# Haemoglobin, EPO and iron indices

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ANZDATA Registry

# Background

- Continuing debate about iron and EPO use
  - What is the optimal level of Hb?
- ANZDATA has recently begun collecting information in this area
  - Whether patient receives an erythropoietic agent
  - Most recent HB
  - Transferrin saturation
  - Ferritin concentration
  - Dialysis parameters

# Who gets erythropoietic agents?

- Australia
  - Subsidised through S100 mechanisms for outpatients
  - "For anaemia associated with renal failure requiring transfusion"
- New Zealand
  - Patients with ESRD treated with dialysis for 3 months and have demonstrated a haemoglobin <70 g/l over a period of 4 months (or <90 g/l in the presence of cardiac disease).
    - Not currently being evaluated for LD TX or expected to receive LD Tx in 3/12
    - Requires application to authority

# Methods

- Data abstracted from ANZDATA
  - Use of erythropoietic agents (EA's)
  - Haemoglobin, ferritin, transferrin saturation
  - Dialysis dose
- This analysis includes all who were recorded in ANZDATA on dialysis in March 2001 for 12 months or more
  - Stratifies people by country because of different criteria
  - Those on dialysis less than 12 months were excluded from analyses as their haemoglobins tended to rise

# Statistical Methods

- URR calculated from Kt/V using formula of Basile (AJKD 15:40-45, 1990)
- Ferritin concentration log-transformed
- All variables examined as categories to avoid assumptions of linearity
- Standard parametric analyses used
  - First order interactions sought
- Kappa used to describe agreement between diagnostic categories

# Results

- The sample is described in Table 1
  - Missing values were an issue for iron indices
    - 15% ferritin values missing and 29% transferrin saturations
      - Missing values more likely in those receiving peritoneal dialysis or being treated in New Zealand.
- Substantially fewer dialysis patients in NZ receive EA's than in Australia ($P<0.001$)
  - Similar ferritin and transferrin saturations values between Australia & NZ

