

RESEARCH ARTICLE

# Performance and comparability of laboratory methods for measuring ferritin concentrations in human serum or plasma: A systematic review and meta-analysis

Maria N. Garcia-Casal<sup>1\*</sup>, Juan P. Peña-Rosas<sup>1</sup>, Eloisa Urrechaga<sup>2</sup>, Jesus F. Escanero<sup>3</sup>, Junsheng Huo<sup>4</sup>, Ricardo X. Martinez<sup>1</sup>, Lucero Lopez-Perez<sup>1</sup>

**1** Evidence and Programme Guidance, Department of Nutrition for Health and Development, World Health Organization, Geneva, Switzerland, **2** Hospital Galdakao Usansolo, Galdakao, Spain, **3** Department of Pharmacology and Physiology, Faculty of Medicine, University of Zaragoza, Zaragoza, Spain, **4** Department of Food Science and Technology, Institute of Nutrition and Food Safety, Beijing, China

\* [garciasalm@who.int](mailto:garciasalm@who.int), [mngarciasasal@gmail.com](mailto:mngarciasasal@gmail.com)



**OPEN ACCESS**

**Citation:** Garcia-Casal MN, Peña-Rosas JP, Urrechaga E, Escanero JF, Huo J, Martinez RX, et al. (2018) Performance and comparability of laboratory methods for measuring ferritin concentrations in human serum or plasma: A systematic review and meta-analysis. PLoS ONE 13(5): e0196576. <https://doi.org/10.1371/journal.pone.0196576>

**Editor:** Pal Bela Szecsi, Holbæk Hospital, DENMARK

**Received:** June 28, 2017

**Accepted:** April 16, 2018

**Published:** May 3, 2018

**Copyright:** © 2018 Garcia-Casal et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Data Availability Statement:** All relevant data are within the paper and its Supporting Information files.

**Funding:** WHO received financial support from several sources including the International Micronutrient Malnutrition Prevention and Control (IMMPaCt) Program, Division of Nutrition, Physical Activity and Obesity at the US Centers for Disease Control and Prevention (CDC) (USA), the United

## Abstract

### Background

Different laboratory methods are used to quantify ferritin concentrations as a marker of iron status. A systematic review was undertaken to assess the accuracy and comparability of the most used methods for ferritin detection.

### Methods and findings

National and regional databases were searched for prospective, retrospective, sectional, longitudinal and case-control studies containing the characteristics and performance of at least one method for serum/plasma ferritin determinations in humans published to date. The analysis included the comparison between at least 2 methods detailing: sensitivity, precision, accuracy, predictive values, inter-methods adjustment, and use of international reference materials. Pooled method performance was analyzed for each method and across methods.

### Outcomes

Search strategy identified 11893 records. After de-duplication and screening 252 studies were assessed, including 187 studies in the qualitative analysis and 148 in the meta-analysis. The most used methods included radiometric, nonradiometric and agglutination assays. The overall within-run imprecision for the most reported ferritin methods was 6.2±3.4% (CI 5.69–6.70%; n = 171), between-run imprecision 8.9±8.7% (CI 7.44–10.35%; n = 136), and recovery rate 95.6% (CI 91.5–99.7%; n = 94). The pooled regression coefficient was 0.985 among all methods analyzed, and 0.984 when comparing nonradiometric and radiometric methods, without statistical differences in ferritin concentration ranging from 2.3 to 1454 µg/L.

States Agency for International Development (USAID) (USA), and the Bill & Melinda Gates Foundation (USA) for its work in nutrition. Donors are not involved in decisions related to WHO's normative work. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing interests:** Maria N Garcia-Casal - is employed as Scientist at the Department of Nutrition for Health and Development at the World Health Organization (WHO). Juan Pablo Peña-Rosas - is employed as Coordinator of the Department of Nutrition for Health and Development at WHO. Eloisa Urrechaga - WHO provided support for travel to meetings and fees for participation in this review. Jesus F Escanero - WHO provided support for travel to meetings and fees for participation in this review. Junsheng Huo - WHO provided support for travel to meetings. Ricardo X Martinez - is a WHO consultant and received consultancy fees, support for travel to meetings and fees for participation in this review. Lucero Lopez-Perez - is a WHO consultant and received consultancy fees, support for travel to meetings and fees for participation in this review. Disclaimer: Maria Nieves Garcia-Casal and Juan Pablo Peña-Rosas are full-time staff members at the WHO. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy or views of the WHO. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

## Conclusion

The laboratory methods most used to determine ferritin concentrations have comparable accuracy and performance. Registered in PROSPERO CRD42016036222.

## Introduction

Ferritin is an iron storage protein present in all cells of the organism. A small amount is found in plasma and serum, which is a reflection of iron stores in healthy individuals [1, 2]. A low serum ferritin concentration is usually regarded as an indicator of iron depletion, although the interpretation of normal or high serum ferritin values is challenging in the presence of acute or chronic inflammatory processes [3, 4], as ferritin is increased in iron overload states and inflammation [5, 6, 7].

Since ferritin concentration is widely used as marker of iron stores and status, it is important to determine if all methods commonly used to assess ferritin concentrations are capable of detecting and discriminating all possible iron statuses (deficiency, repletion, and overload), and to assess the comparability of methods across measurement systems. The World Health Organization (WHO) Expert Committee on Biological Standardization has established international reference materials to develop tests or to evaluate inter-laboratories performance. These reference materials for ferritin have been developed for calibrating working/secondary standards in the routine ongoing assays performed in laboratories and also for evaluating and standardizing new assays for ferritin quantification. At least three international reference materials have been developed: 1<sup>st</sup> (liver), 2<sup>nd</sup> (spleen) and 3<sup>rd</sup> (recombinant) [8, 9, 10].

WHO is updating its global guidelines on the use of serum and plasma ferritin thresholds for diagnosis of iron deficiency and risk of iron overload [11, 12]. While currently WHO recognizes that ferritin is typically assessed in serum or plasma with enzyme immunoassays after venous blood collection, there is no specific recommendation on variability among analytical methods and commutability [13].

The aim of the present review was to analyze the performance and comparability of the most common laboratory methods used for serum or plasma ferritin concentration determinations to detect iron deficiency, repletion or overload in order to inform decisions on the need for adjustments in the interpretation of serum or plasma ferritin using different methods. This was achieved by determining the sensitivity, specificity and predictive value between ferritin methods; assessing the variability of serum or plasma ferritin concentrations using different laboratory methods of detection; and reviewing the use of international standard materials of ferritin for calibration purposes and in global public health surveillance.

## Methods

### Search strategy and selection criteria

A search strategy and structured search was performed and updated in March 27, 2017. The search strategy for MEDLINE is shown in [Table 1](#). The strategy was adapted to the following international and regional databases: Cochrane Central Register of Controlled Trials, MEDLINE, Embase, CINAHL, Science Citation Index, Conference Proceedings Citation Index-Science, BIOSIS Previews, ARIF Reviews Database, PROSPERO, Database of Abstracts of Reviews of Effects (DARE), Cochrane Database of Systematic Review, IBECs, Scielo, Global

**Table 1. Ovid MEDLINE search strategy.**

1 exp Ferritins/ (17454) Note: Lines 1 to 4 are the terms describing the target "ferritin"
2 ferritin*.mp. (25116)
3 isoferritin*.mp. (328)
4 or/1-3 (25330)
5 exp Enzyme-Linked Immunosorbent Assay/ (131202) Note: Lines 5 to 30 are the terms for capturing the five index tests
6 Immunoassay/ (23984)
7 immunoassay*.tw. (51865)
8 assay*.tw. (758672)
9 Radioimmunoassay/ (64971)
10 radioimmunoassay.tw. (47406)
11 RIA.tw. (17348)
12 "Nephelometry and Turbidimetry"/ (6562)
13 turbidimetr*.tw. (8)
14 Nephelometr*.tw. (2416)
15 Luminescence/ (7001)
16 Luminescent Measurements/ (24362)
17 Luminescen*.tw. (12893)
18 chemiluminescen*.tw. (17107)
19 spectrometr*.tw. (160295)
20 (ELISA or CLIA or ECLIA).tw. (115556)
21 Colorimetry/ (18069)
22 colorimetr*.tw. (84)
23 Radiometry/ (28422)
24 radiometr*.tw. (3627)
25 quantum dot*.tw. (6160)
26 micro array*.tw. (790)
27 or/5-26 (1199654)
28 4 and 27 (2646)
29 Ferritins/du [Diagnostic Use] (283)
30 28 or 29 (2922)
31 exp animals/ not humans/ (4109551)
32 30 not 31 (2297)
33 Ferritin bound iron

<https://doi.org/10.1371/journal.pone.0196576.t001>

Index Medicus–AFRO, EMRO, LILACS, PAHO, WPRO, IMSEAR, IndMED, and Proquest Dissertations and Theses. There were no language or publication date restrictions.

The protocol “Accuracy and comparability of methods for measuring ferritin concentration to determine iron deficiency, repletion and overload” was registered in PROSPERO International prospective register of systematic reviews (9 March, 2016 under the number CRD42016036222 ([https://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42016036222](https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016036222)))

Prospective, retrospective, sectional, longitudinal and case-control studies containing the characteristics and performance of at least one method for serum or plasma ferritin determinations for human use were included, as well as studies evaluating the performance of two or more ferritin methods comparing the same human samples or using international reference materials. We also considered studies comparing homemade, commercial, automated or single equipment laboratory methods to determine: method type and sub-type, calibration to international reference material, limit of detection, reference interval, linearity and interferences.

Included studies contained data on participants of any age or gender that reported human serum or plasma ferritin concentrations in apparently healthy, iron deficient and/or iron overloaded populations. Studies from infection/inflammation settings, malaria areas, disaster or emergency areas, bacterial versus viral infections, acute versus chronic conditions, and data from diabetic, obese, overweight and/or, insulin-resistant individuals, were also included. Iron deficiency, iron repletion, and iron overload was defined by the trialists. If not specified, WHO cut-offs [13] were used.

The studies containing data using international reference materials (especially either of the WHO reference materials from spleen, liver or recombinant) to calibrate commercial assays, automated equipment or used in the routine ongoing assays performed in laboratories, were extracted, sub grouped and recorded in order to register the frequency of use in commercial assays and automated equipment developments, and in routine laboratory assays and surveys globally.

The primary outcomes were characteristics and performance indicators of ferritin methods: type (radiometric, nonradiometric, agglutination), sub-type (EIA, turbidimetric, chemiluminescent, RIA, IRMA), origin of the assay (homemade, commercial), detection equipment (single apparatus, automated multiple-analytes detection equipment), sensitivity, specificity, precision, limit of detection, recovery rate, within-run and between-run imprecision. Data comparing at least two methods for ferritin determination and extracted correlation coefficient, coefficient of agreement or Bland-Altman Plot or regression coefficients were also recorded. The use of international reference materials was also summarized including the origin, use for calibration while developing the assay or use on a routine basis.

## Data collection and analysis

The data retrieved in each search was screened independently by two authors to assess eligibility. Selected records were independently extracted using data extraction forms tested and approved by all authors in order to enhance consistency amongst reviewers. Disagreements at any stage of the eligibility assessment process were resolved through discussion and consultation with a third author.

