Fattori nutrizionali e rischio metabolico: aspetti metodologici

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Obiettivo

- Fornire una panoramica dei problemi metodologici associati alla valutazione di un fattore (predittore) nutrizionale di rischio metabolico

Il problema

$$Y = f(X)$$

Y = outcome (metabolico)

X = fattore di rischio o predittore (nutrizionale)

$f(\cdot)$ = funzione

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$f(\cdot)$ = funzione

Y

- È un “hard outcome”?
- È un “outcome surrogato”?
- È un outcome di scarso valore clinico?
  - NB: ciò non implica che sia irrilevante in senso lato

Il problema

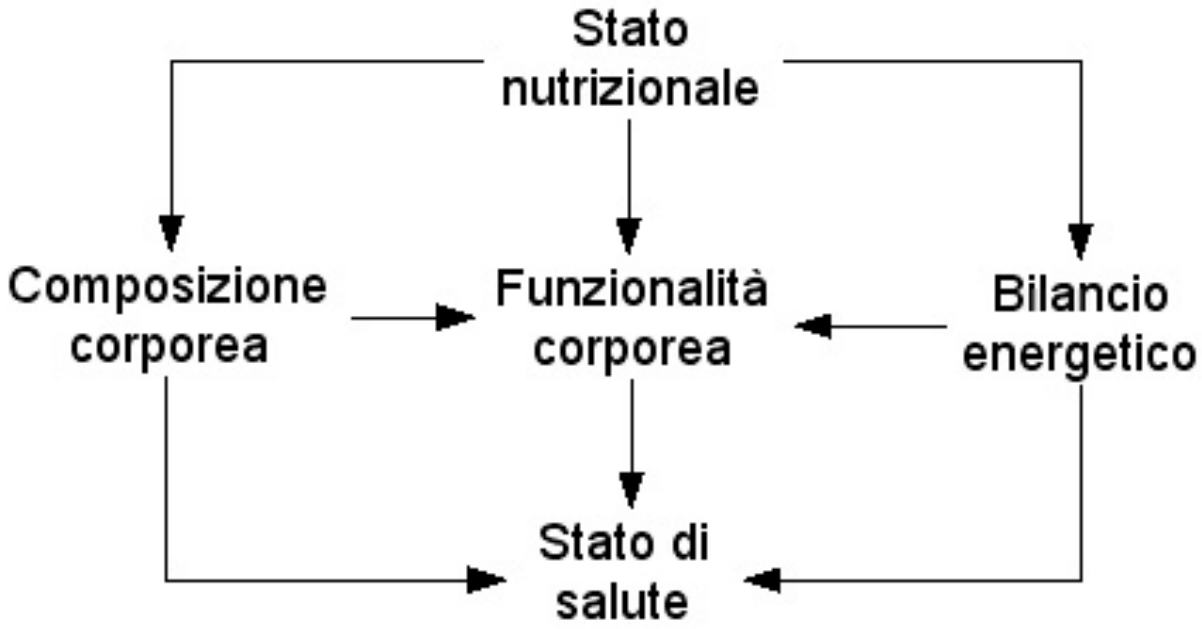
$$Y = f(X)$$

Y = outcome (metabolico)

X = fattore di rischio o predittore (nutrizionale)

$f(\cdot)$ = funzione

X



Bedogni G. Manuale ANDID di valutazione dello stato nutrizionale. SEU: 2009.
http://www.giorgiobedogni.it/mavsn.html

Composizione corporea

- I compartimenti corporei sono stati misurati o stimati?

- Stiamo utilizzando appropriatamente i termini (es. “massa magra”)?

Bilancio di energia e nutrienti

- Come è stato misurato l'introito di nutrienti?

