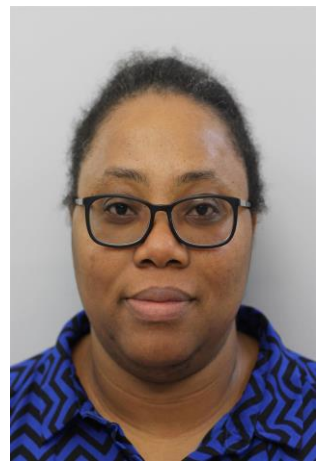




**B. L. Ilesanmi-Oyelere<sup>1,2</sup>, M. McConnell<sup>3</sup>, S. Mros<sup>3</sup>, J. Coad<sup>1</sup>, N. C. Roy<sup>2,4,5</sup>, M. C. Kruger<sup>1,2</sup>,**  
1.Massey Institute of Food Science and Technology, Massey University, Tennent Drive,  
Palmerston North, New Zealand  
2.Riddet Institute, Massey University, Palmerston North, New Zealand  
3.Microbiology and Immunology, University of Otago, Dunedin, New Zealand  
4.Food Nutrition & Health Team, AgResearch Grasslands, Palmerston North, New Zealand  
5.High-Value Nutrition National Science Challenge, Auckland, New Zealand



# Cytokine Production, Ferritin Levels and Bone Health in Postmenopausal women

## ACKNOWLEDGEMENTS

Supporting Technical Staff  
Palmerston North Medical Research Foundation  
Allen Foundation, USA  
Fonterra Cooperative Group Ltd.

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## Background

Osteoporosis is a major public health concern which, as a result of the demineralisation of bones, leads to increased fracture risks<sup>1</sup>. Studies have indicated that low-grade inflammation, due to the effect of pro-inflammatory cytokines such as interleukin (IL)-1 $\beta$  and IL-6 impairs DNA repair and leads to cellular and immunological senescence as well as biological ageing<sup>2</sup>. Ferritin is an acute phase reactant which also serves as a marker of inflammation.

In postmenopausal women, low-grade inflammation, coupled with reduced oestrogen levels, lead to an increase in bone resorption which partly counters increase in bone formation<sup>3</sup> resulting in increased bone turnover.

## Materials and Methods

Eighty-six postmenopausal women aged between 54 and 81 years participated in the “Bug’n’Bones”, a cross-sectional study. Body composition and bone mineral density were measured using the Dual energy X-ray Absorptiometry (DXA). Cytokine assays were prepared according to the BioLegend® LEGENDplex™ Multi-Analyte Flow Assay kit instructions and measured using a Beckman Coulter’s Gallios flow cytometer. Plasma ferritin levels were measured using an electro-chemiluminescence immunoassay (ECLIA).

Massey University Human Ethics Committee approved this study: Southern A, Application 17/17.

## Results

Figure 1 provides an overview of the mean levels of plasma inflammatory markers in the whole group of women. As illustrated, monocyte chemoattractant protein (MCP-1) was observed at the highest levels amongst all the cytokines measured.

Meanwhile the results of analysis of variance among the groups according to the osteoporotic classification are shown in Fig.2. The plasma levels of IFN- $\alpha$ 2 ( $P=0.027$ ), IFN- $\gamma$  ( $P=0.009$ ), IL-12p70 ( $P=0.049$ ), IL-33 ( $P=0.048$ ) and MCP-1 ( $P=0.05$ ) were significantly higher in the osteoporotic group compared to the osteopenic or normal groups. However, rather surprisingly, plasma CRP levels ( $P=0.044$ ) was significantly lower amongst the osteoporotic than osteopenic and normal groups.

In addition, Fig.3 and Fig.4 showed that IL-10 and IL-33 levels were significantly higher in women with low ferritin levels ( $P=0.01$  and  $P=0.02$  respectively).

