

IFCC seminar – Berlin 16th May

Active-B12: A new front line test to diagnose vitamin B₁₂ deficiency



Axis-Shield Sponsored ISW
Monday May 16th
16:45 to 17:45
Hall 10

Refreshments available

You are cordially invited to participate in a stimulating debate to assess the utility of a new and accurate diagnostic test (HoloTranscobalamin or Active B-12) for establishing Vitamin B₁₂ status. Vitamin B₁₂ deficiency is now considered to be a major public health issue, particularly in elderly populations.

www.active-b12.com



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The diagnostic accuracy of Active-B12 using red cell B₁₂ levels to indicate B₁₂ tissue status.

Prof John Scott, Trinity College, Dublin, Ireland



Outcomes of a multi-centre study and experience with introducing and running Active-B12 in the clinical chemistry lab.

Prof Jan Lindemans, Erasmus Medical Centre, Rotterdam, Netherlands

Find out more about Active B-12 testing on the Axis-Shield Booth, Hall 12, Booth 23 or at our web-site

www.active-b12.com



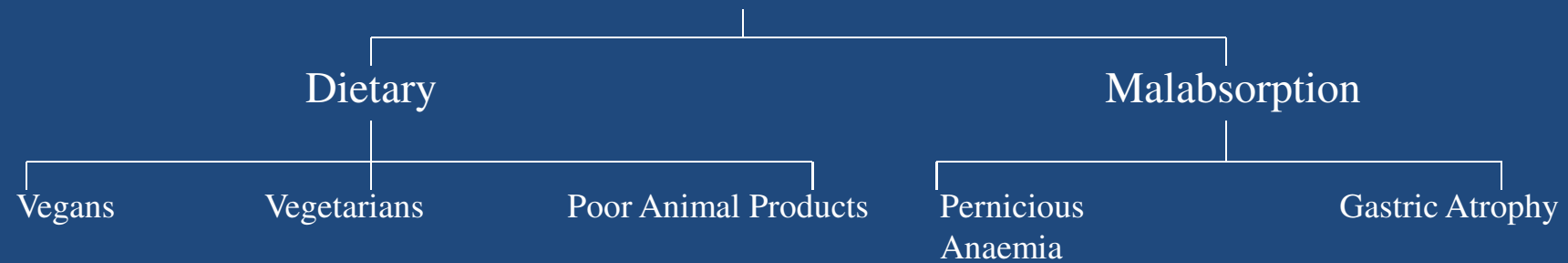
Diagnostic Accuracy of Holotranscobalamin,
Methylmalonic Acid, Serum Cobalamin and other
indicators of tissue vitamin B₁₂ status in the elderly

Professor John Scott
School of Biochemistry and Immunology
Trinity College Dublin
Dublin 2
Ireland