- Da ciò originano in gran parte le controversie relative alla nutrizione come fattore di rischio cardiometabolico

Research Article

Statistics in Medicine

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Using surrogate biomarkers to improve measurement error models in nutritional epidemiology

Ruth H. Keogh,[a,b,c*†] Ian R. White[a] and Sheila A. Rodwell[b‡]

Nutritional epidemiology relies largely on self-reported measures of dietary intake, errors in which give biased estimated diet–disease associations. Self-reported measurements come from questionnaires and food records. Unbiased biomarkers are scarce; however, surrogate biomarkers, which are correlated with intake but not unbiased, can also be useful. It is important to quantify and correct for the effects of measurement error on diet–disease associations. Challenges arise because there is no gold standard, and errors in self-reported measurements are correlated with true intake and each other. We describe an extended model for error in questionnaire, food record, and surrogate biomarker measurements. The focus is on estimating the degree of bias in estimated diet–disease associations due to measurement error. In particular, we propose using sensitivity analyses to assess the impact of changes in values of model parameters which are usually assumed fixed. The methods are motivated by and applied to measures of fruit and vegetable intake from questionnaires, 7-day diet diaries, and surrogate biomarker (plasma vitamin C) from over 25 000 participants in the Norfolk cohort of the European Prospective Investigation into Cancer and Nutrition. Our results show that the estimated effects of error in self-reported measurements are highly sensitive to model assumptions, resulting in anything from a large attenuation to a small amplification in the diet–disease association. Commonly made assumptions could result in a large overcorrection for the effects of measurement error. Increased understanding of relationships between potential surrogate biomarkers and true dietary intake is essential for obtaining good estimates of the effects of measurement error in self-reported measurements on observed diet–disease associations.

Keywords: biomarkers; measurement error; nutritional epidemiology; regression calibration; structural equation models

Funzionalità corporea

- Il criterio scelto per valutare lo stato nutrizionale è funzionalmente rilevante?

- (Si noti che di alcuni nutrienti è possibile solo una valutazione funzionale)

Il problema

$$Y = f(X)$$

Y = outcome (metabolico)

X = fattore di rischio o predittore (nutrizionale)

$f(\cdot)$ = funzione

$f(\cdot)$

- Ogni modello statistico implica delle assunzioni
- Molte assunzioni non sono testabili
  - Problema non risolvibile ma non ignorabile
- Alcune assunzioni testabili ma restano spesso non testate
  - Problema risolvibile e (ovviamente?) non ignorabile

$f(\cdot)$ come relazione causale?

- I filosofi occidentali dibattono cosa sia una "causa" da almeno 2500 anni

- Il concetto di causa è estraneo al mondo della matematica e della statistica
  Baber RL. The Language of Mathematics. Wiley, 2011.
  Freedman D. Statistical models: theory and practice. CUP, 2009.

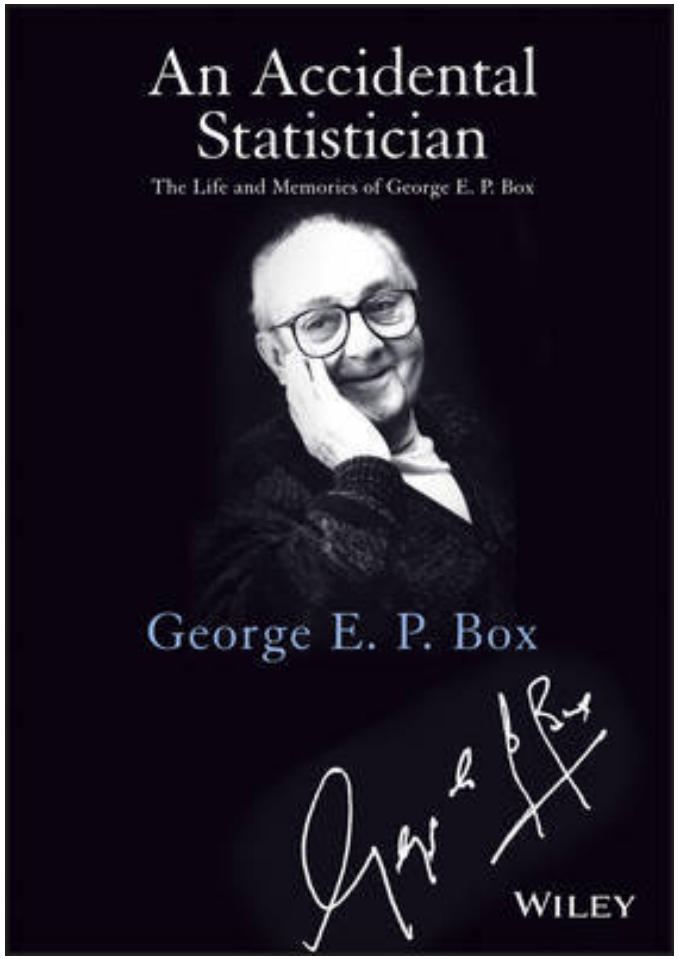
- Una "causa" è operativamente definita attraverso un'associazione praticamente rilevante con un "effetto" di interesse
  Vineis P. Int J Epidemiol 2009;38:675.

