversa tra BMI e AR ACPA-positiva negli uomini.

Table 2. ORs of developing RA when comparing overweight and obese to normal weight according to the World Health Organization classification, stratified by ACPA status and sex*

	No. of exposed cases/controls	OR (95% CI)†	OR (95% CI)‡
All			
ACPA positive			
BMI <25 kg/m²	979/1,815	1.0 (–)	1.0 (–)
BMI ≥25 to <30 kg/m²	572/1,183	0.9 (0.8–1.1)	0.9 (0.7–1.0)
BMI ≥30 kg/m²	216/446	0.9 (0.7–1.1)	0.8 (0.7–1.0)
ACPA negative			
BMI <25 kg/m²	475/1,815	1.0 (–)	1.0 (–)
BMI ≥25 to <30 kg/m²	351/1,183	1.1 (0.9–1.3)	1.1 (0.9–1.3)
BMI ≥30 kg/m²	161/446	1.5 (1.1–1.9)	1.4 (1.1–1.9)
Women			
ACPA-positive RA			
BMI <25 kg/m²	744/1,455	1.0 (–)	1.0 (–)
BMI ≥25 to <30 kg/m²	355/708	1.0 (0.9–1.2)	1.0 (0.8–1.2)
BMI ≥30 kg/m²	159/305	1.0 (0.8–1.3)	1.0 (0.8–1.2)
ACPA-negative RA			
BMI <25 kg/m²	379/1,455	1.0 (–)	1.0 (–)
BMI ≥25 to <30 kg/m²	208/708	1.1 (0.9–1.4)	1.1 (0.7–1.6)
BMI ≥30 kg/m²	117/305	1.6 (1.2–2.2)	1.6 (1.2–2.2)
Men			
ACPA-positive RA			
BMI <25 kg/m²	229/360	1.0	
BMI ≥25 to <30 kg/m²	217/475	0.8 (0.6–1.0)	1.1 (0.7–1.8)
BMI ≥30 kg/m²	57/141	0.7 (0.5–1.0)	0.6 (0.3–0.9)
ACPA-negative RA			
BMI <25 kg/m²	96/360	1.0 (–)	1.0 (–)
BMI ≥25 to <30 kg/m²	143/475	1.0 (0.7–1.5)	1.0 (0.7–1.4)
BMI ≥30 kg/m²	44/141	1.2 (0.7–1.9)	1.1 (0.6–1.8)

* OR = odds ratio; RA = rheumatoid arthritis; ACPA = anti–citrullinated protein antibody; 95% CI = 95% confidence interval; BMI = body mass index.
† Logistic regression model conditional on applicable sex, age, and area of residence.
‡ Logistic regression model conditional on applicable sex, age, and area of residence and adjusted for smoking (ever/never), alcohol consumption (ever/never during the past 12 months), and education (university education; yes/no).

High Body Mass Index Negatively Impacts Time to Achieving Sustained Remission in Early Rheumatoid Arthritis: Results from a Multicenter Early Arthritis Cohort Study

Arthritis Rheumatol. 2015; 67 (suppl 10).

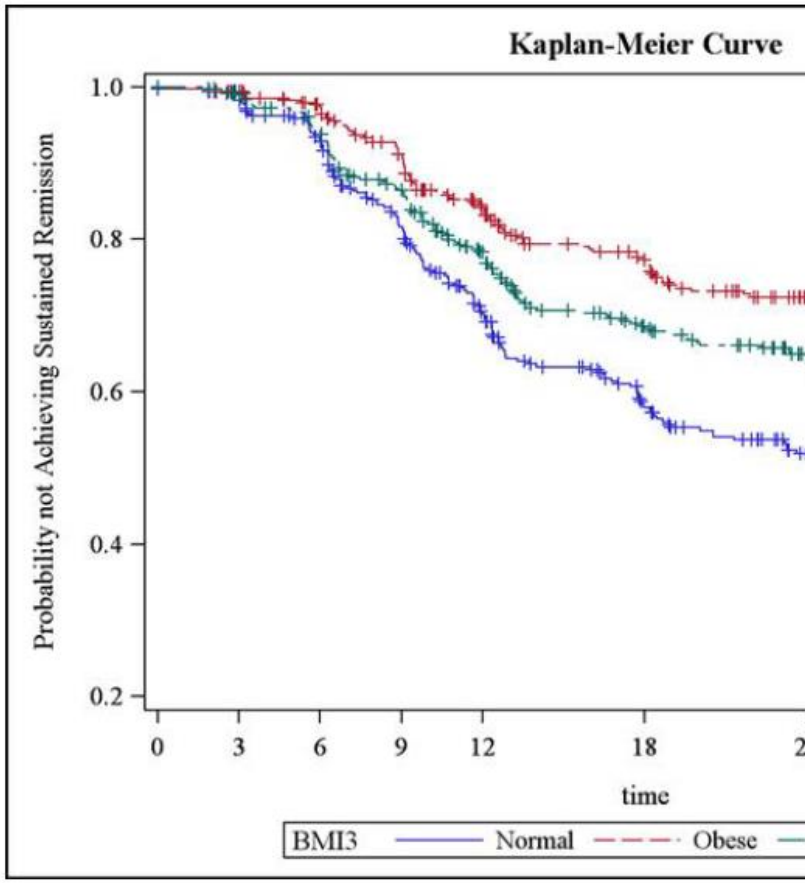


TABLE 1: Multivariate Analysis about the Relationship between Time to Sustained Remission and the Variables of Interest using Cox Regression*

	Hazard ratio Estimate			
Parameter	Point Estimate	95% Confidence Interval		p-value
BMI Overweight vs Normal	0.75	0.59	0.97	**0.03**
BMI Obese vs Normal	0.63	0.48	0.82	**0.0008**
HAQ-DI	0.81	0.65	1.01	0.06
Pain (0-10)	0.99	0.94	1.04	0.74
DAS28<3.2 by 6 months (Yes vs No)	4.21	3.33	5.32	**<0.0001**
Age	1.00	0.99	1.00	0.22
Gender (Female vs Male)	0.80	0.63	1.00	0.07
Ethnicity (Non-Caucasian vs Caucasian)	0.72	0.51	1.02	0.06
Education >high school	1.61	1.00	2.58	**0.05**
Never/Ex smoker	1.35	0.99	1.84	0.06
Symptom Duration	1.00	1.00	1.00	0.88
CRP	1.01	1.00	1.01	0.14
Number of co-morbidities	0.91	0.09	0.98	**0.007**
MTX 1st 3 months	1.40	1.05	1.87	**0.02**
Steroids 1st 3 months	0.76	0.61	0.95	**0.01**

Ann Rheum Dis. 2008 Jun;67(6):769-74. Epub 2007 Oct 26.

A high body mass index has a protective effect on the amount of joint destruction in small joints in early rheumatoid arthritis.

van der Helm-van Mil AH[1], van der Kooij SM, Allaart CF, Toes RE, Huizinga TW.