Fig.1: Mean Plasma Levels of Inflammatory Markers

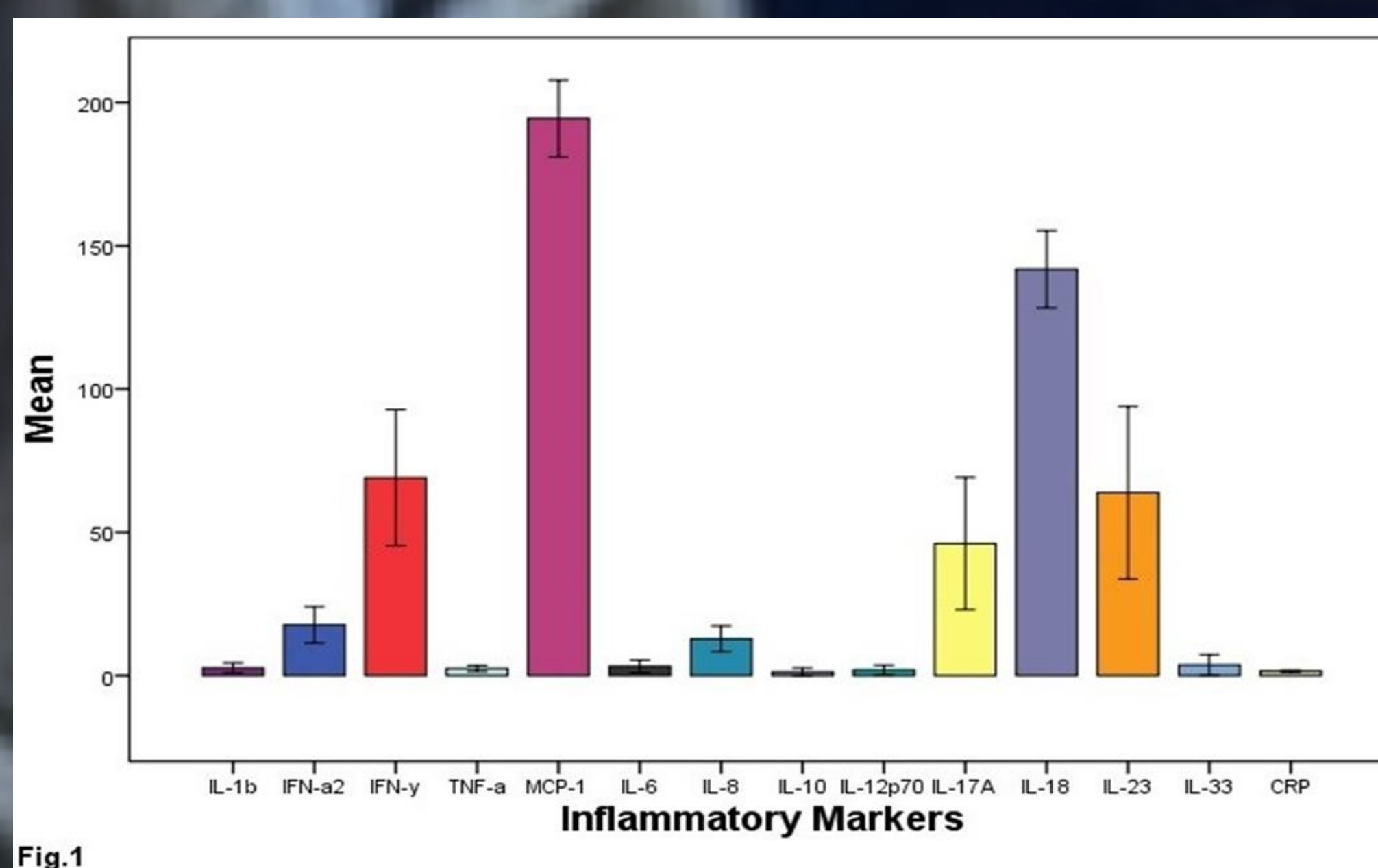
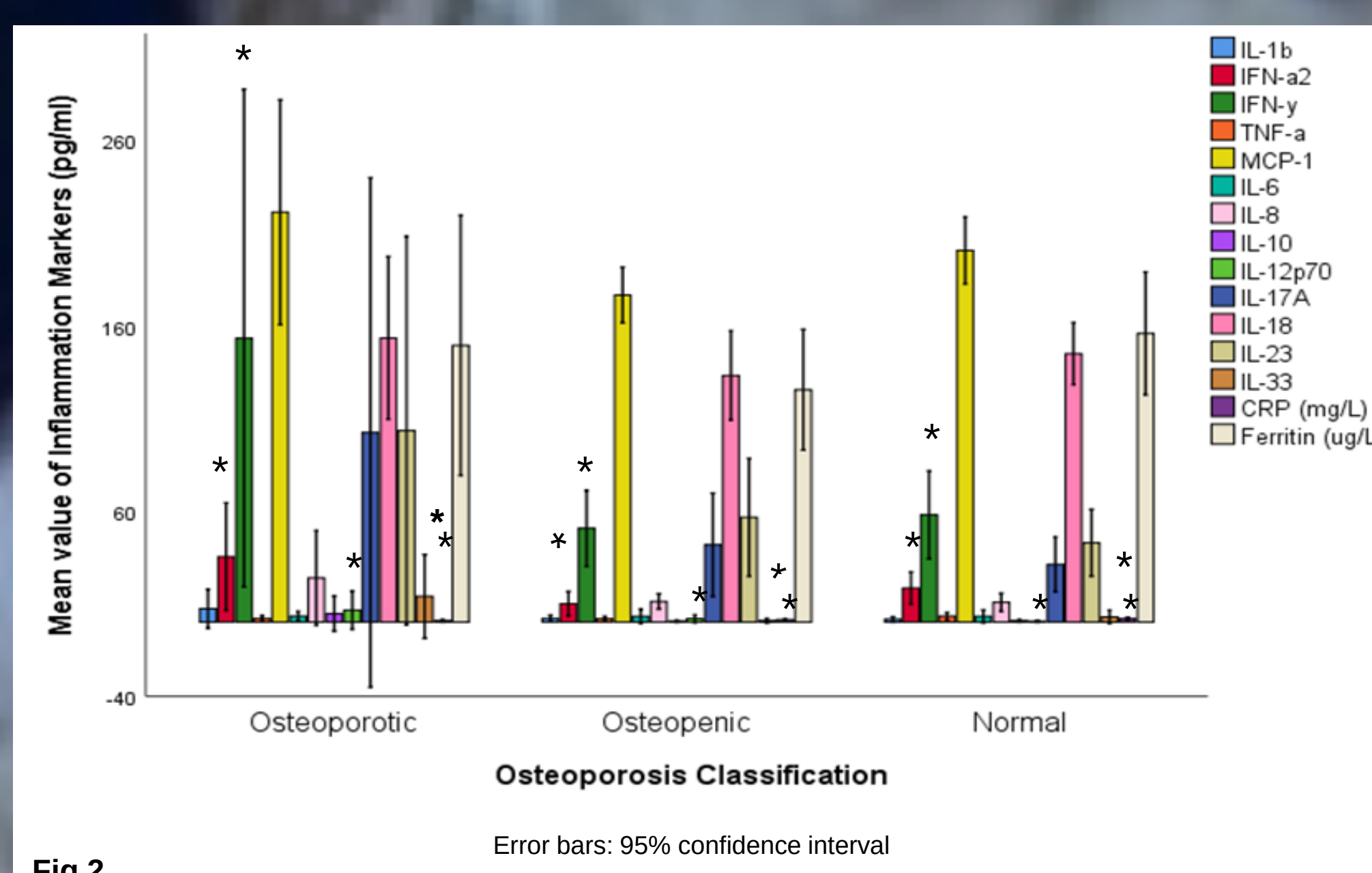