$f(\cdot)$

“All models all wrong but some are useful”

(George Box)

In memoriam



George Box (1919-2013)

Modelli “più utili” 1

$$Y = f(X_1, X_2, \ldots X_n)$$

X_1 = fattore di rischio di interesse

X_2-X_n = fattori di rischio concomitanti (noti o potenziali)

Modelli “più utili” 2

$$(\Delta)Y = f\,(\Delta X_1, \Delta X_{2,} \ldots \Delta X_n)$$

Δ = modificazione temporale

Richiede studio longitudinale (coorte)

Esempio 1

- Il rapporto tra la circonferenza della vita e la statura (WC:Ht) gode di una crescente popolarità tra i pediatri.

Esempio 1

- Y = ?
- X = WC:Ht
- f(·) = ho promesso di non essere tecnico…

Esempio 1

- X = WC:Ht
- Y = massa grassa percentuale (massa grassa / peso corporeo)

International Journal of Obesity (2013), 1–4

www.nature.com/ijo

ORIGINAL ARTICLE

Waist circumference-to-height ratio predicts adiposity better than body mass index in children and adolescents

P Brambilla[1], G Bedogni[2], M Heo[3] and A Pietrobelli[4,5]

OBJECTIVE: Body mass index (BMI) is the surrogate measure of adiposity most commonly employed in children and adults. Waist circumference (WC) and the waist circumference-to-height ratio (WCHt) have been proposed as markers of adiposity-related morbidity in children. However, no study to date has compared WCHt, WC, BMI and skinfolds thickness for their ability to detect body adiposity.

AIM: To compare WCHt, WC, BMI and skinfolds for their accuracy in predicting percent body fat (PBF), percent trunk fat (PTF) and fat mass index (FMI) in a large sample of children and adolescents.

DESIGN, SETTING AND PARTICIPANTS: We studied 2339 children and adolescents aged 8–18 years from the US National Health and Nutrition Examination Survey 2003/2004. Body fat was measured using dual-energy X-ray absorptiometry. Multivariable regression splines were used to model the association between PBF, PTF, FMI and the predictors of interest.

RESULTS: WCHt alone explained 64% of PBF variance as compared with 31% for WC, 32% for BMI and 72% for the sum of triceps and subscapular skinfolds (SF2) ($P<0.001$ for all). When age and gender were added to the predictors, the explained variance increased to 80% for the WCHt model, 72% for the WC model, 68% for the BMI model and 84% for the SF2 model. There was no practical advantage to add the ethnic group as further predictor. Similar relationships were observed with PTF and FMI.

CONCLUSIONS: WCHt is better than WC and BMI at predicting adiposity in children and adolescents. It can be a useful surrogate of body adiposity when skinfold measurements are not available.