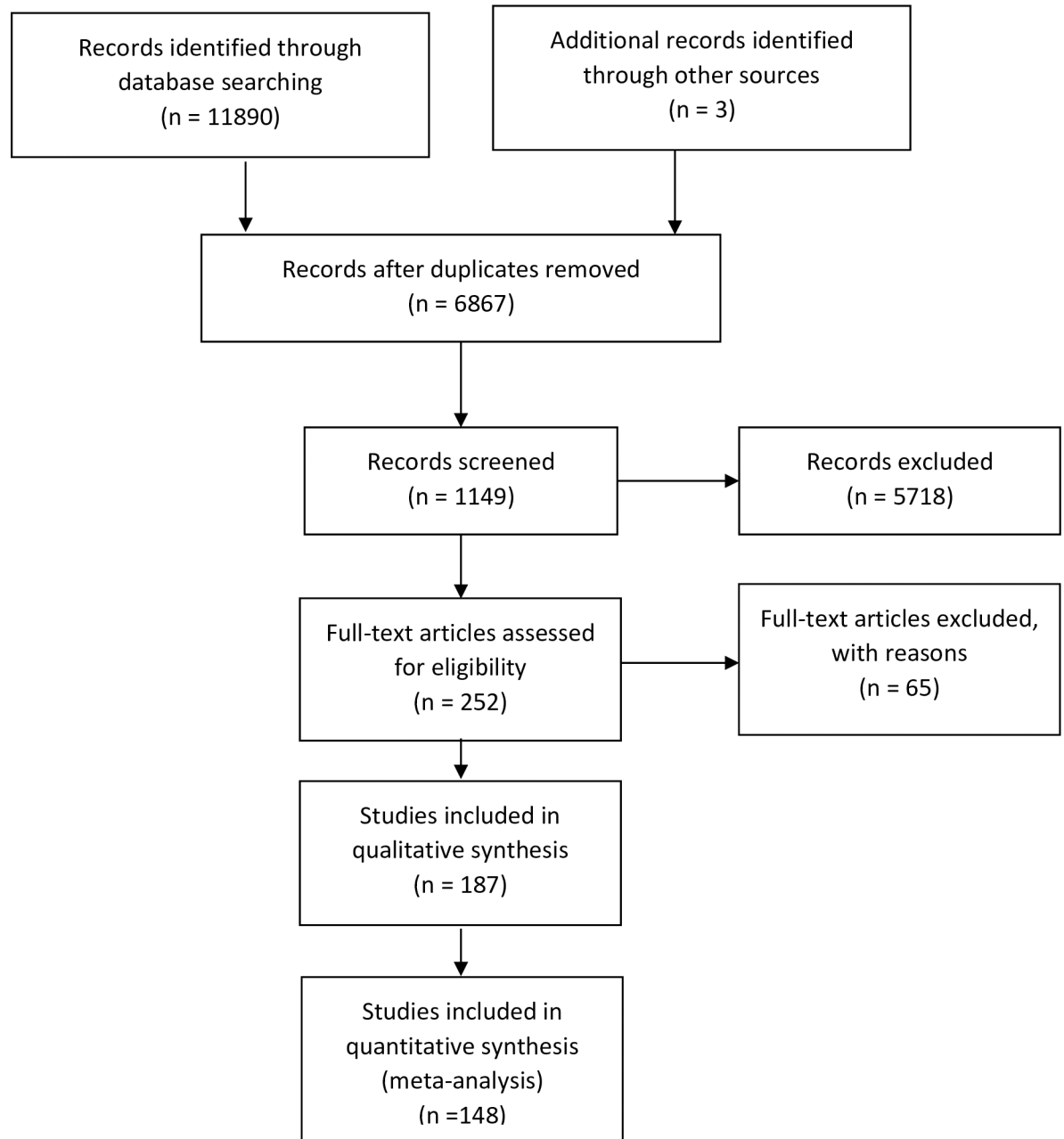
The information collected included: general information, sample size, baseline characteristics (iron status, age, sex, race, presence and severity of infection/inflammation), ferritin detection method(s) used, cutoff points used to define iron deficiency, repletion or overload, methodological details on ferritin quantification (method(s) used for ferritin determination(s) and the characteristics of the test already mentioned as outcomes.

We included a PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow-chart of study selection (Fig 1) [14].

The variability of ferritin determinations was assessed by: 1. intrinsic indicators, commonly used to assess the characteristics of a particular ferritin method (e.g. precision and accuracy); and 2. comparative indicators between two ferritin methods, such as correlation coefficient.

The intrinsic indicators chosen to characterize the different ferritin methods were within-run imprecision, between-run imprecision, recovery rate, minimal level of detection ( $\mu\text{g/L}$ ) and assay linearity.

The comparative indicators between different ferritin methods included correlation coefficient ( $\rho$ ), noise or disturbance term of the regression equation (intercept  $b$ ) and slope of the regression equation ( $m$ ). To assess comparability between methods we compute statistics of the corresponding linear regression equation parameters and fixed effects meta-analysis of the correlation. To estimate inter-methods adjustments, a search for laboratory assessment data was performed. The search included laboratory performance data or reports on internet and



**Fig 1. PRISMA flow-chart of study selection.**

<https://doi.org/10.1371/journal.pone.0196576.g001>

also directly contacted some laboratories to ask for the possibility of data sharing Bland-Altman plots and/or statistics were extracted if present in the selected studies.

The correlation coefficient between methods was performed by standard correlation fixed-effects meta-analysis, because the variance depends strongly on the correlation, the last is converted to the Fisher's z scale, and all analyses were performed using the transformed values. All statistical analysis was performed using Stata ([https://www.jmp.com/en\\_gb/](https://www.jmp.com/en_gb/)), MetaXL (<http://www.epigear.com/>) and CMA (<http://www.comprehensive.com>) softwares.

Originally, covariate analysis, development of Summary Receiver Operating Curves (SROC) and accuracy estimates were planned for the following groups: a) test type or sub-

type: radiometric, nonradiometric, agglutination, other; b) origin of the assay: homemade versus commercial c) detection equipment/system: single apparatus versus automated detection equipment; d) assay performance: variability and reproducibility; e) sample matrix: serum, plasma or erythrocytes; f) age group: infants (less than one year of age), children (two to 11.9 years of age), adolescents (12 to 18.9 years of age), adults (19 years of age or older); g) gender; h) vulnerability to iron deficiency: infants, women of reproductive age, pregnancy; i) body mass index (BMI); j) infection/inflammation: malaria area, emergency settings, groups of patients with inflammatory conditions; k) capability of both-ends detection: iron deficiency, sufficiency and overload; l) correlation of methods by publication year; m) calibration to international reference materials. The analyses were performed for the methods and subgroups with enough available data and included: test type or sub-type (radiometric, nonradiometric, agglutination); origin of the assay (homemade versus commercial); detection equipment/system (single apparatus versus automated detection equipment); assay performance (variability and reproducibility); limit of detection; calibration to international reference materials.

### External laboratory quality assessment data

Data on ferritin measurement precision from laboratory quality assessment programs was searched and extracted to compare reported between-laboratory means and coefficients of variation.

### Use of international reference materials

For assessing the use of international reference materials, we developed comparative tables for the most common used methods sub classified as homemade, commercial and automated.

For all analysis, selection of indicators was dictated by data availability and consistency. At least three studies reporting on a specific indicator detected by the same method type or sub-type were required to perform meta-analysis estimates. Differences between covariates were assessed by visual inspection; non-overlapping confidence intervals (CIs) suggested a statistically significant difference in treatment effect between the subsets.

## Results

The PRISMA flow chart of study selection is presented in [Fig 1](#). Eleven thousand eight hundred ninety three records were obtained from the search strategy depicted in [Table 1](#). From 252 records extracted, 187 studies were included in the qualitative analysis [8,10,15–199] and 148 in the meta-analysis [8,10,15,17,18,22,23,26,28,30–32,34–56,58–64,66–68,72,73,75,77–80,82–85,87–92,94–98,100–102,106–109,111–116,120–137,139–143,145,146,148–151,153–157,159–164,166–175,177,179–181,183,184,186–193,195–199]. Many of the studies included in the meta-analysis provided more than one entry for analysis (some of them compare and analyze up to 11 methods for ferritin determinations [95,112,139,145,193], resulting in some analysis including up to 233 entries. In order to summarize the information from each indicator, pooled estimates were performed for recovery rates and regression coefficients. The characteristics of the studies included in the meta-analysis are presented in [S1 Table](#), as supplementary material.

### Within-run imprecision for method type or sub-type, origin of the assay and detection equipment

For analysis of within-run imprecisions, the methods more commonly used were 94 nonradiometric immunoassays (including 25 enzyme linked immuno sorbent assay (ELISA) and 25 chemiluminescent), 59 radiometric (27 radioimmunoassays (RIA) and 32 immunoradiometric

**Table 2. Within-run imprecision of the methods commonly used for serum or plasma ferritin determinations grouped by method type and sub-type.**

Method type and sub-type <sup>1</sup>	Number of data entries	Mean CV <sup>3</sup> (%)	STD <sup>2</sup> (%)	95% confidence interval (%)	
				Lower limit	Upper limit
<b>Labelled nonradiometric</b>					
EIA	31	5.8	2.5	4.43	6.98
Fluorimetric	7	8.3	6.3	3.66	12.95
ELISA	25	7.5	3.3	6.24	8.80
Chemiluminescent	25	4.8	2.3	3.88	5.72
MEIA	5	4.3	1.8	2.64	5.87
RPIA	1	4.9			
<b>Labelled radiometric</b>					
RIA	27	7.5	4.0	5.97	8.98
IRMA	32	6.7	3.0	5.65	7.74
<b>Agglutination</b>					
Turbidimetric	13	4.3	3.1	2.57	2.94
Nephelometric	3	2.3	0.4	1.84	2.70
LPIA	1	3.1			
<b>Other</b>	1	5.4			
<b>All</b>	<b>171</b>	<b>6.2</b>	<b>3.4</b>	<b>5.69</b>	<b>6.70</b>

<sup>1</sup> EIA: Enzyme immunoassay; ELISA: Enzyme linked immunosorbent assay; MEIA: microparticle enzyme immunoassay; RIA: Radioimmune assay; IRMA: Immunoradiometric assay; LPIA Latex photometric immunoassay; RPIA: Radial partition immunoassay.

<sup>2</sup> Standard deviation.

<sup>3</sup> Coefficient of variance.

<https://doi.org/10.1371/journal.pone.0196576.t002>

assay (IRMA)), and 17 based on agglutination (including 13 turbidimetric and 3 nephelometric).

The overall mean within-run imprecision for the most reported ferritin methods was 6.2 ±3.4% (CI 5.69–6.70%; n = 171). The method with the highest within-run imprecision was the enzyme immunoassay with fluorometric detection (8.3±6.3%; CI 3.66–12.95%; n = 7), and the lowest variation was obtained with nephelometric methods (2.3± 0.4%; CI 1.84–2.70%; n = 3). Differences were not significant between methods except when comparing with nephelometry, although the sample size was only 3 data entries (Table 2).

Table 3 shows the mean within-run imprecision when grouping methods by type as nonradiometric, radiometric and agglutination; by the origin of the assay (homemade, commercial), and by detection equipment (single apparatus, automated detection equipment). As reported before, agglutination methods showed the lowest within-run imprecision (3.8±2.8%; 95% CI 2.5–5.17; n = 17), and radiometric methods the highest (7.1±3.5%; 95% CI 6.16–7.94 n = 59). Commercial assays had lower within-run imprecision s (5.9±3.3%; 95% CI 5.26–6.45; n = 115) than homemade kits (6.9±3.5%; 95% CI 5.96–7.82; n = 56), although differences were not statistically significant. Likewise, automated multiple-analytes detection equipment had lower within-run imprecision s (5.3±2.7%; 95% CI 4.67–5.86; n = 78), compared to single laboratory apparatus (7.0±3.7%; 95% CI 6.22–7.72; n = 93), but differences were not significant.

### Between-run imprecision for detection method, origin of the assay and detection equipment

For analysis of between-run imprecision the methods more commonly used were 75 nonradiometric immunoassays (including 25 ELISA and 17 chemiluminescent), 47 radiometric (22



**Table 3. Within-run imprecision of the methods commonly used for serum or plasma ferritin determinations grouped by method type, by origin of the assay and by detection equipment.**

	Number of data entries	Mean CV <sup>3</sup> (%)	STD <sup>1</sup> (%)	95% confidence interval (%)	
				Lower limit	Upper limit
<b>Method type</b>					
Labelled nonradiometric	94	6.1	3.2	5.43	6.74
Labelled radiometric	59	7.1	3.5	6.16	7.94
Agglutination	17	3.8	2.8	2.50	5.17
Other	1	5.4			
<b>All</b>	<b>171</b>	<b>6.2</b>	<b>3.4</b>	<b>5.69</b>	<b>6.70</b>
<b>Origin of assay</b>					
Commercial	115	5.9	3.3	5.26	6.45
Homemade	56	6.9	3.5	5.96	7.82
<b>Detection equipment</b>					
Automated	78	5.3	2.7	4.67	5.86
Single app <sup>2</sup>	93	7.0	3.7	6.22	7.72

<sup>1</sup> Standard deviation.