RESULTS: Obesity did not influence the likelihood of developing RA. In both RA cohorts, the BMI was inversely correlated with the Sharp-van der Heijde score after 3 years' follow-up ($r = -0.15$, $p = 0.025$ for the Leiden EAC and $r = -0.27$, $p<0.001$ for the replication cohort). Linear regression analyses in both cohorts showed that the BMI was independently and inversely associated with the level of joint destruction in anti-CCP-positive patients with RA, but not in anti-CCP-negative patients.

The Association of Body Mass Index (BMI) and Radiographic Progression of Joint Disease in Rheumatoid Arthritis (RA)

Association of BMI and radiologic progression of joint disease in RA		
Multivariate Logistic Regression Model*	Odds Ratios	Confidence Intervals
BMI (underweight vs. Obese)	**4.85**	**1.34-17.53****
BMI (Normal vs. Obese)	**3.99**	**1.76-9.05**
BMI (Overweight vs. Obese)	1.65	0.68-4.02
DAS28-CRP4 (continuous)	**1.28**	**1.08-1.51**
Anti-CCP Positive	1.85	0.96-3.57
*adjusted for age and gender **test for trend of BMI group and radiologic progression p=0.0006		

Pz sottopeso e normo peso ↑ probabilità di progressione radiografica

Examining the Obesity Paradox in Patients With Rheumatoid Arthritis

Linda Peckel

Having a high BMI [body mass index] may increase the likelihood of developing RA in those who are genetically susceptible, and decrease the likelihood of achieving sustained remission for those with active RA

At the same time, however, patients with obesity also have a lower risk for mortality from RA than patients of normal weight. In what is widely known as the "obesity paradox," patients with RA with a BMI >30 kg/m^2 live longer than patients with BMI <30 kg/m^2.[1,2]

this paradox may be due to *rheumatoid cachexia*, whereby the ratio of fat to lean body mass is altered by RA disease activity.

there is a clear effect on damage mediated through impact and weight that can accelerate joint damage

Weight Loss, the Obesity Paradox, and the Risk of Death in Rheumatoid Arthritis

After multivariable adjustment, low BMI (<20 kg/m^2) was associated with an increased risk of death over the subsequent followup period (Table 2). A modest weight loss (>1 kg/m^2 of BMI) over the preceding observation period was associated with an increased risk of death before and after adjustment for multiple potential confounders (HR 1.99, 95% CI 1.53–2.59, P<0.001) (model 1) (Table 2).

Rate of change in BMI over the previous interval and risk of subsequent death *

Rate of change in BMI (no. of observations)	Risk of death	*P*
No weight loss (8,000)	1 (reference)	
0–<2 kg/m^2 loss/year (6,541)	1.12 (0.85–1.49)	0.4
2–3 kg/m^2 loss/year (1,067)	1.65 (1.09–2.50)	0.02
>3 kg/m^2 loss/year (1,421)	2.49 (1.73–3.57)	<0.001

Figure 1.
Lowess curve illustrating the mean body mass index and 95% confidence interval prior to the date of death in patients who died compared with those who survived to the date when the database was queried.

Arthritis Rheumatol. 2015 July ; 67(7): 1711–1717. doi:10.1002/art.39136.

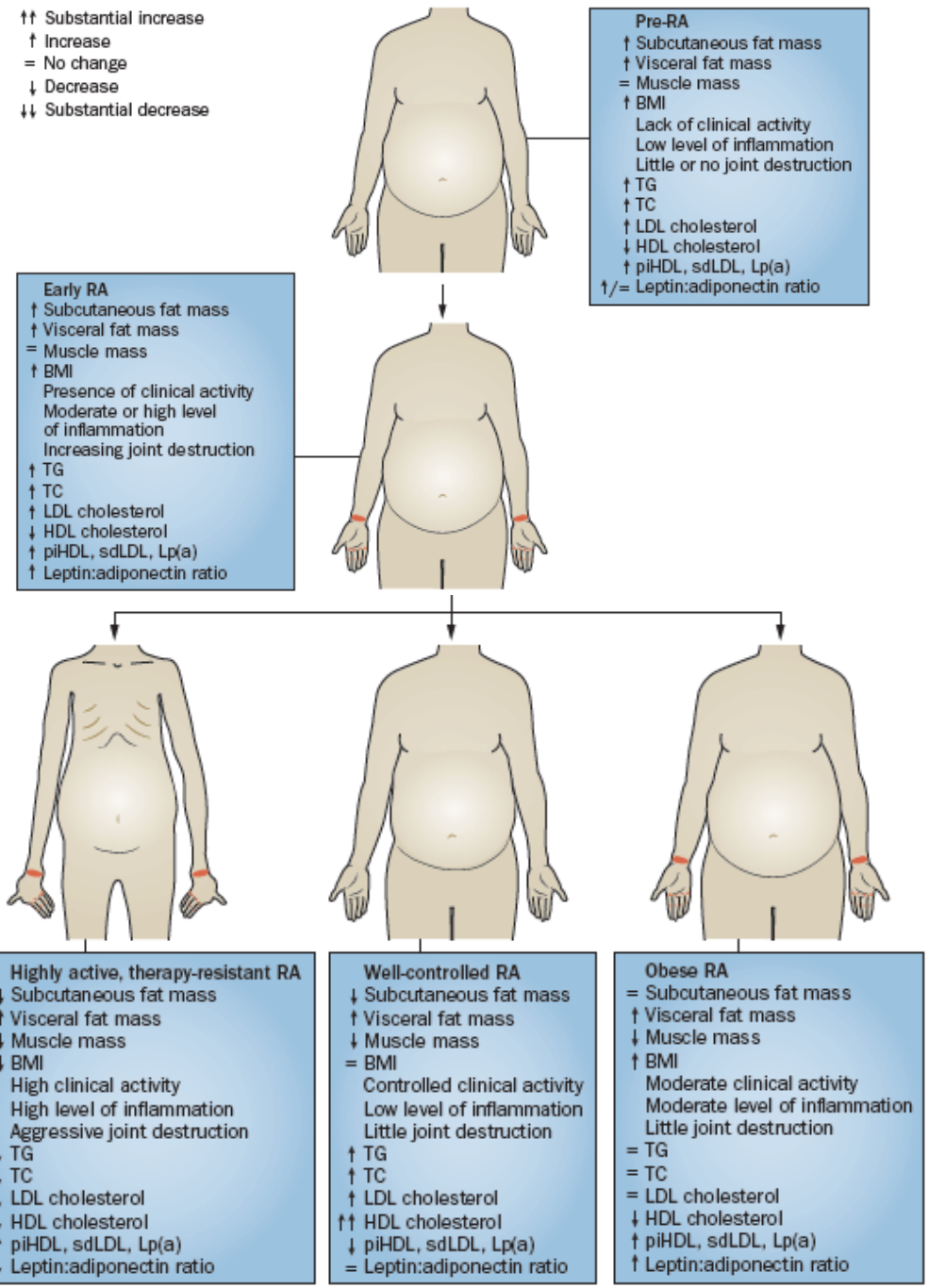
Rheumatoid arthritis and metabolic syndrome

- pre-AR: obesità lieve, ↑ della massa grassa sottocutanea e viscerale, profili lipidici e adipokine proaterogenici

- early AR: ↑ rapporto leptina: adiponectina

- AR consolidata: i pz con malattia altamente attiva hanno profili di massa corporea, lipidi e adipokine che contrastano con quelli dei pazienti con RA ben controllata. L'infiammazione attiva è associata alla cachessia reumatoide.