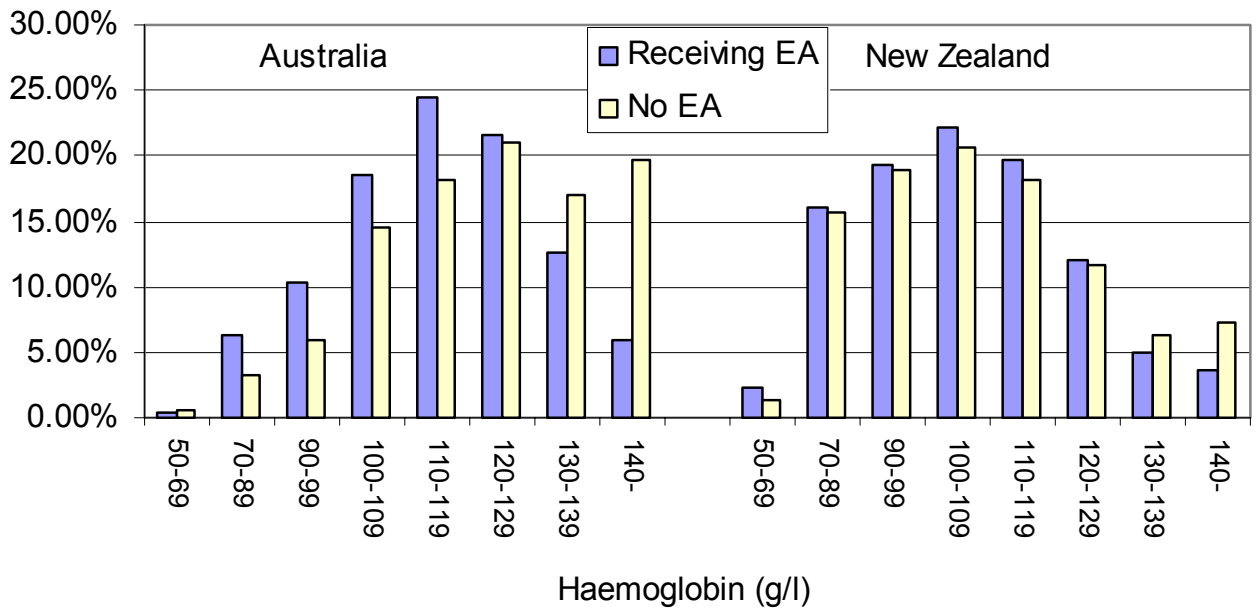
# Study population

| | Australia | | New Zealand | |
|---|---|---|---|---|
| | On EA | No EA | On EA | No EA |
| N | 5975 | 875 | 611 | 848 |
| Dialysis duration ≥12 months | 4564 (76%) | 671 (77%) | 518 (85%) | 551 (65%) |
| Haemodialysis | 3555 (78%) | 430 (64%) | 315 (61%) | 240 (44%) |
| Male | 2504 (55%) | 455 (68%) | 276 (53%) | 346 (63%) |
| Age (median [IQR] | 61.3 [47.1-71.6] | 59.9 [48.7-69.8] | 55.3 [41.0-64.3] | 58.4 [49.0-67.3] |
| Serum Ferritin (μg/l) | 304 [295-314] | 172 [154-191] | 298 [271 – 329] | 197 [178-219] |
| Serum transferrin saturation (%) | 26.6 [26.2-27.1] | 25.5 [23.8-27.3] | 27.1 [25.5-28.7] | 25.5 [23.8-27.3] |
| Haemoglobin (g/dl) | 115 [114-115] | 123 [121-124] | 104 [102-105] | 108 [104-108] |

*Descriptive statistics of those receiving and not receiving erythropoietic agents (EA's) in Australia and New Zealand, March 2001.*