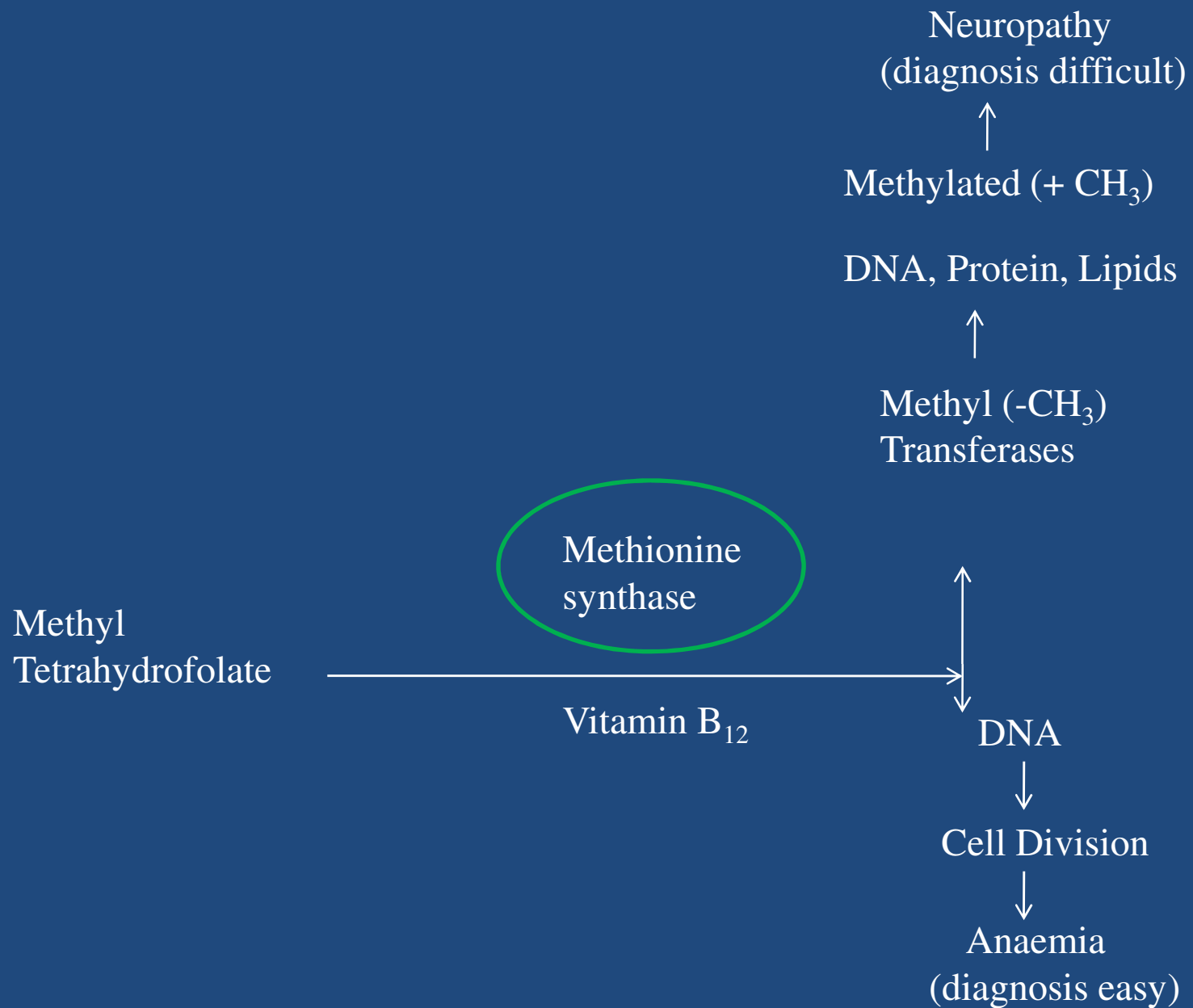


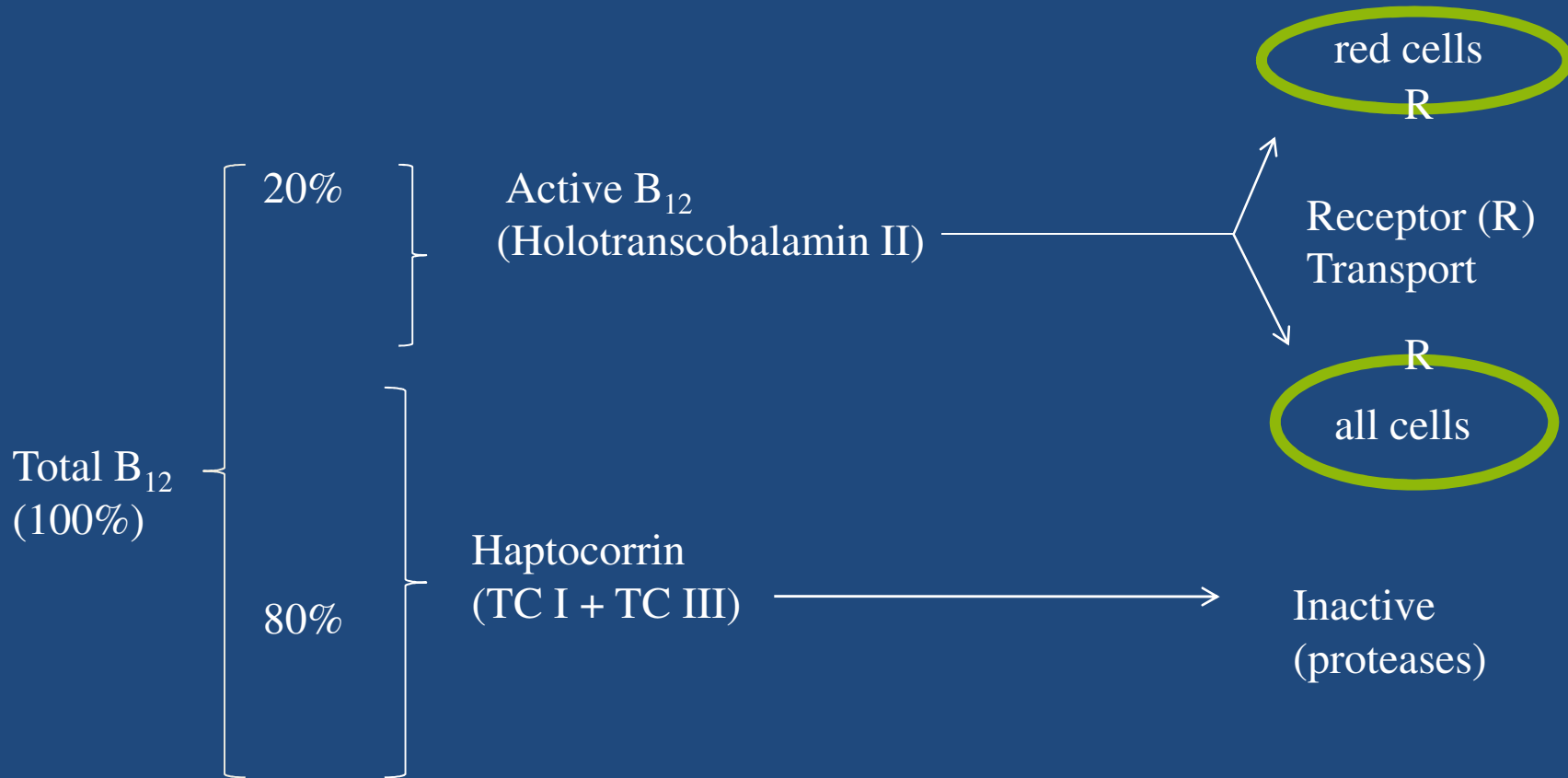
e-mail: jscott@tcd.ie

Vitamin B₁₂ Deficiency [Cobalamin]



Many elderly have diets poor in B₁₂ and varying levels of gastric atrophy





Traditional Diagnosis; Total serum B₁₂

New Diagnosis; Active B₁₂

Active B₁₂ out performs Total B₁₂

- (1) RC-B₁₂ assay reflects tissue B₁₂
- (2) Comparison of ROC plots
- (3) Assay Monoclonal Specific to Active B₁₂
(will not bind to Apotranscobalamin)
- (4) Model: Active B₁₂ in model has superior
specificity and sensitivity than Total B₁₂

EVIDENCE

Red blood cell vitamin B₁₂ (Tissue B₁₂)