- L'obesità in AR è caratterizzata da aumento della massa grassa viscerale ma dalla normale massa adiposa sottocutanea



Kerekes, G. *et al. Nat. Rev. Rheumatol.* **10**, 691–696 (2014); published online 5 August 2014;

ALTERAZIONI QUANTITATIVE

- AR preclinica e early: profilo tipico della sindrome metabolica (Col tot =/↑; LDL e TGD ↑, HDL ↓)
- AR consolidata: ↓ grasso bianco s.c., ↑ grasso viscerale
- AR attiva: ↓ LDL e colest tot

ALTERAZIONI QUALITATIVE

- Modifiche fenotipiche LDL → Lipoteina (a), una particella LDL legata all'apolipoproteina A, è un fattore di rischio moderato indipendente per CVD (più sensibili a stress ox) che risulta ↑ ↑ nei pz AR.
- Alterata distribuzione delle subfrazioni HDL con ↑HDL2 da iper TGD e ↓HDL3 a aumentata clearance; pro-infiammatorie
- Alterazioni della funzione HDL: difesa dell'ospite vs funzione metabolica
- ↓ potere anti-ox

Kerekes, G. *et al. Nat. Rev. Rheumatol.* **10**, 691–696 (2014); published online 5 August 2014;

Table 1 | Independent effects of various RA-related factors on lipid levels

Factor	Cholesterol			Triglycerides	References
	Total	LDL	HDL		
Patient-related					
Obesity and/or metabolic syndrome	↑	↑	↓	↑	6,8,11,15,18,20
Sedentary lifestyle	↑	↑	↓	↑	6,8,18
Ageing	↓	↓	↑	↓	8
Smoking	=	=	↓	=	8
Disease-related					
Acute high-grade inflammation	↓ or =	↓ or =	↓	↑	1,6,8,23,51
Chronic high-grade inflammation	↓	↓	↓	↓	6,8,23,51
Rheumatoid cachexia	↓	↓	↓	⇊	6,11,12,15,16
Treatment-related					
High-dose, long-term corticosteroids	↑	↑	↓	↑	6,8
Low-dose corticosteroids	=	=	↑	=	6,8
Methotrexate	↑ or =	↑ or =	↑	=	8,29,49
Sulphasalazine	↑	=	↑	=	8,29,49
Hydroxychloroquine	↓ or =	↓ or =	↑ or =	↓ or =	8,49
Biologic therapies	↑	↑	↑	↑	6,8,10,39,45,46,48,50

Abbreviations: =, no change; ↑, increase; ↓, decrease; ⇊ substantial decrease; RA, rheumatoid arthritis.

Kerekes, G. *et al. Nat. Rev. Rheumatol.* **10**, 691–696 (2014); published online 5 August 2014;

EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis

Table 1 The 10 recommendations for cardiovascular (CV) risk management in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS)

	Recommendations	Level of evidence	Strength of recommendation
1.	RA should be regarded as a condition associated with higher risk for CV disease. This may also apply to AS and PsA, although the evidence base is less. The increased risk appears to be due to both an increased prevalence of traditional risk factors and the inflammatory burden	2b–3	B
2.	Adequate control of disease activity is necessary to lower the CV risk	2b–3	B
3.	CV risk assessment using national guidelines is recommended for all patients with RA and should be considered annually for all patients with AS and PsA. Risk assessments should be repeated when antirheumatic treatment has been changed	3–4	C
4.	Risk score models should be adapted for patients with RA by introducing a 1.5 multiplication factor. This multiplication factor should be used when the patient with RA meets two of the following three criteria: – Disease duration of more than 10 years – RF or anti-CCP positivity – Presence of certain extra-articular manifestations	3–4	C
5.	TC/HDL cholesterol ratio should be used when the SCORE model is used	3	C
6.	Intervention should be carried out according to national guidelines	3	C
7.	Statins, ACE inhibitors and/or AT-II blockers are preferred treatment options	2a–3	C-D
8.	The role of coxibs and most NSAIDs in CV risk is not well established and needs further investigation. Hence, we should be very cautious about prescribing them, especially for patients with a documented CV disease or in the presence of CV risk factors	2a–3	C
9.	Corticosteroids: use the lowest dose possible	3	C
10.	Recommend smoking cessation	3	C

ACE, angiotensin-converting enzyme; anti-CCP, anti-cyclic citrullinated peptide; AT-II, angiotensin II; coxibs, cyclo-oxygenase-2 inhibitors; HDL, high-density lipoprotein; NSAIDs, non-steroidal anti-inflammatory drugs; RF, rheumatoid factor; SCORE, Systematic Coronary Risk Evaluation; TC, total cholesterol.

Ann Rheum Dis 2010;**69**:325–331. doi:10.1136/ard.2009.113696

METABOLIC EFFECT OF RA THERAPY: rheumatoid cachexia and obesity

Rheumatoid cachexia can persist in patients receiving biologic therapy even after the improvement of arthritis symptoms. In a study of 20 patients with RA and 12 healthy individuals, anti-TNF therapy in the RA group resulted in an improvement of physical activity and protein intake but not in energy expenditure or lean body mass.[44] Further prospective studies in this field are needed.

Treatment with anti-TNF agents and other biologic therapies may result in elevations of lipid subfractions

Indeed, some investigators reported that although short-term anti-TNF treatment increased lipid fractions (including total cholesterol, triglycerides, LDL cholesterol and HDL cholesterol levels), the atherogenic index—defined as the total cholesterol:HDL cholesterol ratio—remained unchanged.[23,45]

Particularly pronounced increases in circulating lipid levels have been associated with the anti-IL-6R antibody tocilizumab and the Janus kinase inhibitor tofacitinib.[23,47] However, according to the lipid paradox, the elevations in lipid levels observed during treatment with these agents, as well as with anti-TNF biologic therapies, might reflect their potent suppressive effects on CRP.[7,8,23]

ApoB:ApoA1 ratio, a biomarker used for CVD risk stratification, remained unchanged in most treated patients with RA.[46]

Kerekes, G. *et al. Nat. Rev. Rheumatol.* **10**, 691–696 (2014); published online 5 August 2014;

METABOLIC EFFECT OF RA THERAPY: altered adipokine levels and insuline sensitivity

- IFX ↓ resistina
- antiTNF ↑ adiponectina in alcuni studi
- = leptina
- ↓ Leptina/adiponectina (marker di resistenza all'insulina e s. metabolica) in corso di bDAMRDs
- DAMRDs+corticosteroidi nel primo trimestre migliora la sensibilità all'insulina e la dislipidemia
- Anti TNF ↑ sensibilità all'insulina

Kerekes, G. *et al. Nat. Rev. Rheumatol.* **10**, 691–696 (2014); published online 5 August 2014;

Joint Bone Spine. 2019 Mar;86(2):173-183. doi: 10.1016/j.jbspin.2018.03.007. Epub 2018 Apr 7.