<sup>2</sup> Single apparatus.

<sup>3</sup> Coefficient of variance.

<https://doi.org/10.1371/journal.pone.0196576.t003>

RIA and 25 IRMA), and 14 based on agglutination (including 10 turbidimetric and 3 nephelometric).

The overall mean between-run imprecision for the most reported ferritin methods was 8.9 ± 8.7% (95% CI 7.44–10.35; n = 136). The method with the highest between-run imprecision was the nonradiometric immunoassay with fluorometric detection (24.8 ± 41.5%; 95% CI 0.00–61.21; n = 5), and the lowest variation was obtained with nephelometric methods (4.1 ± 0.1%; 95% CI 3.99–4.21; n = 3). Variations from chemiluminescent methods (6.9 ± 2.6%; 95% CI 5.70–8.14; n = 17) were not different from light passage ones. Differences were not significant between methods as the confidence intervals with the other assays have subtle intersections (Table 4).

When methods were grouped by type, agglutination methods showed the lowest between-run imprecision (4.1 ± 2.5%; 95% CI 2.81–5.43; n = 14), and nonradiometric methods the highest (9.5 ± 11.0%; 95% CI 7.03–12.03; n = 75), without differences with radiometric ones (9.3 ± 3.8%; 95% CI 8.21–10.39; n = 47). Between-run imprecisions from commercial assays (9.1 ± 10.1%; 95% CI 7.03–11.10; n = 95) were not different than from homemade assays (8.5 ± 3.4%; 95% CI 7.45–9.52; n = 41). Automated multiple-analytes detection equipment had between-run imprecisions (8.9 ± 12.2%; 95% CI 5.89–11.95; n = 62), not statistically different from single laboratory apparatus (8.9 ± 3.8%; 95% CI 7.99–9.74; n = 74) (Table 5).

### Recovery rate for method type and sub-type, origin of the assay and detection equipment

The pooled recovery rate for all assays evaluated (n = 94) was 95.6% (95% CI 91.5–99.7). When grouped by method type, agglutination methods showed the lower recoveries (88.1%; 95% CI 80.7–95.4; n = 18) compared to nonradiometric immunoassays that included 12 ELISA and 12 chemiluminescent methods (97.7%; 95% CI 92.1–103.29; n = 54) or to radioactive methods (103.8%; 95% CI 93.1–114.3; n = 22). There was no difference in recoveries between commercial and homemade assays (94.8%; 95% CI 89.9–99.7; n = 61 vs. 97.6%; 95% CI 89.9–105.2;



**Table 4. Between-run imprecision of the methods commonly used for serum or plasma ferritin determinations grouped by method type and sub-type.**

Method type and sub-type <sup>1</sup>	Number of data entries	Mean CV <sup>2</sup> (%)	STD <sup>3</sup> (%)	95% confidence interval (%)	
				Lower limit	Upper limit
<b>Labelled nonradiometric</b>					
EIA	24	8.1	3.7	7.21	10.06
Fluorimetric	5	24.8	41.5	0.00	61.21
ELISA	25	10.1	3.6	8.68	11.52
Chemiluminescent	17	6.9	2.6	5.70	8.14
MEIA	4	5.2	0.4	4.76	5.59
<b>Labelled radiometric</b>					
RIA	22	10.0	4.3	8.15	11.76
IRMA	25	8.7	3.3	7.45	10.00
<b>Agglutination</b>					
Turbidimetric	10	4.3	3.0	2.41	6.10
Nephelometric	3	4.1	0.1	3.99	4.21
LPIA	1	2.8			
<b>All</b>	<b>136</b>	<b>8.9</b>	<b>8.7</b>	<b>7.44</b>	<b>10.35</b>

<sup>1</sup> EIA: Enzyme immunoassay; ELISA: Enzyme linked immunosorbent assay; MEIA: microparticle enzyme immunoassay; RIA: Radioimmune assay; IRMA: Immunoradiometric assay; LPIA Latex photometric immunoassay; RPIA: Radial partition immunoassay.

<sup>2</sup> Coefficient of variance.

<sup>3</sup> Standard deviation.

<https://doi.org/10.1371/journal.pone.0196576.t004>

n = 33, respectively), or between automated multiple-analytes detection equipment and single laboratory apparatus (94.8%; 95% CI 89.7–99.7; n = 54 vs. 97.4%; 95% CI 90.3–104.5; n = 40, respectively).

The recovery rates did not changed significantly when data was analyzed by the ferritin concentration added. In studies spiking ferritin up to 100 µg/L (n = 32), recovery was 92.2%

**Table 5. Between-run imprecision of the methods commonly used for serum or plasma ferritin determinations grouped by method type, by origin of the assay and by detection equipment.**

Method type	Number of data entries	Mean CV <sup>3</sup> (%)	STD <sup>1</sup> (%)	95% confidence interval (%)	
				Lower limit	Upper limit
Labelled nonradiometric	75	9.5	11.0	7.03	12.03
Labelled radiometric	47	9.3	3.8	8.21	10.39
Agglutination	14	4.1	2.5	2.81	5.43
<b>All</b>	<b>136</b>	<b>8.9</b>	<b>8.7</b>	<b>7.44</b>	<b>10.35</b>
<b>Origin of assay</b>					
Commercial	95	9.1	10.1	7.03	11.10
Homemade	41	8.5	3.4	7.45	9.52
<b>Detection equipment</b>					
Automated	62	8.9	12.2	5.89	11.95
Single app <sup>2</sup>	74	8.9	3.8	7.99	9.74

<sup>1</sup> Standard deviation.

<sup>2</sup> Single apparatus.

<sup>3</sup> Coefficient of variance.

<https://doi.org/10.1371/journal.pone.0196576.t005>

(95% CI 85.0–99.3); 97.0% (95% CI 89.7–104.2) for concentrations up to 350 µg/L (n = 30), and 98.2% (95% CI 83.0–109.5) for concentrations up to 1000 µg/L (n = 25).

### Limit of detection

The lowest average levels of detection were found in nonradiometric methods (2.3±4.5µg/L; n = 72) and agglutination methods (2.6±2.5µg/L; n = 14), compared to radiometric methods (7.3± 12.5µg/L; n = 47). There was no significant difference in average lowest levels of detection between commercial and homemade kits (4.2± 9.4µg/L; n = 96 vs. 3.8± 5.5µg/L; n = 38, respectively), or between automated multiple-analytes detection equipment and single laboratory apparatus (2.6± 3.5µg/L; n = 63 vs. 5.5± 10.9µg/L; n = 71, respectively).

The highest average level of detection was found in agglutination methods 1454± 1517µg/L; n = 14), compared to nonradiometric (1171± 1145µg/L; n = 72), and radiometric methods (808±1068µg/L; n = 47). There was no significant difference in average highest levels of detection between commercial and homemade assays (1070± 1025µg/L; n = 96 vs. 1053± 1494µg/L; n = 38, respectively), or between automated multiple-analytes detection equipment and single laboratory apparatus (1151± 1068µg/L; n = 63 vs. 989± 1258µg/L; n = 71, respectively).

### Assay linearity for method type, origin of the assay and detection equipment

The most reported maximal ferritin concentrations that maintained assay linearity were 500 and 1000µg/L (11 out of 56 assays). The highest concentration reported to maintain linearity of the curve was 6000µg/L. The highest concentrations that maintained linearity (2000–6000µg/L) were no related to a particular method or equipment; they were found with radiometric, nonradiometric or homemade assays as well as with agglutination or commercial assays. Likewise, the lowest linearity concentration reported was 100µg/L, and it was not related to origin of the assay (commercial or homemade), but the 3 studies that reported such linearity threshold, were nonradiometric.

### Correlation between methods

**Table 6** shows a correlation of 0.981 between all methods analyzed. Correlation coefficient was 0.984 when comparing nonradiometric and radiometric methods.

The correlation coefficient was further analyzed at various serum ferritin concentrations. There were no statistically significant differences in correlation coefficients between methods when analyzing samples containing up to 300 µg/L (0.94± 0.06; 95% CI 0.928–0.961; n = 44), up to 800 µg/L (0.99± 0.01; 95% CI 0.984–0.993; n = 42), up to 1500 µg/L (0.98± 0.02; CI 0.972–0.985; n = 45) or even higher concentrations (0.98± 0.03; CI 0.961–0.989; n = 23).

**Table 6. Correlation coefficient fixed effects meta-analysis for all methods and comparison between nonradiometric and radiometric methods (pooled estimate computed using standard Fisher’s Z transform).**

Type of Assay	Correlation coefficient Estimate	95% confidence interval		Number of data entries
		Lower limit	Upper limit	
Nonradiometric vs nonradiometric	0.989	0.988	0.989	107
Nonradiometric vs radiometric	0.984	0.983	0.985	74
Radiometric vs radiometric	0.878	0.869	0.886	51
<b>All</b>	<b>0.981</b>	<b>0.980</b>	<b>0.981</b>	<b>233</b>

<https://doi.org/10.1371/journal.pone.0196576.t006>

### Intercept (b) and slope (m) of the regression equation

These comparative indicators were found in 85% of the selected articles (115/136), with 218 data entries. As seen in Table 7, intercept values were far from 0 although not significantly different from it for the comparisons between nonradiometric methods or between nonradiometric and radiometric methods, showing a high variability with standard deviations between 8.85 and 20.83 µg/L. For the three comparisons, slopes were close to 1.

### Agreement between laboratory methods

It is important to highlight that the use of the correlation, intercept, and slope indicators in our statistical analysis, only indicated the strength of the relationship or the linearity between compared methods, not the agreement between them. The most used agreement indicator Bland-Altman plots [200] and/or statistics, was only reported in seven studies [62, 68, 79, 115, 142, 162, 198] (S2 Table, supplementary material).

A recent study [115] found poor agreement (bias from -11.5 to 44 µg/L and  $\sigma$  higher than 25 µg/L) between ELISA vs microparticle enzyme immunoassay (MEIA) or chemiluminescence. Previously, two other studies [68, 162] found moderate agreement (bias from -8 to 3.7 µg/L and  $\sigma$  from 8.5 to 12 µg/L) between ELISA versus chemiluminescence and radiometric methods, respectively. Zhang 2015 [198], and Dipalo 2016 [62] found moderate to poor agreement between chemiluminescence (bias from 34 to 60 µg/L and  $\sigma$  from 12 to 71 µg/L), while Molinario 2015 [142] and Gomez 2000 [79] found good agreement between agglutination and chemiluminescent methods (bias from -6 to -7.9 µg/L and  $\sigma$  from 1.5 to 8 µg/L).

In these seven studies, the authors stated that when ferritin concentrations were below a certain threshold (75 µg/L for three of the studies) [68, 79, 162], the agreement improved considerably. These results cannot be generalized because of the low number of studies reporting this indicator, although illustrate the limitations in interchangeability, especially above certain ferritin concentrations.

### Laboratory assessment data

Data on ferritin measurement precision were obtained from four laboratory quality assessment programs, two reporting on between-laboratory means and coefficients of variation [201, 202], other [203] on reference range data (lowest limits for ferritin range) and the forth on commutability and deviation from the mean [126]. Based on the highest number of participating laboratories, a report from the XXI Laboratory Quality Assessment Program of the Spanish Society

Table 7. Mean and variance of the regression intercept and slope between nonradiometric and radiometric assays.