Reference population (n = 118) mean 97.2 (32.8) ρ mol/L

- 95% central reference interval

- cut off for deficiency

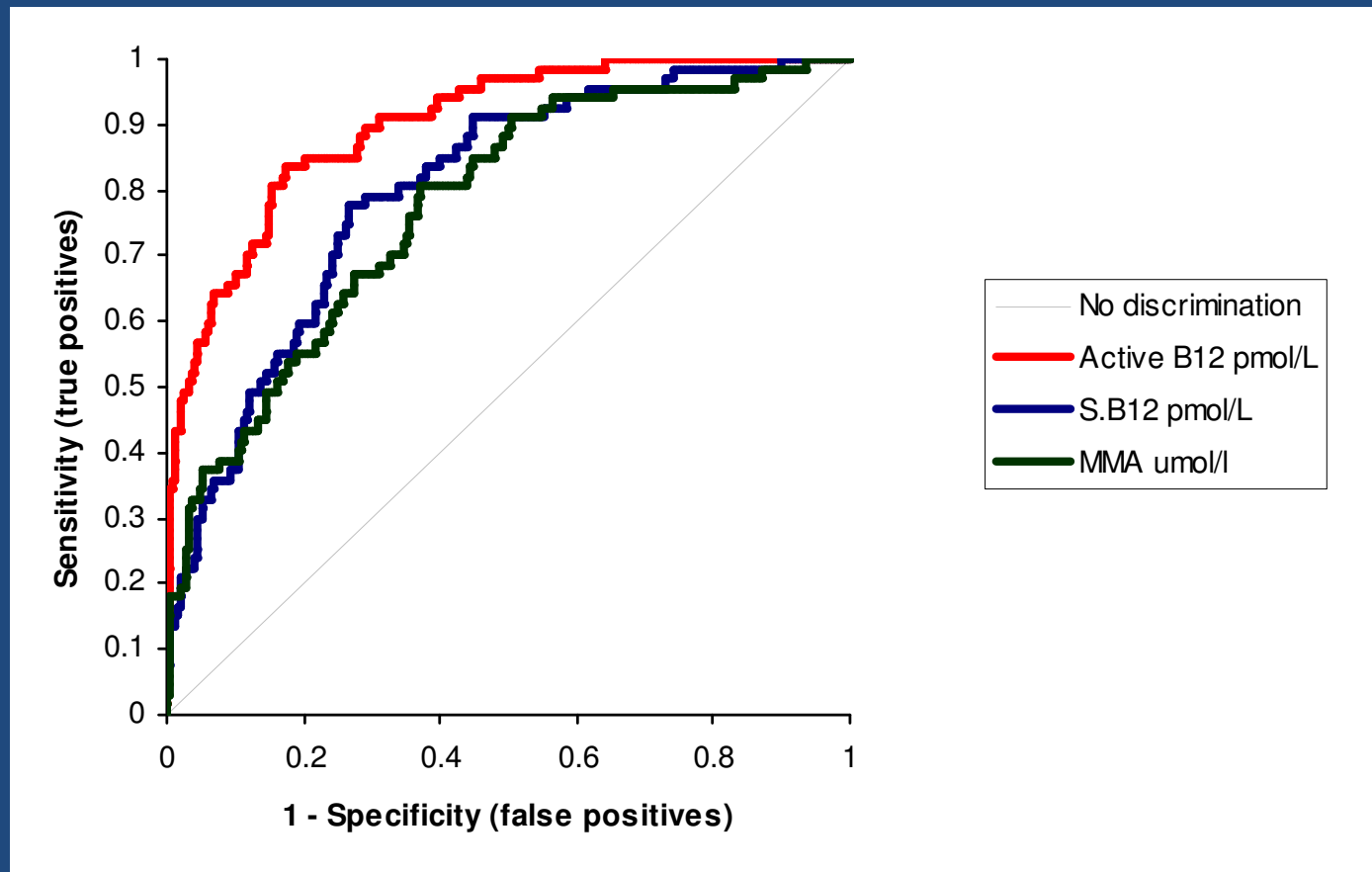
33 < ρ mol/L red cell B₁₂

Elderly (69-92 years) study population (n = 700)

Red cell B₁₂ < 33 ρ mol/L n = 67 deficient

> 33 ρ mol/L n = 633 non-deficient

ROC plots for serum total cobalamin, holoTC and MMA for vitamin B12 deficiency, defined as red cell cobalamin <33 pmol/L



Performance of markers at a single cut-off

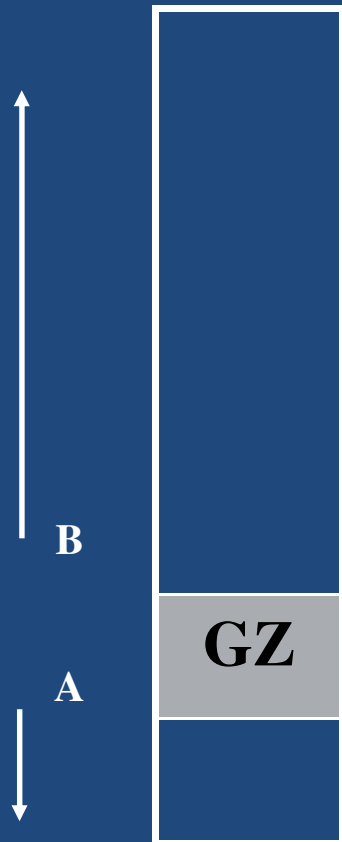
Marker	Cutoff	Sensitivity%	Specificity%	PPV%	NPV%
holoTC	<20pmol/L	55 (43 to 67)	96 (94 to 97)	56 (45 to 70)	95 (93 to 97)
Serum Cbl	<123pmol/L	33 (22 to 45)	95 (93 to 96)	39 (26 to 53)	93 (91 to 95)
MMA	<0.36 μ mol/L	81 (69 to 89)	63 (59 to 66)	19 (14 to 24)	97 (95 to 98)