Impact of obesity on the efficacy of different biologic agents in inflammatory diseases: A systematic review and meta-analysis.

Shan J[1], Zhang J[2].

Table 1
Characteristics and main findings of included studies: obesity and clinical response to anti-TNF agents in AS or axSpA patients.

Refs	Patients			BMI timing	Therapy: anti-TNF agent (n)	Groups (n)			Reported outcomes				Clinical response was assessed by	Study design	
	Rheumatic disease (n)	Obese %	Female %			Obese	Over weight	Normal weight	Clinical response			Other		Type of study	Duration (months)
Ottaviani et al. 2012 [26]	AS (155)	24.5	36.7	Baseline	IFX	38	54	63		BASDAI50 %[a]	BASDAI20 %[a]	BASDAI70 %[a]	BASDAI50 response rate (%) and BASDAI20%; BASDAI70%[a]	Retrospective cohort	6
									Obese[a] Overweight[a] Normal weight[a]	26.5 %[a] 48.9%[a] 77.6%[a]	41.2 %[a] 71.2%[a] 84.5%[a]	5.9 %[a] 29.8%[a] 48.3%[a]			
										P < 0.001[a]	P < 0.001[a]	P < 0.001[a]			
Rosas et al., 2017 [27]	AS (57)	26.3	35	At treatment	ADA (57)	15	25	17	Obese ↓ Achieving BASDAI ≤ 4 (P = 0.05) Achieving ASDAS ≤ 2.1 (P = 0.02)[a]			Blood ADL levels ↓ P = 0.032 Anti-ADL Abp = 0.13[a]	BASDAI index and the ASDAS ESR index[a]	Cross-sectional study	–
Gremese et al. 2014 [28]	Axial SpA (170)	13.5	30.6	Baseline	IFX (104) ETA (31) ADA (35)	23	55	92	BASDAI50% Obese: 30.4%; Overweight: 54.5%; Normal weight: 72.8% P < 0.001[a]				BASDAI50 response rate (%)[a]	Retrospective cohort	12
Micheroli et al., 2017 [29]	Axial SpA (624)	14.1	37.8	Baseline	IFX (137) ADA (215) ETA (167) GOL (105)	88	204	332		ASAS40%[a]	BASDAI50%[a]	ASDAS < 2.1%[a]	BASDAI50 response rate (%) ASAS40 response rate (%) ASDAS ESR index[a]	Retrospective cohort	12
									Obese[a] Overweight[a] Normal weight[a]	29%[a] 34%[a] 44%[a]	33%[a] 40%[a] 48%[a]	25% 41% 56%			
										P = 0.02[a]	P = 0.06[a]	P < 0.001[a]			

AS: ankylosing spondylitis; axSpA: axial spondyloarthritis; ASAS: Assessment in SpondyloArthritis International Society; ASAS40: 40% improvement according to ASAS; BASDAI: Bath ankylosing spondylitis disease activity index; BASDAI50: 50% improvement according to BASDAI; anti-TNF agents include infliximab (IFX), adalimumab (ADA), etanercept (ETA), certolizumab (CTZ) and golimumab (GOL).

[a] Significant difference between groups.

IMPATTO DEL BMI SULLA RISPOSTA AGLI ANTI-TNF

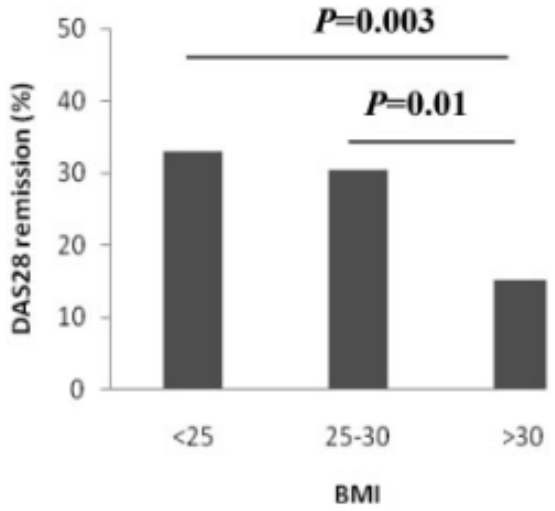


Figure 1. Percentage of Disease Activity Score in 28 joints (DAS28) remission at the 12th month of anti–tumor necrosis factor α therapy in rheumatoid arthritis patients according to body mass index (BMI) categories.

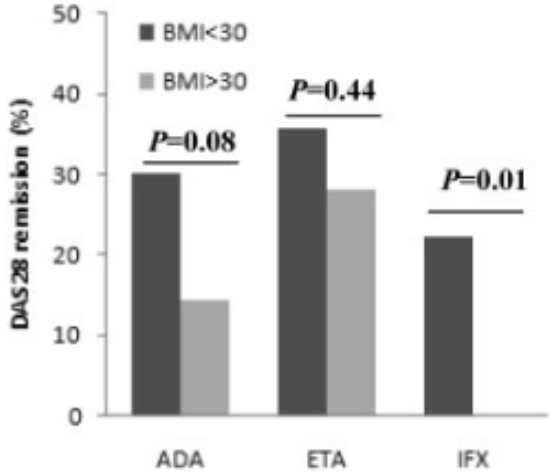


Figure 2. Percentage of Disease Activity Score in 28 joints (DAS28) remission in obese and nonobese rheumatoid arthritis patients treated with adalimumab (ADA), etanercept (ETA), and infliximab (IFX). None of the obese patients responded to IFX. BMI = body mass index.

Aliment Pharmacol Ther. 2017;46:883–891.

J Am Acad Dermatol. 2019 Aug 7. pii: S0190-9622(19)32498-3. doi: 10.1016/j.jaad.2019.07.103.

J Dermatol. 2018 Sep;45(9):1130-1134. doi: 10.1111/1346-8138.14526.

Clin Rheumatol. 2017 Dec;36(12):2655-2665. doi: 10.1007/s10067-017-3788-1.

Arthritis Care Res (Hoboken). 2013 Jan;65(1):94-100. doi: 10.1002/acr.21768.