Type of Assay	Mean intercept ±SD	95% confidence interval		Number of data entries
		Lower limit	Upper limit	
<b>Intercept</b>	µg/L			
Nonradiometric vs nonradiometric	2.72±14.14	-0.070	5.500	99
Nonradiometric vs radiometric	-4.14±20.83	-8.919	0.640	73
Radiometric vs radiometric	3.99±8.85	1.487	6.496	48
<b>Slope</b>				
Nonradiometric vs nonradiometric	0.93±0.57	0.818	1.041	99
Nonradiometric vs radiometric	0.95±0.32	0.875	1.023	73
Radiometric vs radiometric	1.11±0.45	0.981	1.236	48

<https://doi.org/10.1371/journal.pone.0196576.t007>

of Clinical Biochemistry and Molecular Pathology in 2014 was selected for analysis of ferritin results [202].

One hundred and eighty eight laboratories participated in this round, and most of them used automated equipment. The methods used for detection in these automated equipment were immunoenzymatic with different antigen-antibody pairs and detection systems (chemiluminescence, agglutination). The confidence intervals and coefficient of variation calculated from this report are presented in **S3 Table** (supplementary material), showing a between-laboratory coefficient of variation from 7.52% to 13.10%, which is in agreement with our findings of a mean CV of 8.5% for EIA and 6.8% for chemiluminescence.

### Use of international reference materials

As shown in **S1 Table** (supplementary material), some of the studies report calibrating the assays to WHO or other international reference materials, although calibration data is not presented in the articles [8,10,18,36,38,45,54,62,78,79,85,95,112,115, 116, 126,131,136,137,139, 140,142,148,155,156,158,162,164,168,171,187,190]. There were no studies reporting the use of these materials on a laboratory routine basis. Only one study reported results from a serum pool 'spiked' with either the 1<sup>st</sup> and 2<sup>nd</sup> international standard for ferritin. Those sera were measured by 52 laboratories using five automated methods and the recovery of the target values was calculated. The recovery of the first international reference materials by three of the methods was between 104 and 129%; and to the second reference material was between 99 and 125%. Authors recommend manufacturers to calibrate their methods against the 3<sup>rd</sup> international standard (recombinant), and to periodically assess their methods relative to this standard as a means of avoiding assay drift over time [36].

### Discussion

Measurement of iron status in the general population is important to determine the prevalence and distribution of iron deficiency and overload, and thus to decide appropriate interventions, and to monitor and evaluate the impact and safety of implemented public health programmes.

The selection of a test that reflects real ferritin concentration and has been validated through the use of reference materials has important implications from the perspective of the individual and public health pathway. The comparability of results from patients for differential diagnosis of iron deficiency or risk for iron overload has important implications for clinical decisions and also the appropriate use of resources. It is important to determine whether a therapeutic decision and treatment is having the expected effect and is not causing harm, regardless of the laboratory method used. Likewise, in the planning and evaluation of public health interventions it is important to determine the iron status of the targeted population as well as the impact of a nutrition-specific or nutrition-sensitive intervention. If different laboratory methods give different results, this may lead to misinterpretation of the effects and lead to incorrect public health decisions. Additionally, it should be possible to compare data from different surveys performed years apart and performed by different methods.

There are various methods to determine serum, plasma or erythrocyte ferritin concentration. The vast majority of them are based in antigen-antibody reactions that are detected by different methods. The detection could be by radioactive counting or by color development using different enzyme-substrate pairs to measure color development at visible range. Also, light scattering or turbidimetric measurements have been developed as well as fluorescence emission. The first reported methods for ferritin determination were radioactive, using radioisotopes to label the antigen (IRMA) or the antibody (RIA) [16, 61]. Common colorimetric methods include peroxidase or glycosidase based color development [177, 204, 205]. Methods

based in agglutination and light passage could be turbidimetric or nephelometric [35, 206]. More recently, quantum dots, plasma-mass spectrometry, and micro array based technologies have been developed [207, 208].

Another milestone in the development of methods for ferritin determination was automation. Radioactive methods started as home made in a few laboratories, followed in few years by colorimetric tests. Both methodologies were improved and commercialized, making them widely available. More recently, automated equipment that allow the determination of various metabolites, including ferritin, have been developed [34, 157, 209]. The detection method for these equipment vary, but is mainly based on turbidimetry and chemiluminescence.

The evolution of routine medical laboratories is reflected in the different techniques applied for ferritin determination: the principle of the method used for detection has changed, as well as the use of automated equipment. Our results show that the methods used in the included studies and the use of automated or single apparatus equipment for detection, made no difference for ferritin determinations.

This analysis has limitations. It was not possible to identify a gold standard method for ferritin determinations. This precluded the possibility of comparing ferritin methods against a reference method or to develop 2x2 tables. Instead, individual method performance and comparisons between all available methods that contained consistent data were analyzed.

In most of the included studies there were no details on the characteristics of the human serum or plasma used to test or validate ferritin assays, and it was not possible to sub classify studies by iron status (deficiency, repletion or overload), physiological state, age, gender or inflammatory conditions of the samples used to describe or compare ferritin methods. In fact, many valuable studies do not report on the methods used to determine ferritin. A recent systematic review summarized the serum ferritin thresholds recommended by international professional organizations associations worldwide to define iron deficiency in different population groups [210]. There was no mention on the preferred or recommended laboratory methods or the commutability between them to interpret the results.

Although it was not possible to perform comparisons or meta-analysis, available studies report the use of WHO or other international reference materials while developing and calibrating an assay, but also to improve comparability between methods and assays components [10, 36, 87, 88, 96, 139, 140, 181]. Studies reporting on commercial, automated equipment refer the use of international reference materials for calibration while developing an assay [96]. One study on accuracy and precision of seven commercial kits for serum ferritin (3 RIAs and 4 IRMAs), demonstrate that the use of a reference ferritin standard improved the accuracy of serum ferritin determination, but did not eliminate the variability of the determinations particularly for high ferritin concentrations [95].

The main challenges identified with the development of this review were related to the variety of available methods and small practical differences between them, which resulted in a challenge for categorization of methods. Other important issue was the quality of publications, especially for automated and commercial assays. In many cases they were only reports or abstract to scientific meetings, that did not result in a posterior formal, complete publication. The use of a Diagnostic Test Accuracy (DTA) methods approach to develop this review was not possible due to the difficulty to unequivocally identify a gold standard method to perform comparisons.

Regarding statistical analysis, it was not possible to perform meta-analysis of important indicators such as Bland-Altman statistics (mean differences and corresponding variance), repeatability, high dose hook effect and carry over due to the limited amount and quality of data. These limitations also come from the fact that the studies were not trying to compare accuracies of existing methods, but focused on similarities between two methods that were

available to them. In fact, more than 98% of the included articles did not study methods agreement or use proper method comparison techniques such as Passing-Bablok regressions [112, 142], Spearman correlations, and concordance methods [62].

The results from this review show that the methods used to determine ferritin are comparable and there is not preferred /recommended laboratory method, although the risk for radioactive contamination and expensive equipment are important drawbacks of RIA and IRMA. For patient follow-up, public health surveys or evaluations of impact of interventions it is recommended that, once selected, the same ferritin method should be used during the different stages of the intervention.

International reference materials (e.g. WHO standard) should be used for calibration of all commercial assays and probably in the regular laboratory practice for periodical assessment of the reagents and equipment of the routine method used, providing that the reference material has been shown to be commutable for a particular assay. It is important that reference materials are commutable so the results from samples are equivalent among all procedures, in order to obtain results traceable to the reference system and without calibration bias among procedures. Laboratories performing ferritin determinations for patient care or for public health assessments should participate in national or regional quality control surveys.

## Supporting information

**S1 Table. Characteristics of the studies included in meta-analysis.**

(DOCX)

**S2 Table. Summary of studies reporting Bland-Altman (B-A) statistics: Mean and standard deviation of the regression intercept and slope between different detection techniques.**

(DOCX)

**S3 Table. Laboratory assessment data from a quality control program of the Spanish Society of Clinical Biochemistry and Molecular Pathology (2014).**

(DOCX)

**S1 File. PRISMA checklist ferritin methods.**

(DOC)

**S2 File. Review ferritin methods PROSPERO registration.**

(PDF)

## Acknowledgments

The review is the responsibility of the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development at the World Health Organization.

## Author Contributions

**Conceptualization:** Maria N. Garcia-Casal, Juan P. Peña-Rosas.

**Formal analysis:** Maria N. Garcia-Casal, Juan P. Peña-Rosas, Eloisa Urrechaga, Jesus F. Escanero, Ricardo X. Martinez, Lucero Lopez-Perez.

**Funding acquisition:** Juan P. Peña-Rosas.

**Investigation:** Maria N. Garcia-Casal, Eloisa Urrechaga, Jesus F. Escanero, Junsheng Huo, Ricardo X. Martinez, Lucero Lopez-Perez.

**Methodology:** Juan P. Peña-Rosas, Ricardo X. Martinez.

**Project administration:** Juan P. Peña-Rosas.

**Validation:** Maria N. Garcia-Casal.

**Writing – original draft:** Maria N. Garcia-Casal.

**Writing – review & editing:** Maria N. Garcia-Casal, Juan P. Peña-Rosas, Eloisa Urrechaga, Jesus F. Escanero, Junsheng Huo, Lucero Lopez-Perez.

## References

- Harrison PM, Arosio P. The ferritins: molecular properties, iron storage function and cellular regulation. *Bioch Biophys Acta—Bioenergetics* 1996; 1275(3): 161–203.
- Wang W, Knovich M, Coffman L, Torti F, Torti S. Serum ferritin: past, present and future. *Biochim Biophys Acta* 2010; 1800: 760–769. <https://doi.org/10.1016/j.bbagen.2010.03.011> PMID: 20304033
- Grant FK, Suchdev PS, Flores-Ayala R, Cole CR, Ramakrishnan U, Ruth LJ, et al. Correcting for inflammation changes estimates of iron deficiency among rural Kenyan preschool children. *J Nutr* 2012; 142(1):105–111. <https://doi.org/10.3945/jn.111.146316> PMID: 22157541
- Knowles J, Thurnham DI, Phengdy B, Houamboun K, Philavong K, Keomoungkhone I, et al. Impact of inflammation on the biomarkers of iron status in a cross-sectional survey of Lao women and children. *Brit J Nutr* 2013; 110(12): 2285–2297. <https://doi.org/10.1017/S000711451300158X> PMID: 23778021
- Jonker F, Boele van Hensbroek M, Leenstra T, Vet RJWM, Brabin BJ, Maseko N, et al. Conventional and novel peripheral blood iron markers compared against bone marrow in Malawian children. *J Clin Path* 2014; 67(8): 717–23. <https://doi.org/10.1136/clinpath-2014-202291> PMID: 24915849
- Jonker F, Calis J, Phiri K, Kraaijenhagen RJ, Brabin BJ, Faragher B, et al. Low hepcidin levels in severely anaemic Malawian children with high incidence of infectious diseases and bone marrow iron deficiency. *PLoS One* 2013; 8(12): e78964. <https://doi.org/10.1371/journal.pone.0078964> PMID: 24339866
- Nemeth E, Ganz T. Anemia of inflammation. *Hemat/Oncol Clin North America* 2014; 28(4): 671–681.
- Hamwi A, Endler G, Rubi K, Wagner O, Endler AT. Reference values for a heterogeneous ferritin assay and traceability to the 3rd international recombinant standard for ferritin (NIBSC Code 94/572). *Clin Chem Lab Med* 2002; 40(4): 365–370. <https://doi.org/10.1515/CCLM.2002.059> PMID: 12059077
- National Institute for Biological Standards and Control. WHO International Standard Ferritin, human, recombinant NIBSC code: 94/572. National Institute for Biological Standards and Control 2008; 2008: 1–2.
- Thorpe S, Walker D, Arosio P, Heath A, Cook J, Worwood M. International collaborative study to evaluate a recombinant L ferritin preparation as an International Standard. *Clin Chem* 1997; 43: 1582–1587. PMID: 9299937
- Garcia-Casal MN, Peña-Rosas JP, Pasricha SR. Rethinking ferritin cutoffs for iron deficiency and overload. *Lancet Haematol* 2014; 1(3): e92–94. [https://doi.org/10.1016/S2352-3026\(14\)00025-8](https://doi.org/10.1016/S2352-3026(14)00025-8) PMID: 27029234
- Garcia-Casal MN, Pasricha SR, Martinez RX, Lopez-Perez LD, Peña-Rosas JP. Serum or plasma ferritin concentration as an index of iron deficiency and overload. *Cochrane Database of Systematic Reviews* 2015; Issue 7. Art. No.: CD011817 <https://doi.org/10.1002/14651858.CD011817>
- World Health Organization. Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations. Geneva: World Health Organization, 2011.
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic and meta-analyses of studies that evaluate interventions: explanation and elaboration. *PLoS Medicine* 2009; 6(7):1–28.
- Abdul-Ahad W, Luther C, Knight W, Asithy D. An automated sandwich enzyme immunoassay for the measurement of human ferritin. *Clin Chem* 1992; 38: 1098 (abstr).
- Addison GM, Beamish MR, Hales CN, Hodgkins M, Jacobs A, Llewellyn P. An immunoradiometric assay for ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *J Clin Pathol* 1972; 25(4): 326–329. PMID: 5063755
- Aguanno J, McManus C. Evaluation of the new Abbott Ferrizyme assay for serum Ferritin. *Clin Chem* 1984; 30: 985 (abstr).