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Keywords: children; body composition; body fat; body mass index; trunk fat; waist circumference

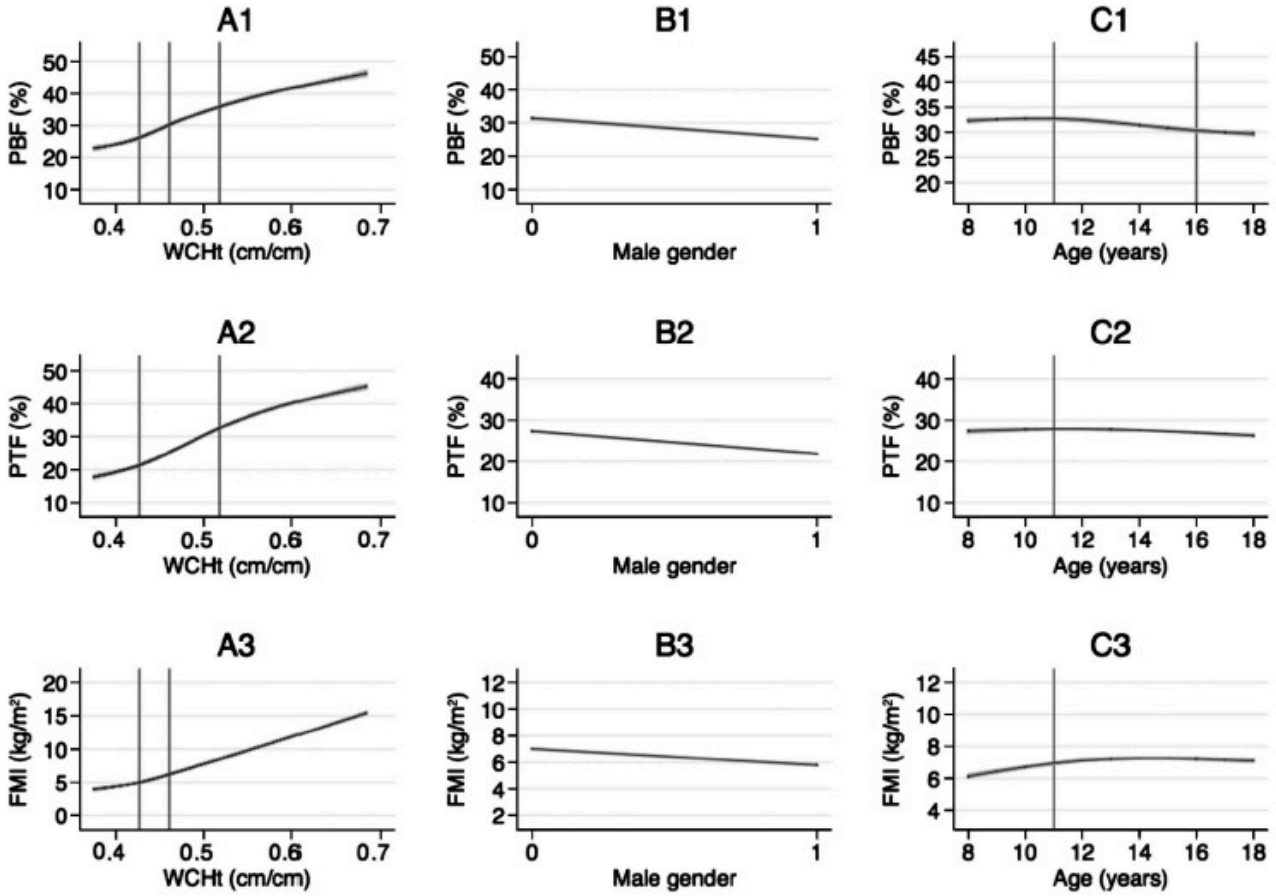


Figure 1. Prediction of PBF, PTF and FMI from the multivariable model using WCHt, age and gender as predictors. Graphs A–C for each outcome (1–3) shows the variability of the outcome explained by each predictor after correction for other predictors (partial residuals). Gray bands are 95% confidence intervals. Vertical lines shows the position of knots selected by multivariable regression spline analysis (see also Supplementary Appendix).