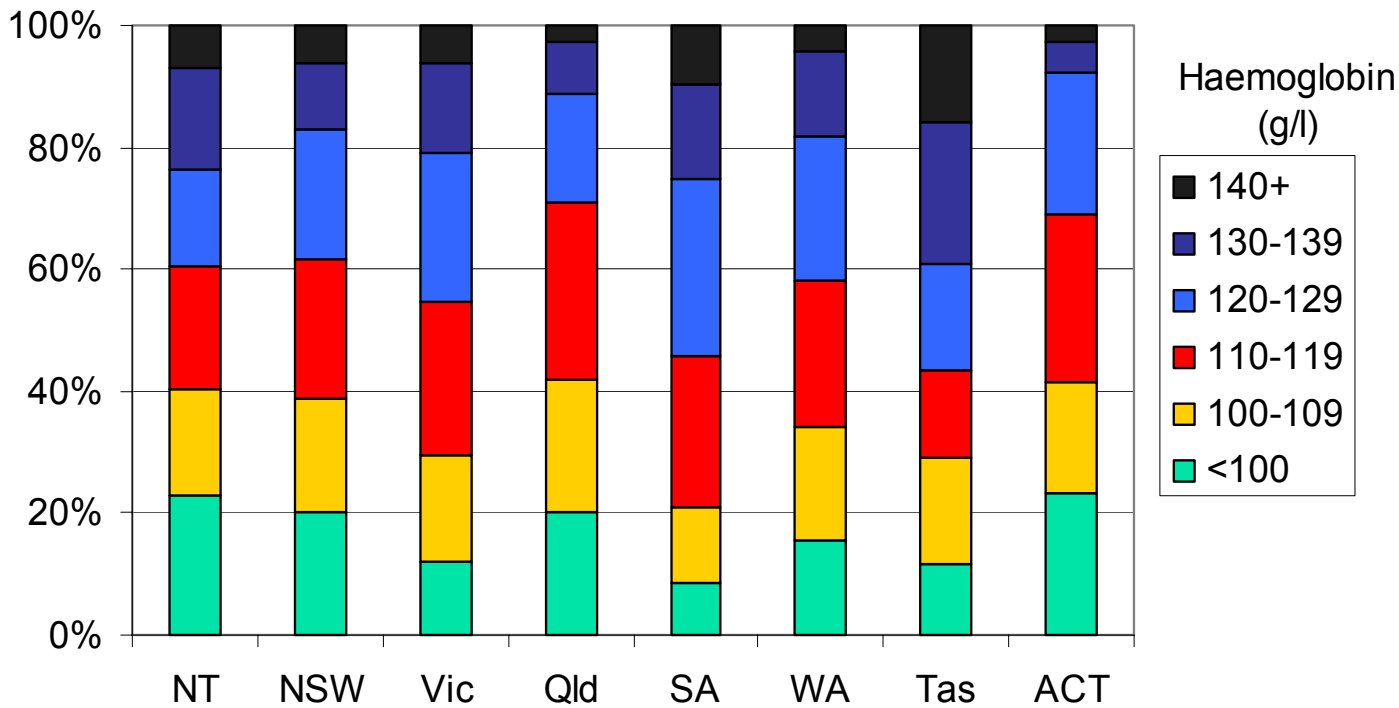
# Variation in haemoglobin levels

- There is considerable variation in haemoglobin values between countries




*Distribution of haemoglobin concentrations at 31 March 2001 for ESRD patients in Australia and New Zealand. EA=erythropoietic agent*

# Haemoglobin by state

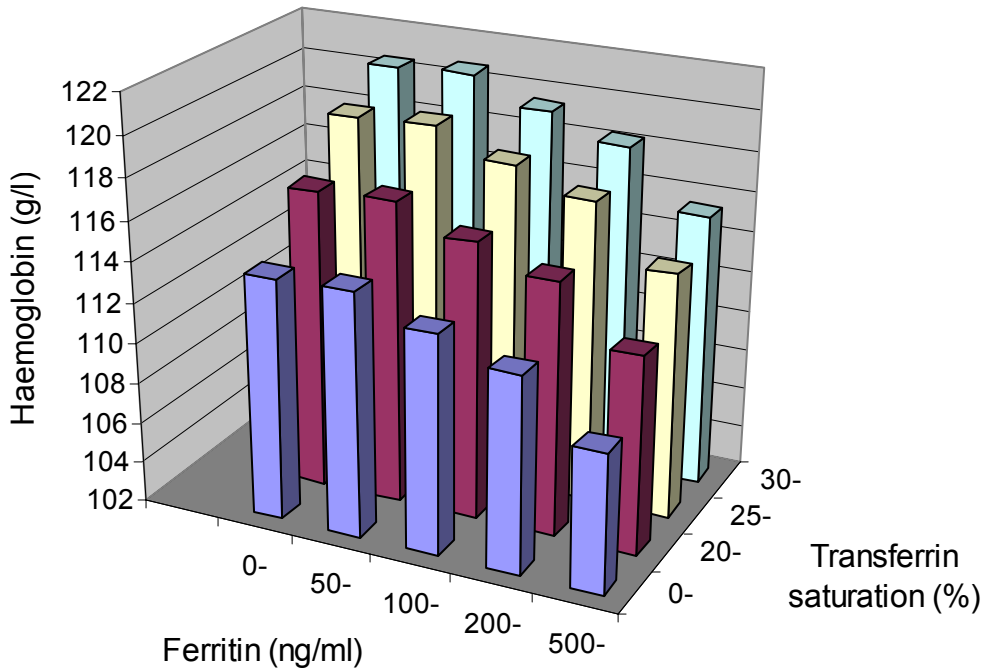



*Haemoglobin concentration by state, 2001, for those on dialysis at least 1 year*

# Iron indices

- Haemoglobin concentration increased with increasing transferrin saturation, but decreased with increasing ferritin concentrations
  - These trends were independent of each other
  - Also independent of age, country and gender (Iron indices 2)
  - Among those on HD, the group with URR<65% had lower Hb
    - Adjusted for ferritin, transferrin, age and gender, the URR<65% group's Hb was 2.9 [1.2-4.6] g/l lower