18. Akbas N, Schryver P, Algeciras-Schimmich A, Baumanna N, Block D, Budd J, Gaston S, Klee G. Evaluation of Beckman Coulter Dxl 800 immunoassay system using clinically oriented performance goals. *Clin Biochem* 2014; 47: 158–163.
19. Aksoy N, Tekin N, Binerotlu N, Serin N. Application of Sigma Metrics for immunoassay tests. *Clin Chem Lab Med* 2014; 52: S1573 (abstr).
20. Albertson D, Ali N. Clinical evaluation of serum ferritin by RIA. *Clin Chem* 1978; 24: 998 (abstr).
21. Alfrey CP. Serum ferritin assay. *Crit Rev Clin Lab Sci* 1978; 9: 179–208.
22. Alshawi A, Dawnay A, Landon J. A novel immunoradiometric assay for human-liver ferritin. *J Clin Path* 1983; 36: 440–444. PMID: [6403597](#)
23. Alshawi A, Dawnay A, Landon J. A two-site immunoradiometric assay with magnetizable particles: human liver ferritin as a model. *Clin Chem* 1984; 30: 38–41. PMID: [6690149](#)
24. Amarasiri F, Wilson G. Studies of the 'hook' effect in the one-step sandwich immunoassay. *J Immunol Meth* 1992; 151: 47–66.
25. Ambayya A, Su A, Osman N, Nik-Samsudin N, Khalid K, Chang K, et al. Haematological Reference Intervals in a Multiethnic Population. *PLoS One* 2014; 9: e91968. <https://doi.org/10.1371/journal.pone.0091968> PMID: [24642526](#)
26. Anaokar S, Garry PJ, Standefer JC. Solid phase enzyme immunoassay for serum ferritin. *Clin Chem* 1979; 25: 1426–1431. PMID: [378465](#)
27. Anaokar S, Fries P, Weiss S. Sensitive enzyme immunoassay for serum ferritin comparison with commercial radio immunoassays. *Clin Chem* 1981; 27: 1112–1113 (abstr).
28. Anderson M, Kelly A. Serum ferritin by a rapid and inexpensive enzyme linked immuno sorbent assay method. *Clin Chim Acta* 1981; 116: 405–408. PMID: [7296902](#)
29. Armbruster D, Jirinz D, Williams J. Evaluation of enhanced luminescence immunoenzymometric assays LIA for ferritin and free T4. *J Clin Lab Anal* 1989; 3: 78–83. PMID: [2659758](#)
30. Armenta R, Tarnowski T, Gibbons I, Ullman EF. Improved sensitivity in homogeneous enzyme immunoassays using a fluorogenic macromolecular substrate an assay for serum ferritin. *Anal Biochem* 1985; 146: 211–219. PMID: [3922243](#)
31. Assink H, Brouwer H, Blijenberg B, Leijnse B. The influence of the label on the quality of a solid phase immunoassay evaluation of a commercial ELISA enzyme linked immune-sorbent assay kit for serum ferritin. *J Clin Chem Clin Biochem* 1983; 21: 695–702. PMID: [6655446](#)
32. Barlow E, Beausang LA, Campbell J, Madden H, Miller T. A chemiluminescent immunoassay for measurement of ferritin. *Clin Chem* 1988; 34: 1162 (abstr).
33. Beamish M, Addison G, Jacobs A, Llewelli P, Hodgkins M, Hales C. Ferritin estimation by a radioimmunoassay technique—serum levels in normal subjects and patients with blood disorders. *Brit J Haematol* 1972; 22: 637 (abstr).
34. Bernard AM, Lauwerys RR. Continuous flow system for automation of latex immunoassay by particle counting. *Clin Chem* 1983; 29(6):1007–1011. PMID: [6342848](#)
35. Bernard A, Lauwerys R. Turbidimetric latex immunoassay for serum ferritin. *J Immunol Meth* 1984; 71(2):141–147.
36. Sheena Blackmore, Malcolm Hamilton, Anne Lee, Mark Worwood, Matthew Brierley, Alan Heath, et al. Automated immunoassay methods for ferritin: recovery studies to assess traceability to an international standard. *Clin Chem Lab Med* 2008; 46: 1450–1457. <https://doi.org/10.1515/CCLM.2008.304> PMID: [18844501](#)
37. Blick K, Fry H, Passey R. An evaluation of an automated ferritin assay using the VITEK systems kinetic-count-48. *Clin Chem* 1988; 34 (6):1173 (abstr).
38. Blunden RW, Farley J, Geary TD, Halliday JW, Hawley D, Rudzki Z. A report on two interlaboratory surveys of serum ferritin estimation. *Pathology* 1980; 12: 575–585. PMID: [7465254](#)
39. Borque L, Rus A, Del Cura J, Maside C, Escanero J. Automated quantitative nephelometric latex immunoassay for determining ferritin in human serum. *J Clin Lab Anal* 1992; 6: 239–244. PMID: [1403343](#)
40. Borque L, Rus A, Gaona N. Nephelometric latex immunoassay for determination of ferritin in human sera. [Spanish] Medida Nefelometrica de la concentracion de ferritina serica mediante un inmunoanálisis de microparticulas. *Rev Soc Esp Quim Clin* 1996; 15: 34–40.
41. Borque L. A sensitive, particle-enhanced assay for Ferritin on IMMAGE(R) Immunochemistry System. *Clin Chem* 1999; 45: A45 (abstr).
42. Borque L, Rus A, Bellod L, Seco M. Development of an automated immunoturbidimetric ferritin assay. *Clin Chem Lab Med* 1999; 37: 899–905. <https://doi.org/10.1515/CCLM.1999.133> PMID: [10596956](#)

43. Bradley CA, Crean DM, Posey YF, Parl FF. A comparison of radioimmunoassay vs. enzyme immunoassay measurement of ferritin concentration in premenopausal and postmenopausal females. *Clin Chem* 1987; 33: 1032 (abstr).
44. Brindle E, Stevens D, Crudder C, Levin C, Garrett D, Lyman C, Boyle D. A multiplex immunoassay method for simultaneous quantification of iron, vitamin A and inflammation status markers. *PLoS One* 2014; 9(12): e115164. <https://doi.org/10.1371/journal.pone.0115164> PMID: 25525806
45. Brotherton J. Ferritin another pregnancy-specific protein in human seminal plasma and amniotic fluid as estimated by six methods. *Andrologia* 1990; 22: 597–607. PMID: 2099678
46. Camara PD, Velletri K, Krupski M, Rosner M, Griffiths WC. Evaluation of the Boehringer Mannheim ES 300 immunoassay analyzer and comparison with enzyme immunoassay fluorescence polarization immunoassay and radioimmunoassay methods. *Clin Biochem* 1992; 25: 251–254. PMID: 1525980
47. Camilo A, Waltrick D, Pereira C. Linearity study to define the Analytical Measurement Range (AMR) for immunoassays. *Clin Chem* 2014; 1: S53.
48. Chida R, Tsujino D, Yamada Y, Kondo Y, Someya K, Sasaki Y. Fundamental and clinical evaluation of measuring plasma ferritin levels by magnetic ferritin kit. *Radioisotopes* 1985; 34: 87–90. PMID: 3991925
49. Chou PP, Toms RA, King B, Chang A. Evaluation of ferritin on the Abbott IMX automated immunoassay systems. *Clin Chem* 1989; 35:1099 (abstr).
50. Christopher CW, Chou PP, Bailey JL. Evaluation of Ciba-Corning Magic Lite ferritin assay. *Clin Chem* 1990; 36: 1189 (abstr).
51. Cloete H, Kleinhans W, Mansvelt EPG. Ferritin assay performed on the Technicon Immuno 1 analyser using serum and plasma samples. *Clin Lab Haematol* 2002; 24: 281–283. PMID: 12358888
52. Conradie JD, Mbhele BE. Quantitation of serum ferritin by enzyme-linked immunosorbent assay (ELISA). *Suid-Afrikaanse Tydskrif Vir Geneeskunde. S Afr Med J* 1980; 57: 282–287. PMID: 6996142
53. Cozzi A, Levi S, Bazzigaluppi E, Ruggeri G, Arosio P. Development of an immunoassay for all human isoforms and its application to serum ferritin evaluation. *Clin Chim Acta* 1989; 184: 197–206. PMID: 2692876
54. Cragle LK, Coleman PF. Solid-phase enzyme immunoassay for the quantitation of ferritin in human serum. *S Afr Med J* 1986; 32:1142 (abstr).
55. Datta P, Dai J. A new, high-throughput assay for ferritin, evaluated on the ADVIA chemistry systems. *Clin Chem* 2011; 1: A111
56. Datta P, Eilert M, Becker D. An automated chemiluminescent assay for ferritin on the IMMULITE. *S Afr Med J*. 1992; 38:1089 (abstr).
57. Dawson DW, Fish DI, Shackleton P. The accuracy and clinical interpretation of serum ferritin assays. *Clinical and Laboratory Haematol* 1992; 14: 47–52.
58. Dcosta M, Feld R, Laxdal V, Trundle D, Collinworth W. A multicenter evaluation of the Boehringer-Mannheim ES-300 immunoassay system. *Clin Biochem* 1993; 26: 51–57. PMID: 8448840
59. Dempster WS, Knight GJ, Jacobs P. Evaluation of the RAMCO kit for serum ferritin assay. *S Afr Med J* 1979; 56: 1132–1133 (abstr). PMID: 550454
60. Denend AR, Zan GT, Murthy HMS, Lamotte GB. A rapid and sensitive immunoradiometric assay for the determination of serum ferritin. *Clin Chem* 1986; 32: 1148 (abstr).
61. Deppe W, Joubert S, Naidoo P. Radio immunoassay of serum ferritin. *J Clin Path (London)* 1978; 31 (9): 872–877.
62. Dipalo M, Gnocchi C, Aloe R, Lippi G. Comparison of the novel Maglumi ferritin immunoluminometric assay with Beckman Coulter Dxl 800 ferritin. *LaboratoriumsMedizin* 2016; 40(3): 221–223.
63. Donnell MC, Kahn DC, Peterson JW. Comparison of 4 ferritin radioassay test systems. *Clin Chem* 1980; 26:1065 (abstr).
64. Dunn CDR, Boden DJ. 3 commercial immuno radiometric kit assays for serum ferritin evaluated. *Clin Chem* 1981; 27: 1280–1283. PMID: 7237798
65. Dupuy A, Debarge L, Poulain M, Badiou S, Ross M, Cristol JP. Determination of serum ferritin using immunoturbidimetry or chemiluminescent detection in comparison with radioimmunoassay a compendium of a methodological juxtaposition. *Clin Lab* 2009; 55: 207–15. PMID: 19728554
66. Ellisor C. Comparison of two methods for ferritin assay. *Clin Chem* 1986; 32: 1066 (abstr).
67. Patrick Englebienne, Van Hoonacker Anne Valsamis Joseph. Rapid homogeneous immunoassay for human ferritin in the Cobas Mira using colloidal gold as the reporter reagent. *Clin Chem* 2000; 46: 2000–2003. PMID: 11106337