IMPATTO DEL BMI SULLA RISPOSTA AGLI ANTI-TNF

Table 3. Baseline characteristics of rheumatoid arthritis patients reaching or not reaching remission after 12 months of anti-TNFα therapy*

	Remission (n = 194)	No remission (n = 447)	P
Age, years	49.2 ± 13.4	53.6 ± 13.2	< 0.001
Disease duration, years	8.2 ± 7.2	8.7 ± 9.3	NS
DAS28	5.1 ± 1.5	5.8 ± 1.3	< 0.001
ESR, mm/hour	27.9 ± 17.7	39.3 ± 23.0	< 0.001
HAQ score	1.1 ± 0.7	1.4 ± 0.7	< 0.001
VAS pain	59.9 ± 25.8	64.8 ± 22.4	NS
Global health	57.4 ± 27.1	61.8 ± 22.3	NS
BMI, kg/m²	24.2 ± 3.6	25.2 ± 4.4	0.02

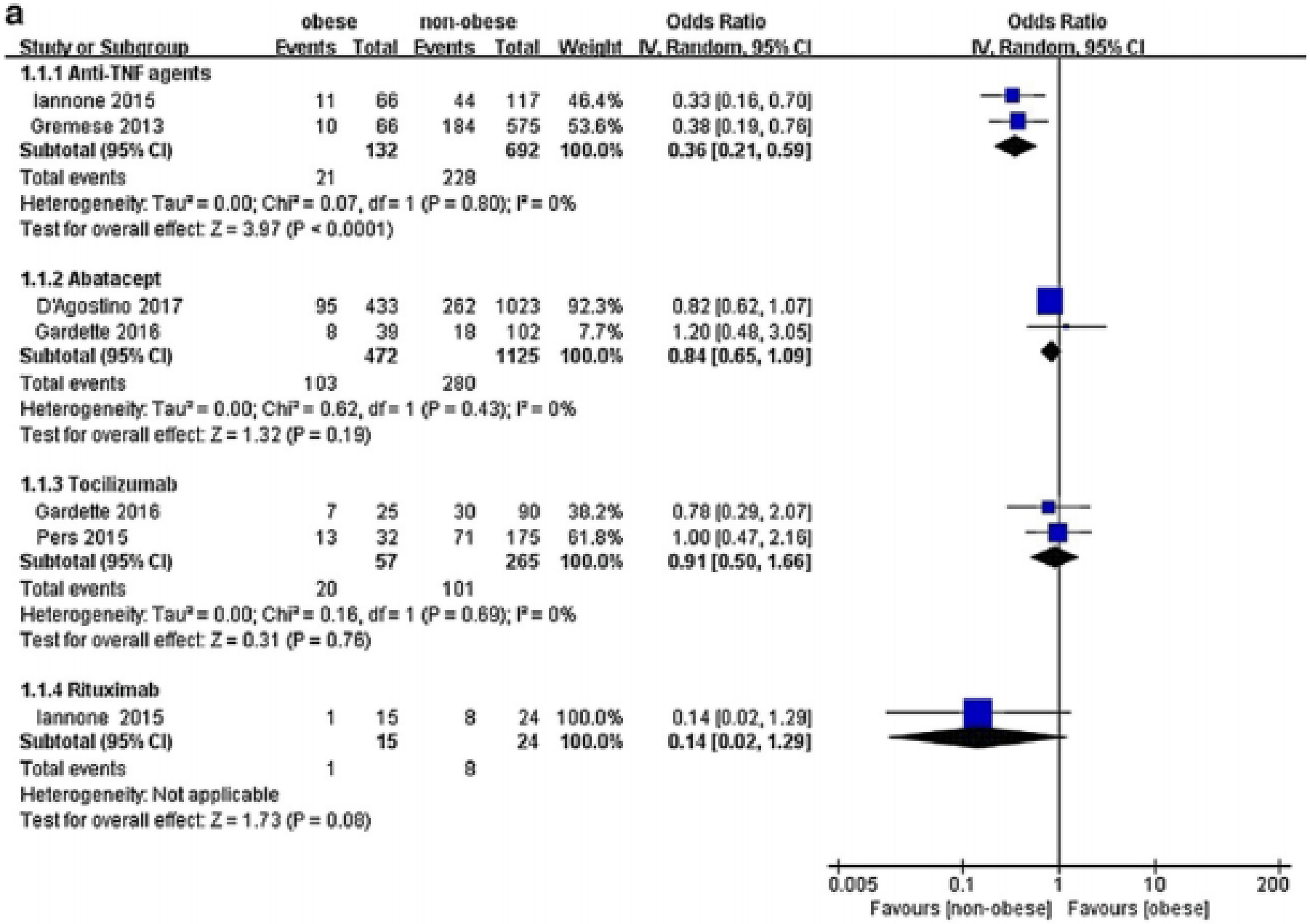
* Values are the mean ± SD. Anti-TNFα = anti–tumor necrosis factor α; NS = not significant; DAS28 = Disease Activity Score in 28 joints; ESR = erythrocyte sedimentation rate; HAQ = Health Assessment Questionnaire; VAS = visual analog scale; BMI = body mass index.

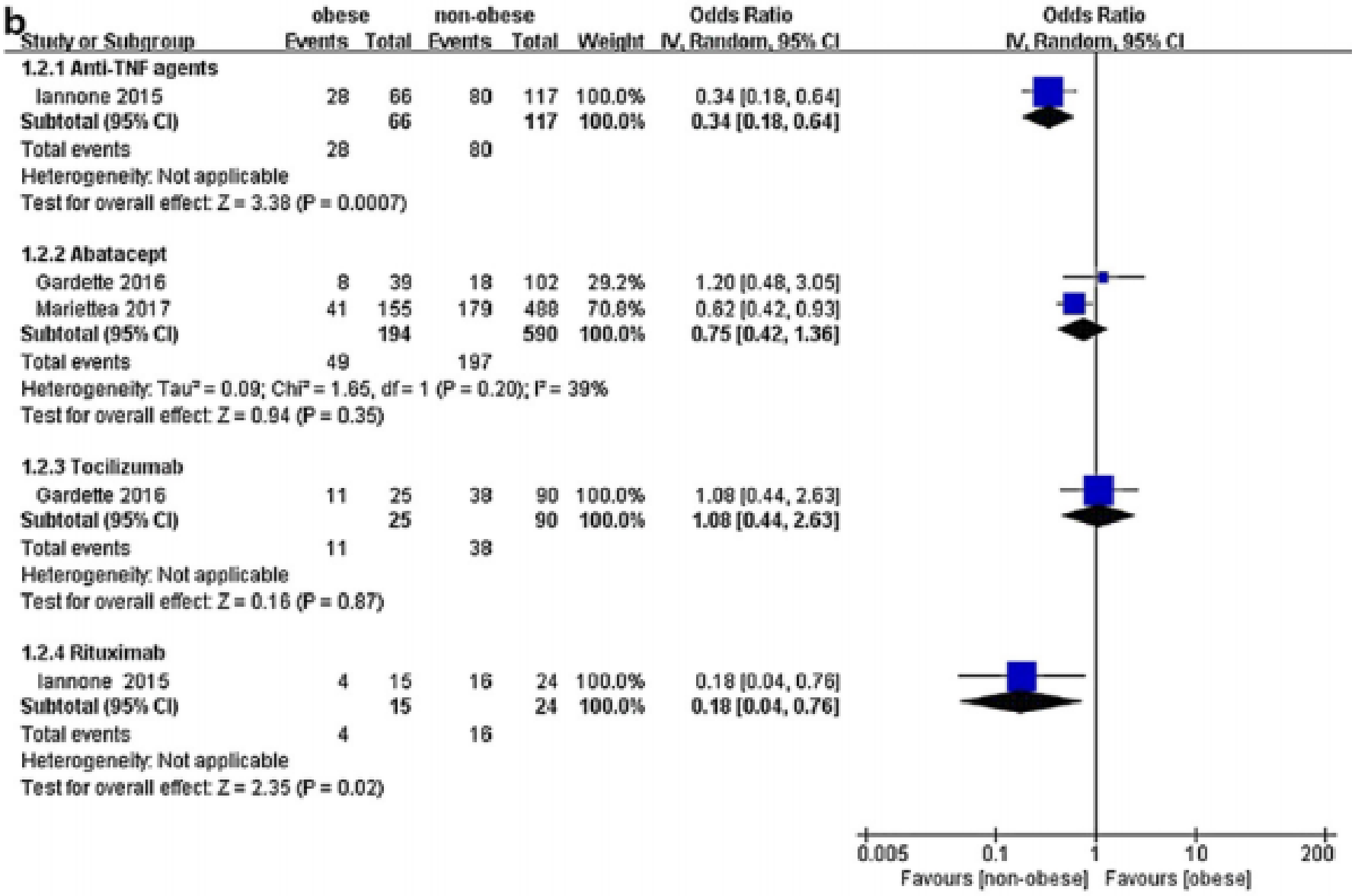
Table 4. Multivariate model predicting the 12-month remission after anti-TNFα therapy in the overall cohort of rheumatoid arthritis patients*