Fig.2: Plasma Levels of Inflammatory Markers by Osteoporosis Classification



## Objectives

1. To examine the relationship between levels of inflammatory markers and bone health status (which is grouped by the World Health Organization (WHO) classification of osteoporosis) in healthy postmenopausal women.
2. To evaluate the differences in the markers of inflammation such as IL-10, (which is known as an anti-inflammatory cytokine), along with pro-inflammatory cytokines and chemokine levels, amongst the normal, osteopenia, and the osteoporotic groups.

Fig.3: Mean Plasma Ferritin Levels by IL-10 status

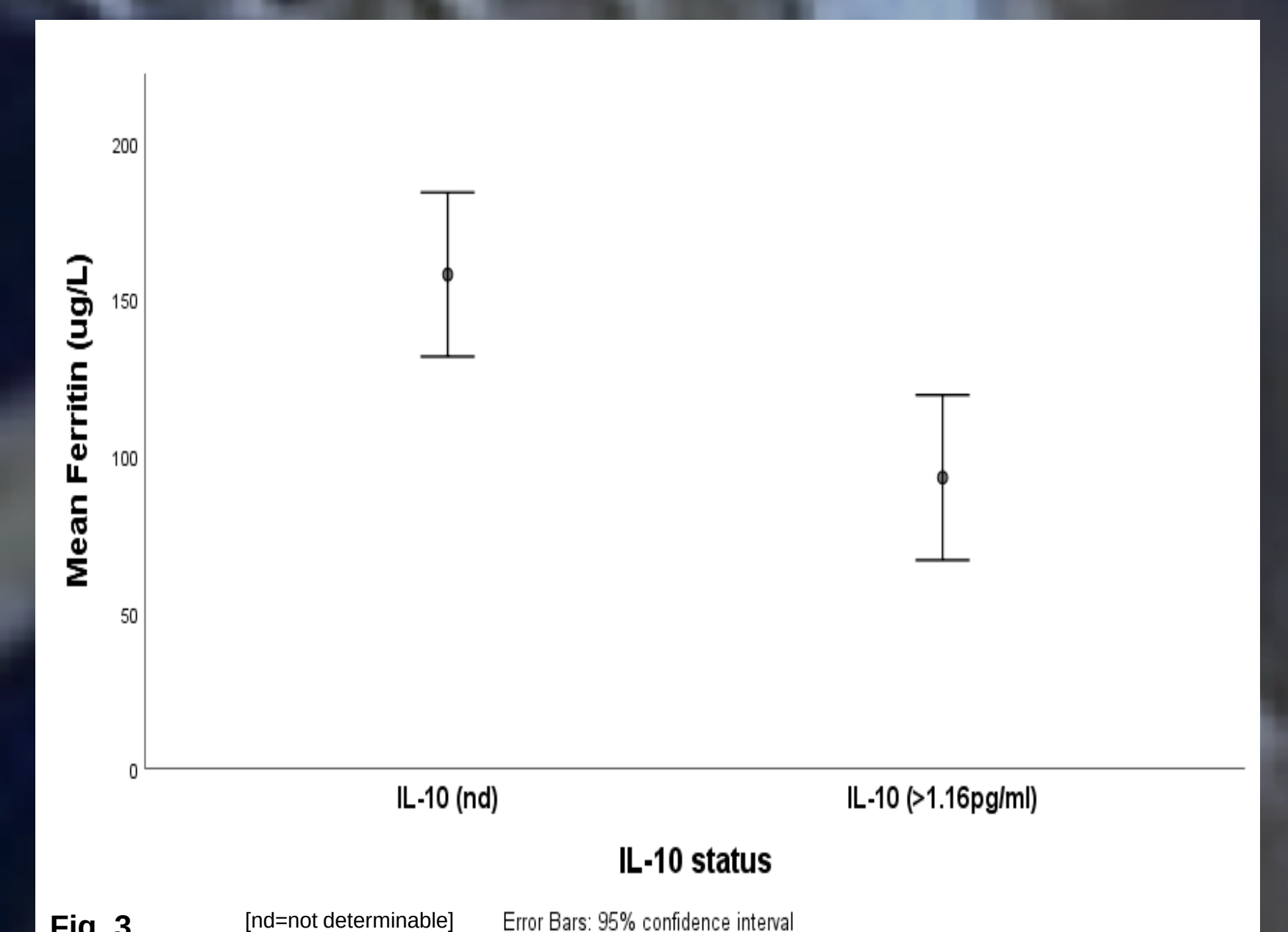
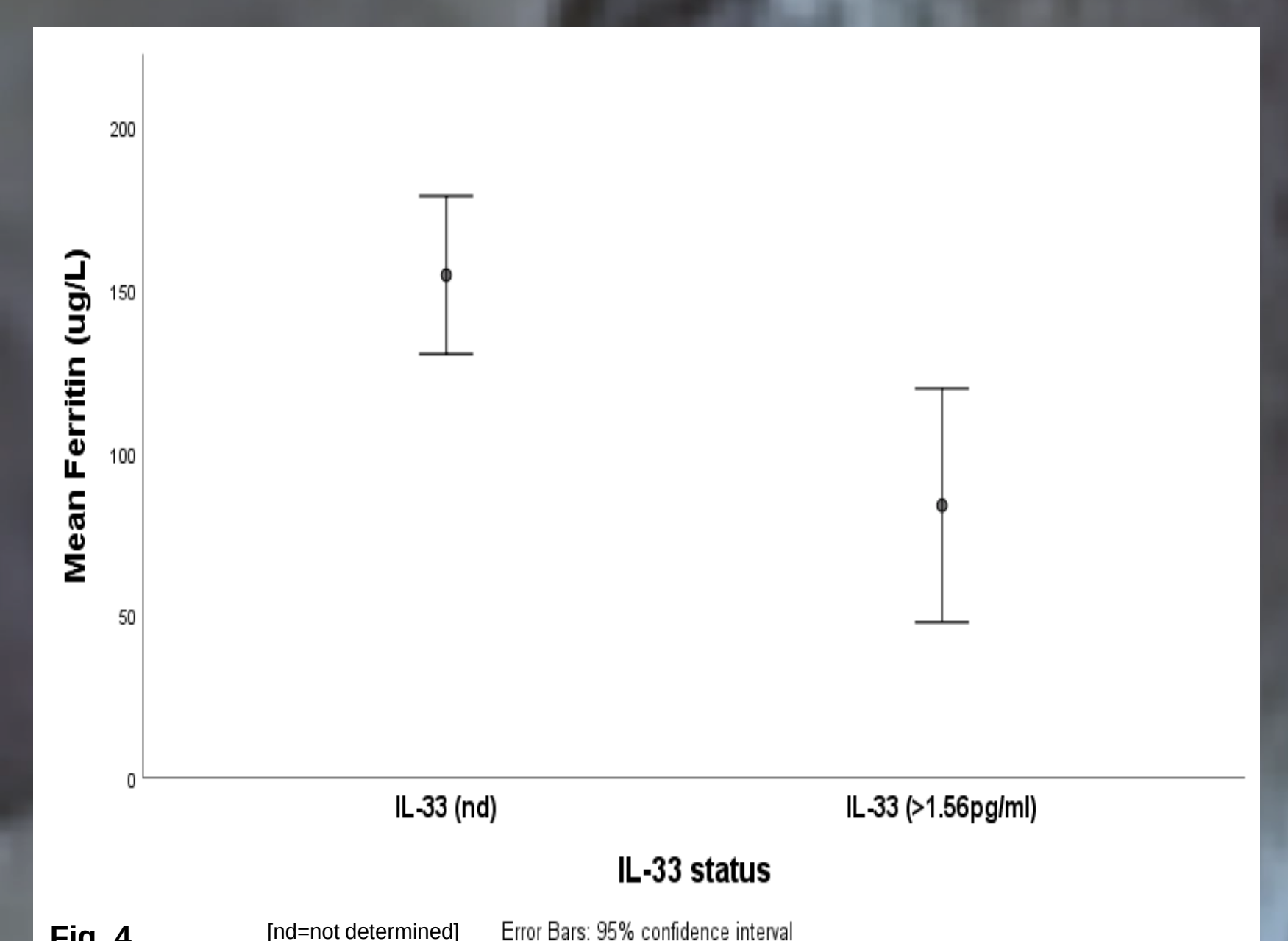


Fig.4: Mean Plasma Ferritin Levels by IL-33 status



## Discussion

The course of inflammageing status is multi-factorial, resulting from not only immunosenescence but also important factors such as dietary pattern, obesity and the gut microbiota status<sup>3</sup>. Studies have indicated the contribution of IL-17 and IL-23 but not interferon- $\gamma$  (IFN- $\gamma$ ) to osteoporosis. Likewise, IL-10 but not IL-33 has been linked to lower ferritin levels and low iron stores<sup>4</sup>.

## Conclusions

High plasma levels of IFN- $\alpha$ 2, IFN- $\gamma$ , IL-12p70, IL-33 and MCP-1 in apparently healthy postmenopausal women are associated with low bone mass. In addition, an increase in levels of IL-10 may be associated with lower ferritin status in women of this age group. This results need to be investigated further due to the complex interplay of comorbidities and cytokines that could potentially affect acute phase reactants such as CRP and ferritin.

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