

Prevalence, incidence and types of mild anemia in the elderly: the “Health and Anemia” population-based study

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Online Supplementary Appendix

Laboratory methods

Venous blood samples were collected from participants in a sitting position by venipuncture. Complete blood counts (CBC) were determined using a SISMEM SE-2100 electronic counter (Sysmex Corporation Kobe, Japan) by the central laboratory of Biella Hospital. Results were received by the Coordinating Center in an electronic format within a few days, printed out and mailed to each participant within 2 weeks after sampling. Any blood finding of clinical relevance was quickly communicated by the laboratory directly to the family doctor.

When a hemoglobin concentration was below WHO reference criteria for anemia, further laboratory investigations were conducted. Serum iron was measured colorimetrically using the MODULAR PPP analyzer (Hitachi High-Technologies Corporation, Hichige, Japan). Serum transferrin was determined by immunoturbidimetric assay using the MODULAR PPP analyzer (Hitachi High-Technologies Corporation, Hichige, Japan). Serum ferritin was measured by a chemiluminescent immunometric assay using the IMMULITE 2000 analyzer (DPC Instrument Systems Division, Flanders, NJ, USA). Serum folic acid and vitamin B12 were determined by a competitive immunoassay using the IMMULITE 2000 analyzer (DPC Instrument Systems Division, Flanders NJ, USA). Transferrin saturation was calculated by dividing serum iron by total iron-binding capacity x 100. These laboratory investigations were also assessed in an equal sample of non-anemic individuals matched for age and sex.

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Online Supplementary Table S1. Characteristics of mildly anemic and non-anemic elderly participants.

| | Non-anemic (n=4,682) | Mildly anemic (n=465) | P value Univariate analysis | P value Adjusted for age, sex, education |
|--|-------------------------|--------------------------|--------------------------------|--|
| Mean age in years (SD) | 75.2 (7.1) | 80.0 (8.6) | <0.0001 | |
| Women (%) | 62.2 | 57.4 | 0.0423 | |
| Mean education in years (SD) | 7.6 (3.8) | 7.0 (3.9) | 0.0012 | |
| Living in institutions (%) | 2.8 | 11.3 | <0.0001 | <0.0001 |
| Smoker (%) | | | 0.0004 | 0.0026 |
| current | 13.5 | 7.4 | | |
| former | 31 | 29.9 | | |
| never | 55.6 | 62.7 | | |
| Alcohol use (%) | | | <0.0001 | <0.0001 |
| current | 71.2 | 60.9 | | |
| former | 3.2 | 5.3 | | |
| never | 25.6 | 33.9 | | |
| Mean body mass index (SD) | 24.8 (4.1) | 23.9 (4.4) | <0.0001 | 0.0015 |
| Underweight (%) | 4.7 | 10.5 | <0.0001 | 0.0006 |
| Overweight (%) | 35.1 | 29.8 | | |
| Obese (%) | 10.1 | 7.2 | | |
| Mean hemoglobin in g/dL (SD) | 14.2 (1.2) | 11.6 (0.7) | | |
| Mean hematocrit (SD) in fL | 44.5 (3.5) | 37.2 (2.4) | | |
| Mean vitamin B ₁₂ (SD) in pg/mL | 374.0 (225.1) | 383.7 (243.5) | 0.5032 | 0.7416 |
| Mean folates (SD) in ng/mL | 5.3 (3.4) | 5.4 (4.6) | 0.7688 | 0.3828 |
| Mean systolic blood pressure in mmHg (SD) | 141.7 (18.7) | 138.8 (19.4) | 0.0022 | 0.0058 |
| Mean diastolic blood pressure in mmHg (SD) | 79.5 (10.1) | 75.4 (10.3) | <0.0001 | <0.0001 |
| Mean heart rate in beats/min (SD) | 69.4 (9.7) | 71.0 (9.5) | 0.0006 | 0.0312 |
| Diabetes (%) | 9.3 | 15.9 | <0.0001 | 0.0006 |
| Hypertension (%) | 54.4 | 56.4 | 0.3975 | 0.7988 |
| Heart failure (%) | 7.5 | 14.6 | <0.0001 | 0.0538 |
| Myocardial infarction (%) | 5.2 | 7.8 | 0.0189 | 0.4514 |
| Respiratory insufficiency (%) | 5.8 | 10.5 | 0.0008 | 0.0117 |
| Renal insufficiency (%) | 1.6 | 13.5 | <0.0001 | <0.0001 |
| Stroke or transient ischemic attack (%) | 6.4 | 12.5 | <0.0001 | 0.1285 |
| Parkinsonism (%) | 1.3 | 3.2 | 0.0029 | 0.1584 |
| Cancer, last 5 years (%) | 3.9 | 7.4 | 0.0007 | 0.0055 |

Online Supplementary Table S2. Diseases associated with anemia of chronic disease in the Health and Anemia Study