Esempio 1

- X = WC:Ht
- Y = fattori di rischio per malattia cardiometabolica

Esempio 1

A POPULATION-BASED COMPARISON OF BMI PERCENTILES AND WAIST-TO-HEIGHT RATIO FOR IDENTIFYING CARDIOVASCULAR RISK IN YOUTH

HENRY S. KAHN, MD, GIUSEPPINA IMPERATORE, MD, PHD, AND YILING J. CHENG, MD, PHD

Objective Determine whether waist-to-height ratio (WHtR) or sex- and age-specific percentiles of body mass index (BMI) better identifies cardiovascular risk.

Study design The third National Health and Nutrition Examination Survey (NHANES III) provided measurements on 7657 participants statistically weighted to represent 50.05 million youth 4 to 17 years of age. We estimated the subpopulations corresponding to BMI strata that were normal (<85th percentile), at risk for overweight (85th to <95th percentile), and overweight (≥95th percentile). We chose WHtR cutoff points (0.490 and 0.539) so that subpopulation sizes in the three WHtR strata would equal those in the three BMI strata. For 13 cardiovascular risk factors we compared mean levels among youth discordant for their BMI and WHtR strata.

Results 726 participants (representing 3.69 million youth) were identified as having WHtR stratum >BMI stratum. Compared with the 603 participants (representing 3.70 million youth) who were discordant in the opposite direction, weighted analyses showed they had higher mean levels of heart rate, low-density lipoprotein (LDL) cholesterol, fasting triglycerides, and total cholesterol (P <.015, adjusted for sex, age, and race-ethnicity). Their mean systolic blood pressure was lower, but this difference was eliminated after adjustment for their shorter stature.

Conclusion WHtR, a simpler anthropometric index than sex- and age-specific BMI percentiles, better identifies youth with adverse cardiovascular risk factors. ***(J Pediatr 2005;146:482-8)***

Esempio 1

Our population-based comparison of two anthropometric indices demonstrated that WHtR could serve better than sex- and age-specific BMI percentiles for identifying US youth with high heart rate or adverse concentrations of LDL cholesterol, triglycerides, and total cholesterol. There also was a suggestion (nonsignificant) that youth with elevated total cholesterol/HDL cholesterol, apolipoprotein B, or apolipoprotein B/apolipoprotein AI would be better identified by WHtR. For adverse levels of HDL cholesterol, glucose, HbA_{1c}, uric acid, and diastolic blood pressure, there was no clear difference in the predictive ability of the alternative anthropometric indices.

On the other hand, BMI percentiles better identified which youth had relatively high systolic blood pressure. Youth

Esempio 1

- X = WC:Ht
- Y = malattia (cardiometabolica) incidente = nessuno studio disponibile.
  - Questo è l'Y maggiormente rilevante da un punto di vista clinico

Esempio 2

- Il BMI è un'indice di adiposità non particolarmente accurato in età pediatrica ma è un predittore di outcome clinicamente rilevanti