68. Erhardt Juergen G, Estes John E, Pfeiffer Christine M, Biesalski Hans K, Craft Neal E. Combined measurement of ferritin, soluble transferrin receptor, retinol binding protein, and C-reactive protein by an inexpensive, sensitive, and simple sandwich enzyme-linked immunosorbent assay technique. *J Nutr* 2004; 134: 3127–3132. <https://doi.org/10.1093/jn/134.11.3127> PMID: 15514286
69. Flowers CA, Kuizon M, Beard JL, Skikne BS, Covell AM, Cook JD. A serum ferritin assay for prevalence studies of iron deficiency. *Am J Hematol* 1986; 23: 141–152. PMID: 3529940
70. Flowers Carol H, Cook James D. Dried plasma spot measurements of ferritin and transferrin receptor for assessing iron status. *Clin Chem* 1999; 45: 1826–1832. PMID: 10508130
71. Forman DT, Vye MV. Immuno radiometric serum ferritin concentration compared with stainable bone marrow iron as indices to iron stores. *Clin Chem* 1980; 26: 145–147. PMID: 7356550
72. Fortier R, Twomey S, McGrath WP. Enzyme immunoassay for serum ferritin method evaluation and comparison to radio immunoassay. *Clin Chem* 1978; 24:1017 (abstr).
73. Fortier RL, McGrath WP, Twomey SL. Enzyme labeled immuno sorbent assay for serum ferritin method evaluation and comparison with 2 radioassays. *Clin Chem* 1979; 25: 1466–1469. PMID: 455688
74. Fortier RL. Ferritin by IRMA enzyme linked immuno sorbent assay or radio immunoassay? Factors to consider in the choice. *Clin Chem* 1980; 26: 1063 (abstr).
75. Gaida U, Wood WG. Establishment and evaluation of immunometric assays for the determination of human ferritin in serum using enzyme luminescent and time-resolved fluorescent labels. *Fres J Anal Chem* 1992; 343: 180–181.
76. George H, Wabner A, Flamenbaum W. Serum ferritin radio immunoassay a comprehensive clinical evaluation of a commercial method. *Clin Chem* 1979; 25: 1135 (abstr).
77. Ghielmi S, Pizzoccolo C, Iacobello C. Methodological effects on the quantitation of serum ferritin by radio- and enzymoimmunoassays. *Clin Chim Acta* 1982; 120: 285–294. PMID: 7074965
78. Goldie DJ, Thomas MJ. Measurement of serum ferritin by radio immunoassay. *Ann Clin Biochem* 1978; 15: 102–108. <https://doi.org/10.1177/000456327801500123> PMID: 637507
79. Gomez F, Simo J, Camps J, Cliville X, Bertran N, Ferre N, et al. Evaluation of a particle-enhanced turbidimetric immunoassay for the measurement of ferritin: 76. Application to patients participating in an autologous blood transfusion program. *Clin Biochem* 2000; 33: 191–196. PMID: 10913517
80. Goodnow T, Timmons R, Koski K, Soto A, Kennedy S, Evans S. Radial partition immunoassay monitoring ferritin levels in serum and plasma. *Clin Chem* 1986; 32: 1143 (abstr).
81. Grail A, Hancock B, Harrison P. Serum ferritin in normal individuals and in patients with malignant lymphoma and chronic renal failure measured with 7 different commercial immunoassay techniques. *J Clin Pathol (London)* 1982; 35: 1204–1212.
82. Guerra-Shinohara E, Paiva R, Santos H, Sumita N, Mendes M, Nunez L, et al. Determinacao da ferritina serica por dois metodos imunologicos automatizados. *Rev Bras Anal Clin* 1998; 30: 39–40 (abstr).
83. Guilleux F, Wagner A. A new radio immunoassay of serum ferritin use of Iodine-125 labeled human spleen antigen and a solid phase 2nd antibody. *Int J Nuc Med Biol* 1981; 8: 17–26.
84. Haden B, Cragle L, Kubasik N, Cook J. Comparison of eight immunoassay procedures for ferritin in human serum. *Clin Chem* 1987; 33: 958 (abstr).
85. Hallberg L, Bengtsson C, Lapidus L, Lindstedt G, Lundberg PA, Hulten L. Screening for iron-deficiency—an analysis based on bone-marrow examinations and serum ferritin determinations in a population-sample of women. *Brit J Haematol* 1993; 85: 787–798.
86. Hamilton MS, Blackmore S, Lee A. Variable recovery of the 3rd international ferritin standard 94/572 shown by UKNEQAS haematitics survey of ferritin immunoassays. *Brit J Haematol* 2004; 125: 60 (abstr).
87. Harries H, Shankland D, Henley R. An automated-assay for serum ferritin. *Med Lab Sci* 1985; 42: 230–232. PMID: 4046769
88. Hashida S, Ishikawa E. Detection of one milliatomole of ferritin by novel and ultrasensitive enzyme immunoassay. *J Biochem (Tokyo)* 1990; 108: 960–964.
89. Haux P, Dubois H, McGovern M, Stockmann W, Ehrhardt V, Kattermann R. Evaluation of the Tinaquant ferritin assay on the Boehringer Mannheim-Hitachi 704 system. *Clin Chem* 1988; 34: 1174 (abstr).
90. Hendriks HA, Kortlandt W, Verweij WM. Analytical performance comparison of five new generation immunoassay analyzers. *Nederlands Tijdschrift voor de Klinische Chemie* 2000; 25: 170–177.
91. Hebert S, Hillock R. A rapid and sensitive radio immunoassay for serum ferritin. *Clinical Chemistry* 24: 998 (1978).

92. Herrera J, Offe M, Ashwood ER. Ferritin assay on the Becton Dickinson affinity. *Clin Chem* 1992; 38: 1041 (abstr).
93. Hoover D, Goad E, Feldkamp C, Patt D. Ferritin radio immunoassay evaluation abnormalities in Scatchard plots. *Clin Chem* 1978; 24: 998–999 (abstr).
94. Hubl W, Zogbaum M, Boyd J, Savory J, Schubert M, Meyer D, et al. Evaluation of analytical methods and workflow performance of the Architect Ci-8200 integrated serum/plasma analyzer system. *Clin Chim Acta* 2005; 357: 43–54. <https://doi.org/10.1016/j.cccn.2005.01.032> PMID: 15963793
95. Iacobello C, Ghielmi S, Belloli S, Arosio P, Albertini A. Use of a reference standard to improve the accuracy and precision of seven kits for determination of ferritin in serum. *Clin Chem* 1984; 30: 298–301. PMID: 6692540
96. Iacobello C, Ruggeri G, Signorini C, Di Cello GC, Albertini A. A semi-automated ELISA for serum ferritin determination. *Clin Chem* 1986; 32: 899 (abstr).
97. Ihara K, Watanabe N. Development of a highly sensitive enzyme immunoassay for serum ferritin and its application for serodiagnosis of iron deficiency anemia. *Sapp Med J* 1987; 56: 503–516.
98. Imagawa M, Yoshitake S, Ishikawa E, Niitsu Y, Urushizaki I, Kanazawa R, et al. Development of a highly sensitive sandwich enzyme immunoassay for human ferritin using affinity purified anti ferritin labeled with beta d galactosidase from escherichia-coli. *Clin Chim Acta* 1982; 121: 277–290. PMID: 6809359
99. Imagawa M, Hashida S, Ishikawa E, Niitsu Y, Urushizaki I, Kanazawa R, et al. Comparison of beta-d galactosidase EC-3.2.1.23 from escherichia-coli and horseradish peroxidase as labels on anti-human ferritin FAB' by sandwich enzyme immunoassay technique. *J Bioch (Tokyo)* 1984; 96: 659–664.
100. International Committee for Standardization in Hematology (ICSH). Preparation, characterization and storage of human ferritin for use as a standard for the assay of serum ferritin. *Clin Lab Haemat* 1984; 6: 177–191.
101. International Committee for Standardization in Hematology (ICSH). Proposed international standard of human ferritin for the serum ferritin assay. *Br J Haematol* 1985; 61: 61–64. PMID: 4052332
102. Ishikawa E, Imagawa M, Yoshitake S, Niitsu Y, Urushizaki I, Inada M, et al. Major factors limiting sensitivity of sandwich enzyme-immunoassay for ferritin, immunoglobulin-e, and thyroid-stimulating hormone. *Ann Clin Biochem* 1982; 19: 379–384. <https://doi.org/10.1177/000456328201900511> PMID: 6814337
103. Ishikawa K, Narita O, Saito H, Kato K. Determination of ferritin in urine and in serum of normal adults with a sensitive enzyme immunoassay. *Clin Chim Acta* 1982; 123: 73–82. PMID: 6749338
104. Jacobs A, Peters S, Bauminger ER, Eikelboom J, Ofer S, Rachmilewitz EA. Ferritin concentration in normal and abnormal erythrocytes measured by immuno radiometric assay with antibodies to heart and spleen ferritin and Moessbauer spectroscopy. *Brit J Haematol* 1981; 49: 201–208.
105. Jagannathan N, Thiruvengadam C, Ramani P, Premkumar P, Natesan A, Sherlin HJ. Salivary Ferritin as a Predictive Marker of Iron Deficiency Anemia in Children. *J Clin Ped Dent* 2012; 37: 25–30.
106. Jennifer S, Rainer F, Barbara P, Susann N, Christiane G, Kathrin B, et al. Comparison of different immuno-luminometric methods. *Clin Chem Lab Med* 2014; 52: S1649 (abstr).
107. Jirinz DC, Scarbrough R, Williams J. Evaluation of fluorometric enzyme immunoassay for ferritin. *Clin Chem* 1988; 34: 1153 (abstr).
108. Johnson F, Klonizchi W, Worthy TE. Application of the Microgenics Cedia(r) ferritin assay to the BM/Hitachi-911. 20th National Meeting, Clinical Ligand Assay Society, April 26–30, 1994, Kissimmee, Florida: Syllabus 1994; 106 (abstr).
109. Jones BM, Worwood M. Automated immunoradiometric assay for ferritin. *J Clin Path* 1975; 28: 540–542. PMID: 1150895
110. Jones BM, Worwood M. An immuno radiometric assay for the acidic ferritin of human heart application to human tissues cells and serum. *Clin Chim Acta* 1978; 85: 81–88. PMID: 647967
111. Kahn DC, Peterson JW. A rapid double antibody radio immunoassay for human ferritin. *Clin Chem* 1979; 25: 1135 (abstr).
112. Kamei D, Tsuchiya K, Miura H, Nitta K, Akiba T. Inter-method variability of ferritin and transferrin saturation measurement methods in patients on haemodialysis. *Therap dialysis* 2017; 21(1): 43–51.
113. Kanamori I, Matsuo S, Higuchi C, Ichikawa H, Kimura T, Nakano S, et al. [Fundamental studies on the determination of serum ferritin by a radioimmunoassay kit]. *Radioisotopes* 1983; 32: 77–80. PMID: 6306736
114. Kano M, Tachibana R, Sato Y, Ito Y. Development of a new homogeneous immunoassay for Ferritin with ultra-sensitivity. *Clin Chem* 2013; 1: A220.