Dependent variables	OR (95% CI)	P
Age, years	0.985 (0.957–1.015)	NS
Female sex	0.457 (0.171–1.225)	NS
Disease duration	0.961 (0.91–1.015)	NS
DAS28†	0.436 (0.327–0.582)	< 0.0001
ESR, mm/hour	0.985 (0.962–1.01)	NS
VAS pain	1.005 (0.985–1.025)	NS
Global health	0.999 (0.979–1.019)	NS
HAQ score	0.778 (0.41–1.475)	NS
BMI, kg/m²†	0.892 (0.806–0.987)	0.02
Baseline steroids, no vs. yes†	0.399 (0.218–0.729)	0.003
RF, positive vs. negative	0.882 (0.376–2.071)	NS
Anti-CCP, positive vs. negative	1.04 (0.474–2.282)	NS
Adalimumab vs. infliximab†	2.435 (1.022–5.802)	0.04
Etanercept vs. infliximab†	3.253 (1.334–7.929)	0.01

* OR = odds ratio; 95% CI = 95% confidence interval; NS = not significant; DAS28 = Disease Activity Score in 28 joints; ESR = erythrocyte sedimentation rate; VAS = visual analog scale; HAQ = Health Assessment Questionnaire; BMI = body mass index; RF = rheumatoid factor; anti-CCP = anti–cyclic citrullinated peptide.
† Variables independently associated with DAS28 remission at 12 months of anti–tumor necrosis factor α (anti-TNFα) therapy.

Arthritis Care Res (Hoboken). 2013 Jan;65(1):94-100. doi: 10.1002/acr.21768.


a
obese
non-obese
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M, Random, 95% CI
M, Random, 95% CI
1.1.1 Anti-TNF agents
Iannone 2015 11 66 44 117 46.4% 0.33 [0.16, 0.70]
Gremese 2013 10 66 184 575 53.6% 0.38 [0.19, 0.76]
Subtotal (95% CI) 132 692 100.0% 0.36 [0.21, 0.59]
Total events 21 228
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.80); I² = 0%
Test for overall effect: Z = 3.97 (P < 0.0001)
1.1.2 Abatacept
D'Agostino 2017 95 433 262 1023 92.3% 0.82 [0.62, 1.07]
Gardette 2016 8 39 18 102 7.7% 1.20 [0.48, 3.05]
Subtotal (95% CI) 472 1125 100.0% 0.84 [0.65, 1.09]
Total events 103 280
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 1.32 (P = 0.19)
1.1.3 Tocilizumab
Gardette 2016 7 25 30 90 38.2% 0.78 [0.29, 2.07]
Pers 2015 13 32 71 175 61.8% 1.00 [0.47, 2.16]
Subtotal (95% CI) 57 265 100.0% 0.91 [0.50, 1.66]
Total events 20 101
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)
1.1.4 Rituximab
Iannone 2015 1 15 8 24 100.0% 0.14 [0.02, 1.29]
Subtotal (95% CI) 15 24 100.0% 0.14 [0.02, 1.29]
Total events 1 8
Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)
0.005
0.1
1
10
200
Favours [non-obese]
Favours [obese]


b
obese
non-obese
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M, Random, 95% CI
M, Random, 95% CI
1.2.1 Anti-TNF agents
Iannone 2015 28 66 80 117 100.0% 0.34 [0.18, 0.64]
Subtotal (95% CI) 66 117 100.0% 0.34 [0.18, 0.64]
Total events 28 80
Heterogeneity: Not applicable
Test for overall effect: Z = 3.38 (P = 0.0007)
1.2.2 Abatacept
Gardette 2016 8 39 18 102 29.2% 1.20 [0.48, 3.05]
Mariettea 2017 41 155 179 488 70.8% 0.62 [0.42, 0.93]
Subtotal (95% CI) 194 590 100.0% 0.75 [0.42, 1.36]
Total events 49 197
Heterogeneity: Tau² = 0.09; Chi² = 1.65, df = 1 (P = 0.20); I² = 39%
Test for overall effect: Z = 0.94 (P = 0.35)
1.2.3 Tocilizumab
Gardette 2016 11 25 38 90 100.0% 1.08 [0.44, 2.63]
Subtotal (95% CI) 25 90 100.0% 1.08 [0.44, 2.63]
Total events 11 38
Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)
1.2.4 Rituximab
Iannone 2015 4 15 16 24 100.0% 0.18 [0.04, 0.76]
Subtotal (95% CI) 15 24 100.0% 0.18 [0.04, 0.76]
Total events 4 16
Heterogeneity: Not applicable
Test for overall effect: Z = 2.35 (P = 0.02)
0.005
0.1
1
10
200
Favours [non-obese]
Favours [obese]

Body mass index as a driver of selection of biologic therapy in rheumatoid arthritis. Results from the US-CLARA study

BMI does not influence the abatacept response in RA patients with active disease. During abatacept treatment, the clinical response can be achieved despite a condition of overweight or obesity.

Body mass index and treatment response to subcutaneous abatacept in patients with psoriatic arthritis: a *post hoc* analysis of a phase III trial

In the abatacept group, there were no significant differences in the likelihood of achieving treatment outcomes at week 24 in the obese or overweight versus underweight/normal subgroup ($p \geq 0.17$ for all measurements)

Eur J Intern Med. 2019 Aug;66:57-61. doi: 10.1016/j.ejim.2019.05.017. Epub 2019 May 18.