# Iron indices 2

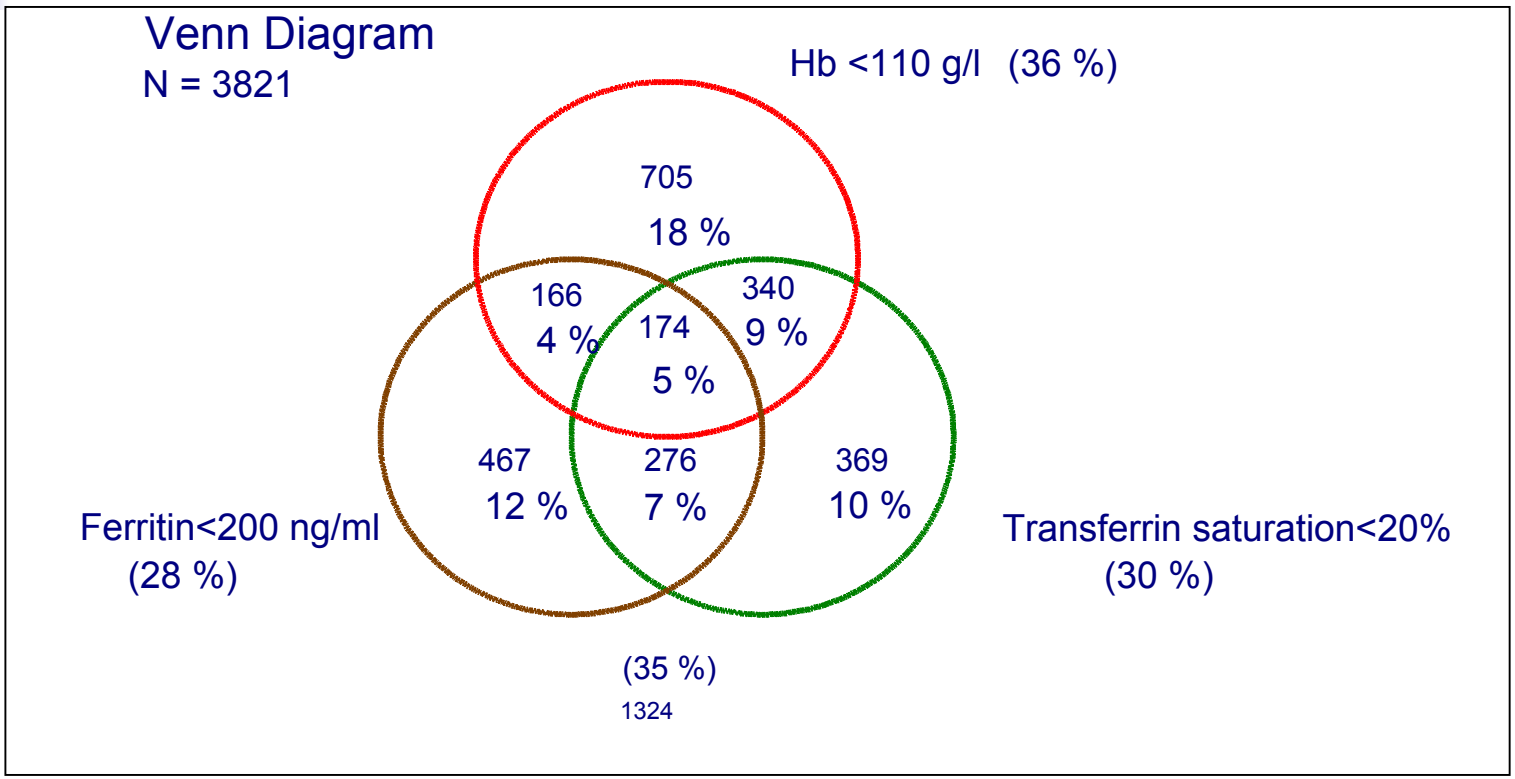



*Mean Hb concentrations by ferritin and transferrin categories. The Hb concentrations are adjusted for age, gender and country.*

# Iron indices 3

- Of those receiving EA's
  - 1242/4458 (28%) had a serum ferritin <200 ng/ml
  - 1172/3867 (30%) had a transferrin saturation less than 20%
  - 47% of people had either Ferritin <200 or Tfsat<20%
- But these groups were not the same
  - 65% agreement vs 58% by chance alone
  - Kappa=0.15
- A similar proportion (34%) of Australian patient had a haemoglobin less than 110g/l
  - But these did not overlap (Iron indices 4)

# Iron indices 4




*Overlap between indicators of iron deficiency (Tfsat <20% and ferritin<200) and Hb<110 g/l EA's recipients only.*

# Conclusions

- There is substantial variation in the haemoglobin concentration among dialysis patients
  - Major regulatory differences in availability of erythropoietic agents exist between Australia and NZ
  - Considerable variation between Australian states
  - Presumably reflects differing views about target haemoglobin

# Conclusions 2

- The associations between transferrin, ferritin and haemoglobin are from a cross-sectional study, and causality should not be inferred
- Reinforces the fact that ferritin marks many processes, not just iron availability
- Categories based on transferrin and ferritin do not agree well with each other, and are not interchangeable

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Disclaimer

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