115. Karakochuk C, Whitfield K, Rappaport A, Barr S, Vercauteren S, McLean J, Hou K, Talukder A, Houghton L, Bailey K, Boy E, Green T. Comparison of four immunoassays to measure serum ferritin concentrations and iron deficiency prevalence among non-pregnant Cambodian women and Congolese children. *Clin Chem Lab Med* 2017; 55(1): 65–72. <https://doi.org/10.1515/cclm-2016-0421> PMID: [27337742](https://pubmed.ncbi.nlm.nih.gov/27337742/)
116. Khosravi MJ, Chan MA, Bellem AC, Diamandis EP. A sensitive time-resolved immunofluorometric assay of ferritin in serum with monoclonal antibodies. *Clin Chim Acta* 1988; 175: 267–276. PMID: [3416487](https://pubmed.ncbi.nlm.nih.gov/3416487/)
117. Kim HS, Kang HJ, Whang DH, Lee SG, Park MJ, Park JY, et al. Lot-to-lot Reagent Variation in Immunoassay: Retrospective Analysis of Daily Quality Control Results. *J Lab Med Qual Ass* 2010; 32: 243–253.
118. Kim HS, Kang H, Dong H, Whang D, Gyu S. Analysis of Reagent Lot-to-Lot Comparability Tests in Five Immunoassay Items. *Ann Clin Lab Sci* 2012; 42(2): 165–173 PMID: [22585613](https://pubmed.ncbi.nlm.nih.gov/22585613/)
119. Kimiyama H, Takabe M. Serum ferritin determination by means of radioimmunoassay technique improved rapid method and normal reference value. *Radioisotopes* 1985; 34: 91–94. PMID: [3991926](https://pubmed.ncbi.nlm.nih.gov/3991926/)
120. Kimura F, Miyoshi S, Mishima Y, Shigeto N, Fukuda T, Yamahara S, et al. Development and evaluation of a quantitative lateral flow immunoassay for the detection of ferritin as point-of-care testing. *Am J Hematol* 2013; 88: E173 (abstr).
121. Konig B, Oed M, Kunz A, Schlett R, Mack M. LIAISON Ferritin—an automated chemiluminescent immunoassay for the determination of Ferritin. *Anticancer Res* 1999; 19: 2739–2741. PMID: [10470232](https://pubmed.ncbi.nlm.nih.gov/10470232/)
122. Konijn AM, Levy R, Link G, Hershko C. A rapid and sensitive enzyme linked immuno sorbent assay for serum ferritin employing a fluorogenic substrate. *J Immunol Meth* 1982; 54: 297–308.
123. Koseki J, Niitsu Y, Goto Y, Urushizaki I. [An evaluation of Spac Kit for serum ferritin measurement (author's transl)]. *Radioisotopes* 1979; 28: 639–641. PMID: [531244](https://pubmed.ncbi.nlm.nih.gov/531244/)
124. Kotajima N, Ishizaka M, Oshitani S, Fukumura Y, Ushijima Y, Murakami M. Latex agglutination test for ferritin measurement. *J Clin Lab Anal* 2003; 17: 223–228. <https://doi.org/10.1002/jcla.10096> PMID: [14614745](https://pubmed.ncbi.nlm.nih.gov/14614745/)
125. Kousaka T, Tomida K, Koujida Y, Endo K, Konishi J, Torizuka K. Fundamental and clinical evaluation of magnetic ferritin kit. *Radioisotopes* 1984; 33: 883–886. PMID: [6528069](https://pubmed.ncbi.nlm.nih.gov/6528069/)
126. Kristensen G, Rustad P, Berg J, Aakre K. Analytical bias exceeding desirable quality goal in 4 out of 5 common immunoassays: Results of a native single serum sample external quality assessment program for cobalamin, folate, ferritin, thyroid-stimulating hormone, and free t4 analyses. *Clin Chem* 2016; 62(9): 1255–1263. <https://doi.org/10.1373/clinchem.2016.258962> PMID: [27384539](https://pubmed.ncbi.nlm.nih.gov/27384539/)
127. Kubasik NP, Cordy PA, Murray C, Sine HE, Mayer TK, Dsouza JP. Evaluation of a new ferritin enzyme-immunoassay (EIA) based on monoclonal-antibodies. *Clin Chem* 1987; 33: 958–959 (abstr).
128. Kubo A, Takagi Y, Ando Y, Yamashita S, Kinoshita F, Hashimoto S. [An immunoradiometric assay for ferritin in normal subjects and cancer patients (author's transl)]. *Radioisotopes* 1978; 27: 730–733. PMID: [746177](https://pubmed.ncbi.nlm.nih.gov/746177/)
129. Kubota R, Kanamori K, Kawai Y, Sakai N, Shiba K. Evaluation of the newly-developed serum ferritin measurement system, Point Reader<sup>TM</sup> and point Strip<sup>TM</sup> ferritin. *Clin Chem* 2014; 1: S88.
130. Kwiatkowski M, Buehler R. Paramagnetic solid-phase radioimmunoassay for ferritin. *Clin Chem* 1984; 30: 984 (abstr).
131. Lavigne L, Merrifield S, Foster K, Fitzgerald N, Saul R, Metzmann E. A rapid self-contained immunoassay for human ferritin. *Clin Chem* 1992; 38: 1081 (abstr).
132. Lee M, Burgett MW. A solid phase enzyme immunoassay for the quantitation of serum ferritin. *Clin Chim Acta* 1981; 112: 241–246. PMID: [7016377](https://pubmed.ncbi.nlm.nih.gov/7016377/)
133. Lee M, Chang J, Carlson D, Burgett M. A biotin-avidin enzyme immunoassay for the quantitation of serum ferritin. *Clin Chim Acta* 1985; 147: 109–116. PMID: [3886204](https://pubmed.ncbi.nlm.nih.gov/3886204/)
134. Lee C-Y, Leung WY, Tung JK. Applications of a monoclonal antibody to human ferritin in various immunoassays. *Biotech Appl Biochem* 1987; 9: 31–38.
135. Marc Letellier, Ann Levesque, Francine Daigle, Andrew Grant. Performance evaluation of automated immunoassays on the Technicon Immuno 1 system. *Clin Chem* 1996; 42: 1695–1701. PMID: [8855156](https://pubmed.ncbi.nlm.nih.gov/8855156/)
136. Lipschitz DA, Skikne BA, Thompson C. Precision and accuracy of serum ferritin measurements. *Am J Clin Nutr* 1981; 34: 951–956. <https://doi.org/10.1093/ajcn/34.5.951> PMID: [7234722](https://pubmed.ncbi.nlm.nih.gov/7234722/)



137. Johannes Lotz, Gerd Hafner, Winfried Prellwitz. Reference values for a homogeneous ferritin assay and traceability to the 3rd international recombinant standard for ferritin (NIBSC code 94/572). *Clin Chem Lab Med* 1999; 37: 821–825. <https://doi.org/10.1515/CCLM.1999.123> PMID: 10536931
138. Mejia LA, Viteri FE. Ferritin concentrations in plasma from capillary (finger prick) blood and venous blood compared. *Clin Chem* 1983; 29: 871–873. PMID: 6839470
139. Milman N, Graudal N, Juuljorgensen B, Bentzon MW. Calibration of the Amersham-ferritin-RIA kit using the WHO human liver ferritin International Standard 80/602. *Eur J Clin Chem Clin Biochem* 1994; 32: 41–42 (abstr). PMID: 8167193
140. Milman N, Juul-Jørgensen B, Bentzon MW. Calibration of Abbott AxSYM Ferritin kit using the WHO Human Liver Ferritin International Standard 80/602. *Eur J Clin Chem Clin Biochem* 1997; 35(8): 631–632 (abstr). PMID: 9298354
141. Mitsuma T, Chaya M, Kato T, Murakami K, Nakao N. The measurement of serum ferritin by radioimmunoassay method the evaluation of magnetic ferritin kit. *Radioisotopes* 1984; 33: 804–807. PMID: 6522661
142. Molinaro R, Autilio C, Pocino K, Daloso P, Di Leva S, Zuppi C, Antenucci M. Analytical evaluation of a new liquid immunoturbidimetric assay for the determination of ferritin in serum. *Clin Chem Lab Med* 2015; 53(12): E351–E353. <https://doi.org/10.1515/cclm-2015-0270> PMID: 26087064
143. Murthy Jayasimha N, Hicks Jocelyn M, Soldin Steven J. Evaluation of the technicon immuno I random access immunoassay analyzer and calculation of pediatric reference ranges for endocrine tests, T-uptake, and ferritin. *Clin Biochem* 1995; 28: 181–185. PMID: 7628078
144. Muylle L, Blockx P, Becquart D, Vandevyver F. Ferritin concentration in serum, erythrocytes, polymorphs and mononuclear-cells in healthy people by immunoradiometric assays with monoclonal and polyclonal antibodies. *Eur J Nuclear Med* 1984; 9: A76 (abstr).
145. Ng R, Brown B, Valdes R. Three commercial methods for serum ferritin compared and the high-dose “hook effect” eliminated. *Clin Chem* 1983; 29(6): 1109–1113. PMID: 6851105
146. Novembrino C, Porcella A, Conte D, de Vecchi A F, Buccianti G, Lonati S, et al. Erythrocyte ferritin concentration: analytical performance of the immunoenzymatic IMx-Ferritin (Abbott) assay. *Clin Chem Lab Med* 2005; 43: 449–453. <https://doi.org/10.1515/CCLM.2005.079> PMID: 15899663
147. O’Broin S, McCarthy N. Ferritin assays on the Beckman Access using EDTA-plasma samples. *Int J Lab Hematol* 2010; 32: e186–187 (abstr). <https://doi.org/10.1111/j.1751-553X.2009.01151.x> PMID: 19254347
148. Picelli G, Moutal C, Meunier V, Fleury B, Aubry C. Performance of the ferritin assay on BIOMERIEUX VIDAS. *Clin Chem* 1992; 38: 1085 (abstr).
149. Pierson-Perry JF, Freehafer SV, Moran WJ, Vaidya HC, Tuhy PM. Analytical performance of a method for ferritin on the DuPont ACA plus immunoassay system. *Clin Chem* 1994; 40: 1020 (abstr).
150. Pocekay J. A new highly sensitive ferritin EIA for the Bio-Rad RADIUS system. *Clin Chem* 1992; 38: 1079 (abstr).
151. Polson RJ, Kenna JG, Shears IP, Bomford A, Williams R. Measurement of ferritin in serum by an indirect competitive ELISA. *Clin Chem* 1988; 34: 661–664. PMID: 3359597
152. Pootrakul P, Skikne BS, Cook JD. The use of capillary blood for measurements of circulating ferritin. *Am J Clin Nutr* 1983; 37: 307–310. <https://doi.org/10.1093/ajcn/37.2.307> PMID: 6823894
153. Prior TW, Beinlich CJ, Gruemer HD. Analytical evaluation of immunoenzymetric assays for serum ferritin. *Clin Chem* 1985; 31: 972 (abstr).
154. Ramakrishnan K, Sackrison J, Todtleben J. A simple solid-phase chemiluminescence assay for ferritin. *Clin Chem* 1991; 37: 1027 (abstr).
155. Ramm GA, Duplock LR, Powell LW, Halliday JW. Sensitive and rapid colorimetric immunoenzymometric assay of ferritin in biological samples. *Clin Chem* 1990; 36: 837–840. PMID: 2357818
156. Ranjitkar P, Turtle C, Harris N, Holmes D, Pyle-Eilola A, Maloney D, Greene D. Susceptibility of commonly used ferritin assays to the classic hook effect. *Clin Chem Lab Med* 2016; 54(2): E41–E43. <https://doi.org/10.1515/cclm-2015-0604> PMID: 26351953
157. Raymond A, Hanbery J, Trundle DS. Evaluation of four assays on the Ciba corning ACS 180 automated chemiluminescence system. *Clin Chem* 1992; 38: 1055 (abstr).
158. Revenant MC, Beaudonnet A. Serum ferritin determination by enzyme-immunoassay—importance of sample dilution (the hook effect). *Clin Chem* 1982; 28: 253–254 (abstr). PMID: 7035002
159. Revenant MC. Sandwich enzyme immunoassay for serum ferritin with poly propylene test tubes as the solid phase. *Clin Chem* 1983; 29: 681–683. PMID: 6403260