McInnes IB, *et al. RMD Open* 2019;**5**:e000934. doi:10.1136/rmdopen-2019-000934

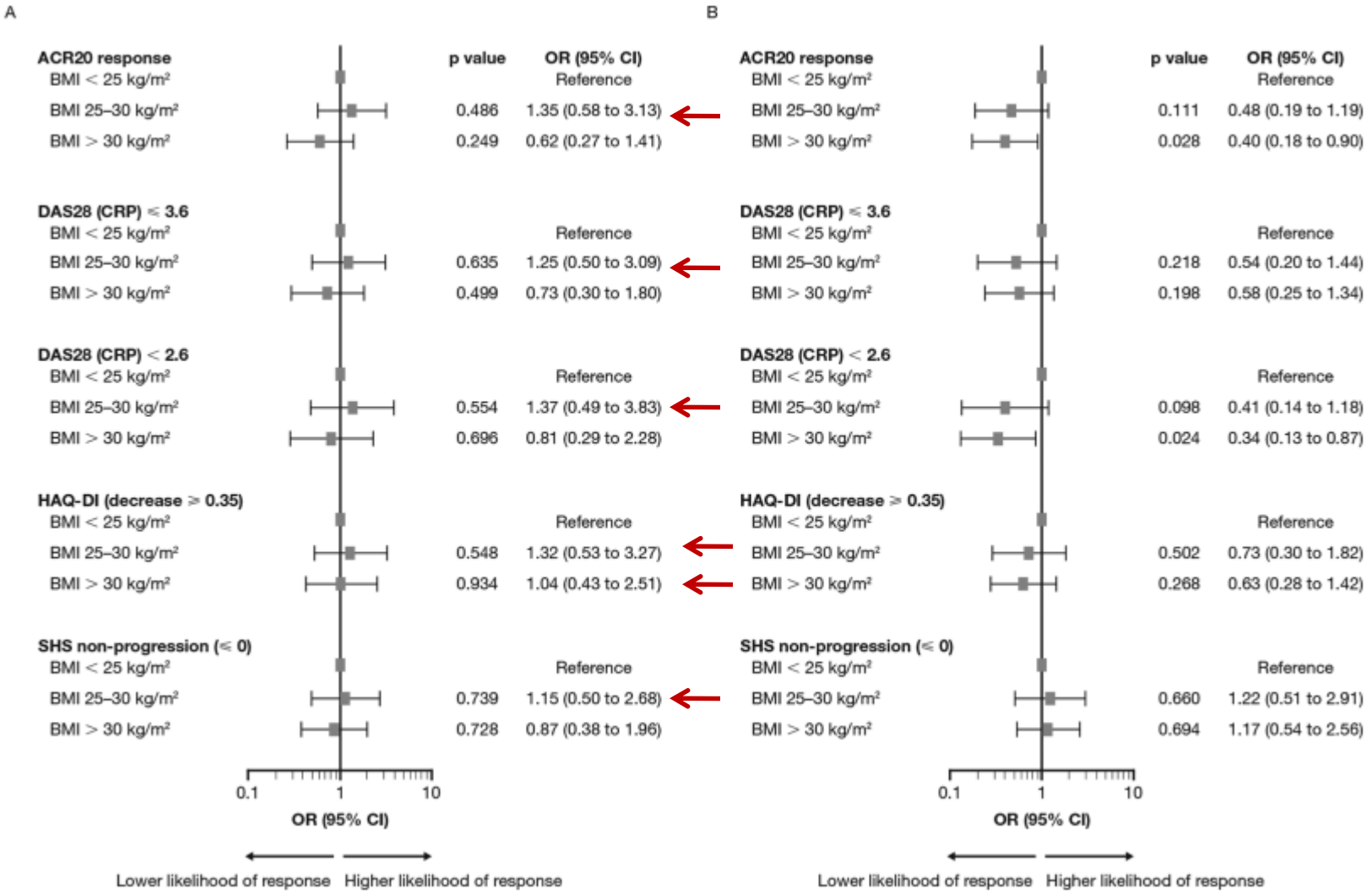


Figure 1 Univariate model of adjusted* comparisons of treatment response at week 24 between BMI subgroups in patients receiving (A) abatacept and (B) placebo. An OR >1 indicates a higher likelihood of response, while an OR <1 indicates a lower likelihood of response. ORs are significant when 95% CIs do not overlap 1. *The model was adjusted for the following baseline factors: treatment, BMI, MTX use, prior TNFis, CRP, erosion, enthesitis, dactylitis, BASDAI and DAS28 (CRP). ACR20, American College of Rheumatology 20% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CRP, C reactive protein; DAS28, Disease Activity Score in 28 joints; HAQ-DI, Health Assessment Questionnaire-Disability Index; MTX, methotrexate; SHS, Sharp/van der Heijde score; TNFis, tumour necrosis factor inhibitors.

PSORIASI

Table 3
Characteristics and main findings of included studies: obesity and clinical response to anti-TNF agents in psoriasis patients.

Refs	Patients					Groups (*n*)			Reported outcomes						Study design	
	Rheumatic disease (*n*)	Obese %	Female %	BMI timing	Therapy: anti-TNF agent (*n*)	Obese	Over weight	Normal weight	Clinical response				Other	Clinical response was assessed by:	Type of study	Duration (months)
Bardazzi et al., 2010 [37]	Ps (24)	45.8	–	Baseline	ETA, ADA and IFX	11	13		Mean PASI:[a] Obese: 15.55 ± 3.195;[a] Non-obese: 5.538 ± 1.228[a] *P* = 0.0051[a]				–[a]	Mean PASI at month 4 and 8[a]	Retrospective cohort	8
Lafuente-Urrez and Pérez-Pelegay 2014 [38]	Ps (30)	33.3	56.7	Baseline	ADA	10	7	13		Non-obese[a]	Obese[a]		Drug discontinue%[a]	Percentage of patients achieve PASI100/90/75 at different visit time[a]	Retrospective cohort	20.8
									PASI75 %[a] PASI90%[a] PASI100%[a]	80 %[a] 80% 70%[a]	80 %[a] 50%[a] 40%[a]	*P* = 1[a] *P* = 0.116[a] *P* = 0.139[a]		Percentage of patients achieve PASI90/75[a]	Prospective cohort	4
Prussick et al., 2015 [34]	Ps (99)	31.3	32.3	Baseline	ADA	31	28	40		Non-obese[a]	Obese[a]		–[a]			
									PASI90 %[a] PASI75 %[a] *P* < 0.05[a]	63.2 %[a] 85.3 %[a]	35.5 %[a] 61.3 %[a]					
Giunta et al., 2016 [35]	Ps (66)	18.2	42.4	Baseline	ETA	12	21	33	Mean PASI:[a] Obese: 2.94 ± 2.81; *P* < 0.001[a] Overweight: 1.86 ± 2.88;[a] Normal weight: 1.72 ± 3.02[a]				–[a]	Mean PASI at month 12[a]	Retrospective cohort	12

Ps: psoriasis; Anti-TNF agents include adalimumab (ADA); infliximab (IFX) and etanercept (ETA); PASI: psoriasis area and severity index.
[a] Significant difference between groups.