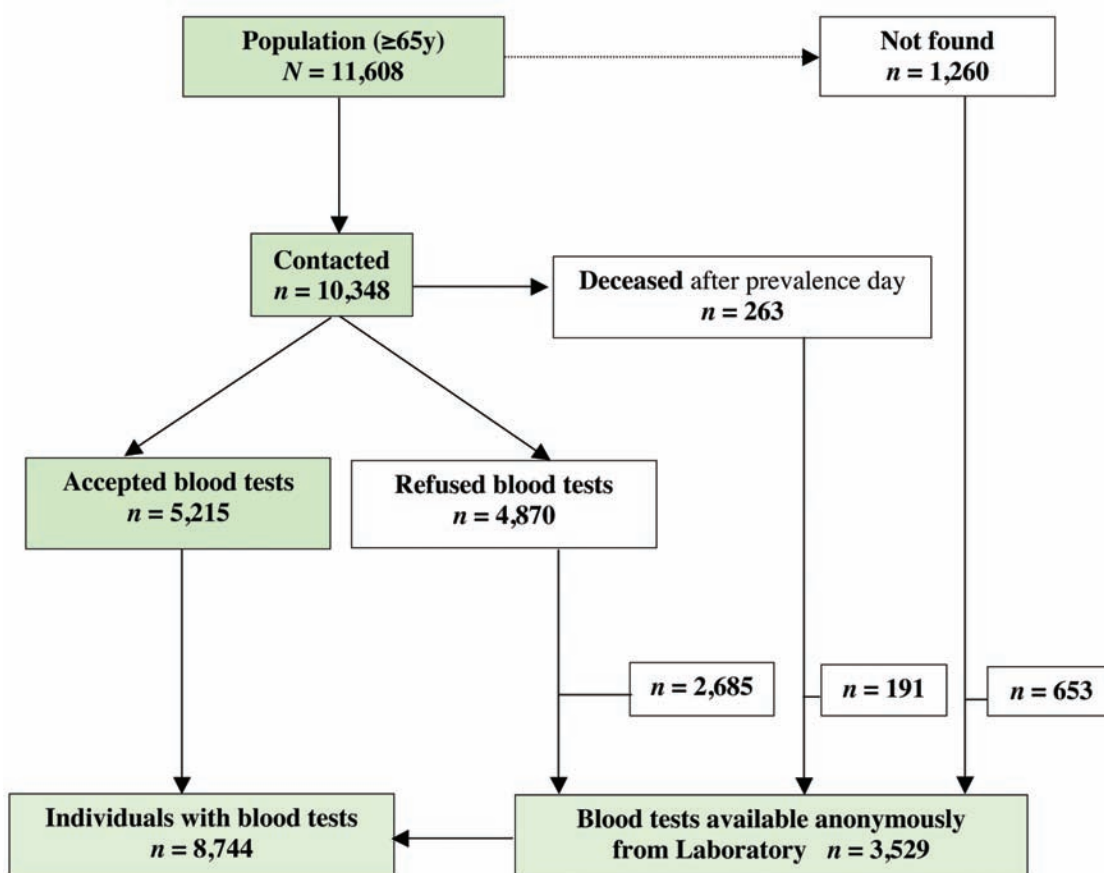
| | n | % |
|----------------------------------|-----------|------------|
| Infections | 3 | 3.5 |
| Autoimmune and infections | 5 | 5.8 |
| Autoimmune | 20 | 23.3 |
| Cancer and autoimmune | 4 | 4.7 |
| Cancer | 32 | 37.2 |
| Chronic non-infectious disorders | 17 | 19.8 |
| None | 5 | 5.8 |
| <i>All</i> | <i>86</i> | <i>100</i> |

Online Supplementary Table S3. Prevalence of mild grade anemia^a in the elderly in population-based studies.

| Study | Country | Age range | N. | Inclusion rate ^b (%) | Mild anemia prevalence (%) |
|---|---------------|-----------|-------|---------------------------------|----------------------------|
| Hobson <i>et al.</i> , 1953 ¹ | Great Britain | 64-86 | 399 | Not reported | ~ 11.0 |
| Parsons <i>et al.</i> , 1965 ² | Great Britain | 65+ | 208 | 77 | ~ 9.1 |
| Elwood <i>et al.</i> , 1971 ³ | Great Britain | 65+ | 533 | 82 | 9.4 |
| Milne <i>et al.</i> , 1972 ⁴ | Great Britain | 62-90 | 472 | 63 | ~ 8.5 |
| McLennan <i>et al.</i> , 1973 ⁵ | Great Britain | 65+ | 475 | ~ 65 | 12.8 |
| Hill, 1976 ⁶ | Great Britain | 65+ | 220 | 89 | 12.3 |
| Salive <i>et al.</i> , 1992 ⁷ | United States | 71+ | 3,946 | 60 | ~ 11.9 |
| Guralnick <i>et al.</i> , 2004 ⁸ | United States | 65+ | 4,199 | ~ 63 | 9.9 |
| Skjelbakken <i>et al.</i> , 2005 ⁹ | Norway | 65+ | 4,228 | 75 | ~ 6.9 |
| Present study | Italy | 65+ | 8,744 | 75 | 11.8 |

^aHemoglobin concentration: women: 10.0-11.9 g/dL; men: 10.0-12.9 g/dL. ^bCalculated or estimated from the initial population.

Online Supplementary Figure S1. Flow chart of the The “Health and Anemia” population-based study (2003-2008).



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