160. Revenant MC, Goudable J, Beaudonnet A, Mailliavin A, Pichot J, Monnet L. Determination of serum ferritin by a one-step immunoenzymoassay, and comparison of four liver-ferritin standards. *Clin Chem* 1985; 31: 640–642 (abstr). PMID: [3884184](#)
161. Robinson CA Jr, Stabler TV, Ketchum CH. Comparison of ferritin by two non-isotopic methods with IRMA. *Clin Chem* 1991; 37: 1038 (abstr).
162. Rohner R, Zeder C, Zimmermann MB, Hurrell RF. Comparison of manual and automated ELISA methods for serum ferritin analysis. *J Clin Lab Anal* 2005; 19: 196–198. <https://doi.org/10.1002/jcla.20077> PMID: [16170808](#)
163. Sampson M, Glickman J, Ruddel M, Murray N, Elin R, Zweig M. A comparison of four methods for the determination of ferritin. *Clin Chem* 1994; 40: 1055 (abstr).
164. Schneider MC, Heath V, Ziegler S, Crews V, Vallejo R. A new extended range automated non-isotopic immunoassay for the determination of serum ferritin on the affinity system. *Clin Chem* 1991; 37: 1036 (abstr).
165. Schrott W, Nebyla M, Meisterova L, Pribyl M. Fast ferritin immunoassay on PDMS microchips. *Chem Papers* 2011; 65: 246–50.
166. Shimakawa A, Kano M, Tachibana R, Ito, Y. Evaluation of the performance characteristics of a new assay for Ferritin on Toshiba 2000FR. *Clin Chem* 2014; 1: S101.
167. Shindelman J, Singh H, Hertle V, Davoudzadeh F, Lingenfelter D, Loor R, et al. Homogeneous enzyme immunoassay for measurement of human ferritin using recombinant enzyme fragments. *Clin Chem* 1992; 38: 1078–1079 (abstr).
168. Signo P, Barassi A, Novario R, d'Eiril Gi. Preliminary evaluation of the performance of a new, highly sensitive commercial immunoassay for serum ferritin determination. *Clin Chem Lab Med* 2005; 43: 883–885. <https://doi.org/10.1515/CCLM.2005.149> PMID: [16201902](#)
169. Simo J, Joven J, Cliville X, Sans T. Automated latex agglutination immunoassay of serum ferritin with a centrifugal analyzer. *Clin Chem* 1994; 40: 625–629. PMID: [8149621](#)
170. Simonsen R, Sebek L, Moster J, Osikowicz G, Brandt D. Microparticle enzyme immunoassays for creatine kinase MB and ferritin on the Abbott AxSYM system. *Clin Chem* 1993; 39: 1979 (abstr). PMID: [8375084](#)
171. Skikne BS, Linpisarn S, Cook JD. An evaluation of monoclonal antibodies for serum ferritin measurements. *Am J Clin Nutr* 1984; 40: 346–350. <https://doi.org/10.1093/ajcn/40.2.346> PMID: [6465064](#)
172. Smith C, Fleisher M, Schwartz MK. Performance characteristics of the Sanofi Access immunoassay analyzer. *Clin Chem* 1994; 40: 1052–1053 (abstr).
173. Spillane D, O'Mullane J. Development of an affinity-column-mediated enzyme-linked immunosorbent assay for ferritin. *Clin Chim Acta* 1998; 273: 81–87. PMID: [9620472](#)
174. Standefer J, Limmity A, Ito M, Anaokar S. Evaluation of an automated latex photometric immunoassay for serum ferritin. *Clin Chem* 1993; 39: 1250 (abstr).
175. Steele BW, Wang E, Palmer-Toy DE, Killeen AA, Elin RJ, Klee GG. Total long-term within-laboratory precision of cortisol, ferritin, thyroxine, free thyroxine, and thyroid-stimulating hormone assays based on a College of American Pathologists fresh frozen serum study: do available methods meet medical needs for precision? *Arch Pathol Lab Med* 2005; 129: 318–322. [https://doi.org/10.1043/1543-2165\(2005\)129<318:TLWPOC>2.0.CO;2](https://doi.org/10.1043/1543-2165(2005)129<318:TLWPOC>2.0.CO;2) PMID: [15737024](#)
176. Steen G, Klerk A, van der Laan K, Eppens EF. Evaluation of the interference due to haemoglobin, bilirubin and lipids on Immulite 2500 assays: a practical approach. *Ann Clin Biochem* 2011; 48: 170–175. <https://doi.org/10.1258/acb.2010.010187> PMID: [21355012](#)
177. Theriault L, Page M. A solid phase enzyme immunoassay for serum ferritin. *Clin Chem* 1977; 23: 2142–2144. PMID: [912877](#)
178. Thorpe SJ. The development and role of international biological reference materials in the diagnosis of anaemia. *Biologicals* 2010; 38: 449–458. <https://doi.org/10.1016/j.biologicals.2010.02.007> PMID: [20338782](#)
179. Timmons R, Soto A. A radial partition sandwich enzyme-immunoassay for ferritin. *Clin Chem* 1984; 30: 984 (abstr).
180. Trefz G, Achana E, Eberle J, Erismann R, Schweizer E. Unimate 3 FERR an immunoturbidimetric assay for the measurement of ferritin in human serum on COBAS instruments. *Clin Chem* 1994; 40: 997 (abstr).
181. Van Oost BA, Willekens FL, van Neerbos BR, Van Den Beld B. Implications of using different tissue ferritins as antigens for ferritin in serum: four radioimmunoassay kits compared. *Clin Chem* 1982; 28: 2429–2433. PMID: [6183028](#)



182. van Eijdsden M, van der Wal MF, Hornstra G, Bonsel GJ. Can whole-blood samples be stored over 24 hours without compromising stability of C-reactive protein, retinol, ferritin, folic acid, and fatty acids in epidemiologic research? *Clin Chem* 2005; 51: 230–232 (2005). <https://doi.org/10.1373/clinchem.2004.042234> PMID: 15613719
183. Vasileff J, Phan Y, Peele J. Evaluation of the Abbott AxSYM random/continuous access immunoassay analyzer. *Clinical Chemistry* 1994; 40:1054 (abstr).
184. Velazquez F, Upham S, Altaffer M, Philipp K. Enzyme-linked immunosorbent ferritin assay compared to an isotopic assay. *Clin Chem* 1993; 39: 1166 (abstr).
185. Velletri K, Krupski CM, Rosner M, Griffiths WC. Evaluation of the BMD ES300 immunoassay analyzer and comparison with EIA FPIA and RIA methods. *Clin Chem* 1991; 37: 970 (abstr).
186. Vernet M, Revenant MC, Bied A, Naudin C, Jauneau M, Olivier F, et al. Rapid determination of ferritin in serum by the stratus fluoroenzymometric assay. *Clin Chem* 1989; 35: 672–673 (abstr). PMID: 2649278
187. Vernet M, Valadoux C, Doffoel S. Evaluation of analytical performances of ferritin assay with Vitros ECi(R). *Ann Biol Clin* 1999; 57: 351–355.
188. Wang XL, Tao GH, Meng YH. Nanogold hollow microsphere-based electrochemical immunosensor for the detection of ferritin in human serum. *Microchim Acta* 2009; 167: 147–152.
189. Watanabe N, Niitsu Y, Ohtsuka S, Koseki JI, Kohgo Y, Urushizaki I, et al. Enzyme immunoassay for human ferritin. *Clin Chem* 1979; 25: 80–82. PMID: 104809
190. Wells T, Hawkins K, Danielzadeh B, Hammad N, Shimizu S. Development of a ferritin assay on the Vista immunoassay system. *Clin Chem* 1993; 39: 1261 (abstr).
191. Wide L, Birgegard G. A solid phase radio immunoassay method for ferritin in serum using Iodine-125 labeled ferritin. *Upsala J Med Sci* 1977; 82:15–20. <https://doi.org/10.3109/03009737709179053> PMID: 20078269
192. Wilding P, Senior M, Hendricks M, Sawycky R. A multicenter evaluation of the TECHNICON IMMUNO 1 system assays for reproductive hormones and ferritin. *Clin Chem* 1993; 39: 1219 (abstr).
193. Wood W. A comparison of eleven commercial kits for the determination of serum ferritin levels. *J Clin Chem Clin Biochem* 1981; 19: 947–952. PMID: 7288374
194. Worwood M, Thorpe SJ, Heath A, Flowers CH, Cook JD. Stable lyophilized reagents for the serum ferritin assay. *Clinical and Laboratory Haematology* 1991; 13: 297–305. PMID: 1794232
195. Yajima T. An improved method for serum ferritin determination and the variation of serum ferritin values in patients suffering from traffic trauma. *J Nippon Med School* 1984; 51: 25–37.
196. Yamamoto M, Sekiya K, Ikegami T, Sato Y, Saito Y, Maeda M, et al. A fully automated chemiluminescent enzyme immunoassay for ferritin. *Clin Chem* 1992; 38: 1087 (abstr).
197. Zhang S, Jiao K, Chen H, Wang M. Detection of ferritin in human serum with a MAP-H<sub>2</sub>O<sub>2</sub>-HRP voltammetric enzyme-linked immunoassay system. *Talanta* 1999; 50: 95–101. PMID: 18967699
198. Zhang X, Lu Y, Ma L, Peng Q, Qin X, Li S. A comparison study between two analyzers for determining serum ferritin. *Clin Lab* 2015; 61(1–2): 169–174. PMID: 25807651
199. Zhang X, Wang S, Hu M, Xiao Y. An immunosensor for ferritin based on agarose hydrogel. *Biosen Bioelec* 2006; 21: 2180–2183.
200. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986; 1(8476):307–310. PMID: 2868172
201. Report of the XX Programa de Garantía Externa de la Calidad de Bioquímica (proteínas) de la Sociedad Española de Bioquímica Clínica y Patología Molecular, 2013. <http://www.seqc.es/>
202. Report of the XXI Programa de Garantía Externa de la Calidad de Bioquímica (proteínas) de la Sociedad Española de Bioquímica Clínica y Patología Molecular, 2014, Page 163. <http://www.seqc.es/>
203. Report of the United Kingdom National External Quality Assessment Service UKNEQAS, July 2007. <http://www.ukneqas.org.uk/content/PageServer.asp?S=287263466&C=1252&Type=N&AID=16&contact=p>
204. Denisov VN, Metelitsa DI. Immunoenzyme system for ferritin detection. *Biotekhnologiya* 1990; 5: 85–88.
205. Terry A, Spencer D, Krauth G. A non-isotopic immuno-enzymetric assay for serum ferritin. *Clin Chem* 1987; 33: 936 (abstr).
206. Limet JN, Collet-Cassart D, Magnusson CGM, Sauvage P, Cambiaso CL, Masson PL. Particle counting immunoassay of ferritin *Clin Chem Lab Med* 1982; 20(3): 141–146.

207. Liu P, Na N, Liu T, Huang L, He D, Hua W, et al. Ultrasensitive detection of ferritin in human serum by Western blotting based on quantum dots-labeled avidin-biotin system. *Proteomics* 2011; 11(17): 3510–3517. <https://doi.org/10.1002/pmic.201000742> PMID: 21751359
208. Yin JY, Sun J, Huang J, Li WX, Huo JS. Study on the method of quantitative analysis of serum ferritin and soluble transferrin receptor with protein microarray technology. *Biomed Environ Sci* 2012; 25(4): 430–439. <https://doi.org/10.3967/0895-3988.2012.04.008> PMID: 23026523
209. Pankratz T, Leflar C, Loreili W. A fluorometric enzyme immunoassay for ferritin using chromium dioxide magnetic particles as solid phase. *Clin Chem* 1988; 34: 1278–1279 (abstr).
210. Peyrin-Biroulet L, Williet N, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. *Am J Clin Nutr* 2015; 102(6):1585–1594. <https://doi.org/10.3945/ajcn.114.103366> PMID: 26561626