TNF correlato con ↑BW e BMI in psoriasi
indifferente vs anti IL-12/23 e IL-17

M. Di CROHN

Table 2
Characteristics and main findings of included studies: obesity and clinical response to anti-TNF agents in CD patients.

Refs	Patients					Groups (*n*)			Reported outcomes			Study Design	
	Rheumatic disease (*n*)	Obese %	Female %	BMI timing	Therapy: anti-TNF agent (*n*)	Obese	Over weight	Normal weight	Clinical response	Other	Clinical response was assessed by	Type of study	Duration (months)
Harper et al., 2013 [30]	CD (99)	–	52.5	Baseline	IFX (99)	–	–	–	Time to LOR: Earlier in obese group $P<0.001$[a]	–[a]	A clinical flare or loss of response (LOR)[a]	Retrospective cohort	36
Bhalme et al., 2013 [31]	CD (130)	14.8	66.7	Baseline	ADA (54)	8	46		Time to LOR: Earlier in obese group $P=0.013$[a]	–[a]	Loss of response (LOR)[a]	Retrospective cohort	10.5
		18.4	55.3	Baseline	IFX (76)	14	62		Time to LOR: Two groups are close $P=0.164$[a]	–[a]			13.0
Brown et al., 2016 [32]	CD (388)	11.9	54	Baseline	IFX (388)	46	91	218	Risk of LOR (%): Obese: 45.7%: Overweight: 41.8%; Normal weight: 39.1%[a]	Any CD-related surgery or CD-related intestinal resectional surgery[a]	A clinical flare or loss of response (LOR)[a]	Retrospective cohort	12
Guerbau et al., 2017 [33]	CD (140)	16.4	51	Baseline	IFX (140)	23	21	96	IFX dose optimization (%) Obese: 56%: Overweight: 52%; Normal weight: 20% $P=0.0002$[a]	Introduction of surgery, CT or IS; IFX discontinuation[a]	IFX dose optimization[b]	Prospective cohort	12

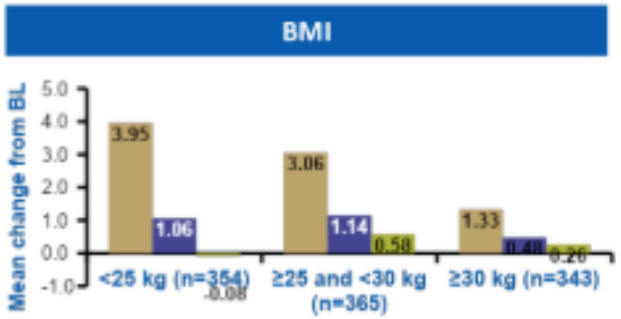
CD: Crohn's disease; LOR: loss of response. A clinical flare or LOR in ref [30,32]was defined as the first occurrence of any of the following: (1) dose escalation of IFX from 5 mg/kg every 8 weeks to either 10 mg/kg per dose and/or a shortening of the dosing interval; (2) loss of response to IFX as manifested by switching to an alternative biologic agent; (3) hospitalization for IBD; (4) need for a course of corticosteroids for disease activity; or (5) need for IBD-related surgery. But the detail definition of LOR was not elaborated in ref [31]. IFX dose optimization was defined as increasing the dosage to more than 5 mg/kg (without limit of IFX dose in patients with a weight excess 100 kg) and/or shortening the interval between infusions to less than 8 weeks.

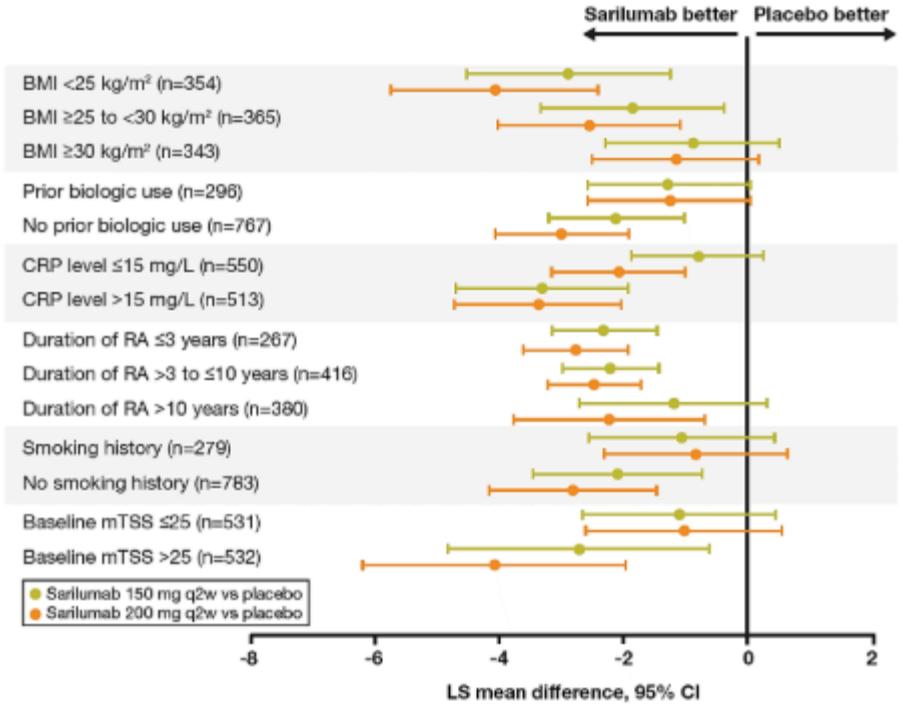
[a] Significant difference between groups.

Miopenia predittore di cattiva risposta nel m. di Crohn

Anti-IL-6

SARILUMAB





JAK-i

DAS28 score <2.6, were 11% for obese patients, 24% for overweight patients, and 20% for normal weight patients. The regression model indicated a significant negative effect of obesity on low disease activity achievement compared with normal weight.

Neither the dosage of JAK inhibitors nor combination/mono-therapy had an effect on treatment response.

Obesity but not overweight had a negative impact on the achievement of LDA in RA patients treated with JAKi.

ACR/ARHP 2018.

CONCLUSIONI 1

- Il tessuto adiposo influenza lo stato infiammatorio nell'AR
- La cachessia reumatoide è il risultato di una prolungata attività infiammatoria
- L'obesità influenza negativamente il raggiungimento della remissione
- La cachessia reumatoide, piuttosto che l'obesità, è stata associata ad un aumento della mortalità per CVD nell'AR.

CONCLUSIONI 2

- RA attiva è associata ad alterazione dell'assetto lipidico
- Un controllo ottimale della malattia comporta un aumento dei livelli lipidici non aterogeni
- Un elevato BMI correla con una peggiore risposta ai farmaci antiTNF e JAK-i
- La risposta ai farmaci anti-IL6, anti CTLA4, anti il 17 e anti-IL12/23 non è influenzata da BMI