- Questa la ragione per cui viene (dovrebbe?) essere calcolato di routine

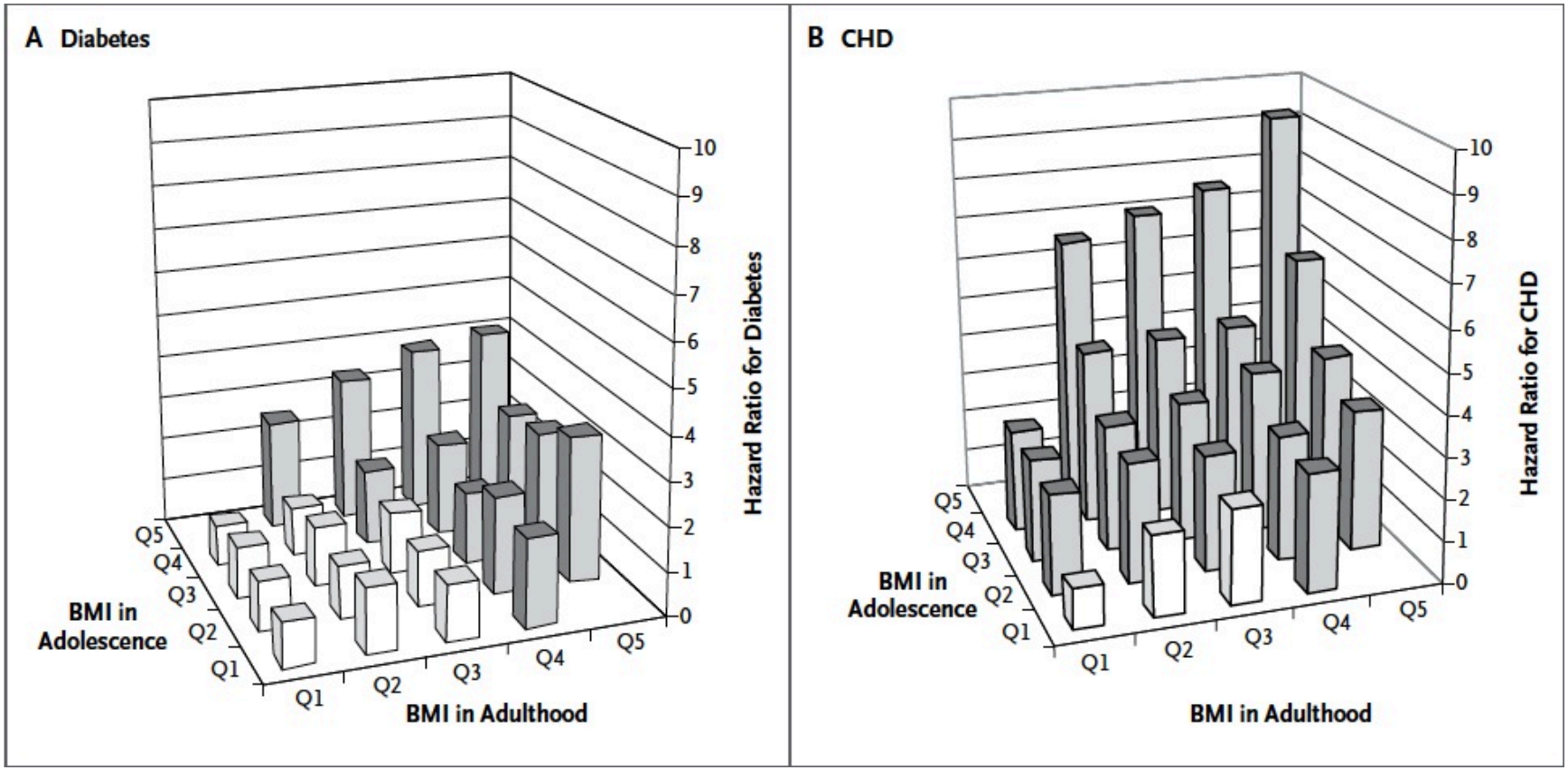
- (La classificazione IOTF del BMI pediatrico è basato sulla predizione del BMI adulto)
  Cole TJ et al. *BMJ.* 2000;320:1240-1243.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adolescent BMI Trajectory and Risk of Diabetes versus Coronary Disease

Amir Tirosh, M.D., Ph.D., Iris Shai, R.D., Ph.D., Arnon Afek, M.D., M.H.A., Gal Dubnov-Raz, M.D., Nir Ayalon, M.D., Barak Gordon, M.D., Estela Derazne, M.Sc., Dorit Tzur, M.B.A., Ari Shamis M.D., M.P.A., Shlomo Vinker, M.D., and Assaf Rudich, M.D., Ph.D.



N Engl J Med 2011;364:1315-25.

Take-home message

$$Y = f(X)$$

Y = outcome clinicamente rilevante

X = fattore di rischio o predittore scelto in base all'associazione con Y

$f(\cdot)$ = "tutti i modelli sono sbagliati, qualcuno è utile"

Grazie