HoloTC was superior to MMA and Cobalamin as predictor of B12 deficiency

3-zone partition with deliberate grey-zone

Any result above the test value B has a very high probability of no B12 deficiency, set at 98% for a negative result

Any result below the test value A has a very high probability of B12 deficiency, set at 60% for a positive result



The “grey” or indeterminate zone, test values in this region have neither a high or low probability for deficiency. Further evaluation of the patient would be required.

We would be interested to estimate how wide this “grey-zone” is in terms of percentage of patients whose results would be within this area.

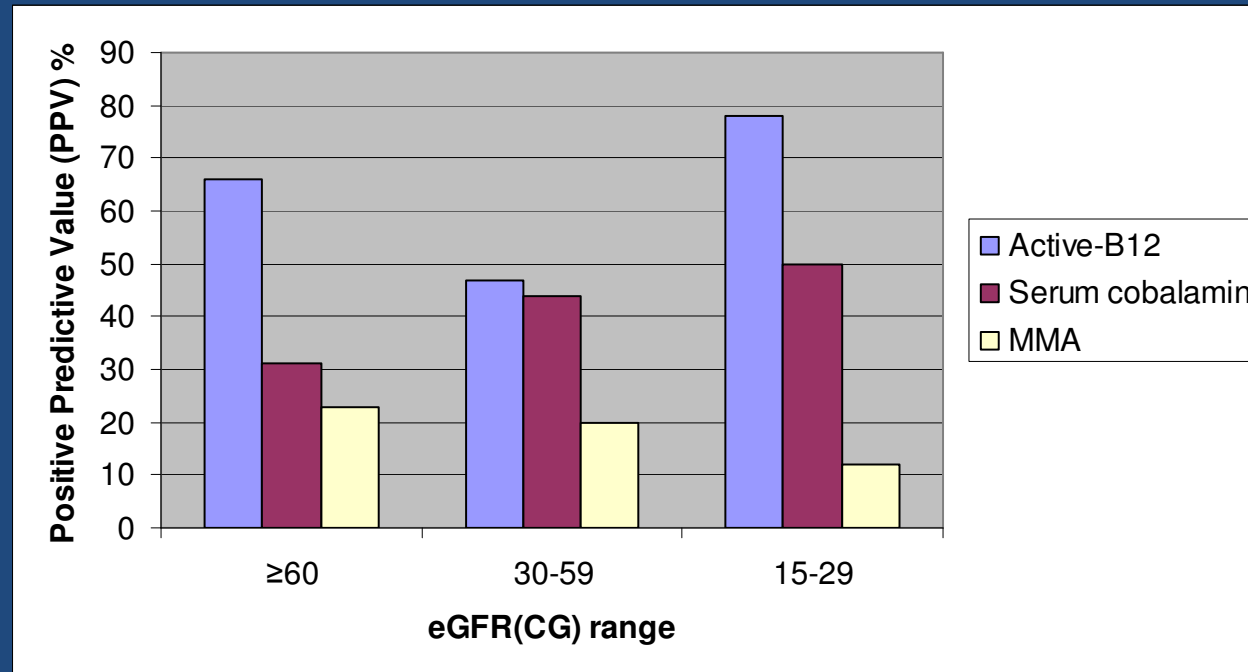
Note: this is written for total B12 and Active B12 where low values indicate deficiency- the same principle applies for MMA, but in this case high values indicate deficiency

Proportion of samples in grey-zone

	MMA (uM)	Active B12 (pM)	B12 (pM)
LR+ =14	1.40	19.6	79
LR- = 0.23	0.31	29.9	238
Samples in Grey-Zone (N)	349/700	96/699	313/700
Samples in Grey-Zone (%)	50	14	45

For MMA and total vitamin B12 a very high proportion of the population would be unclassified, restricting the utility of these tests. HoloTC measurement has clearly superior clinical utility with only 14% of samples in the grey-zone.

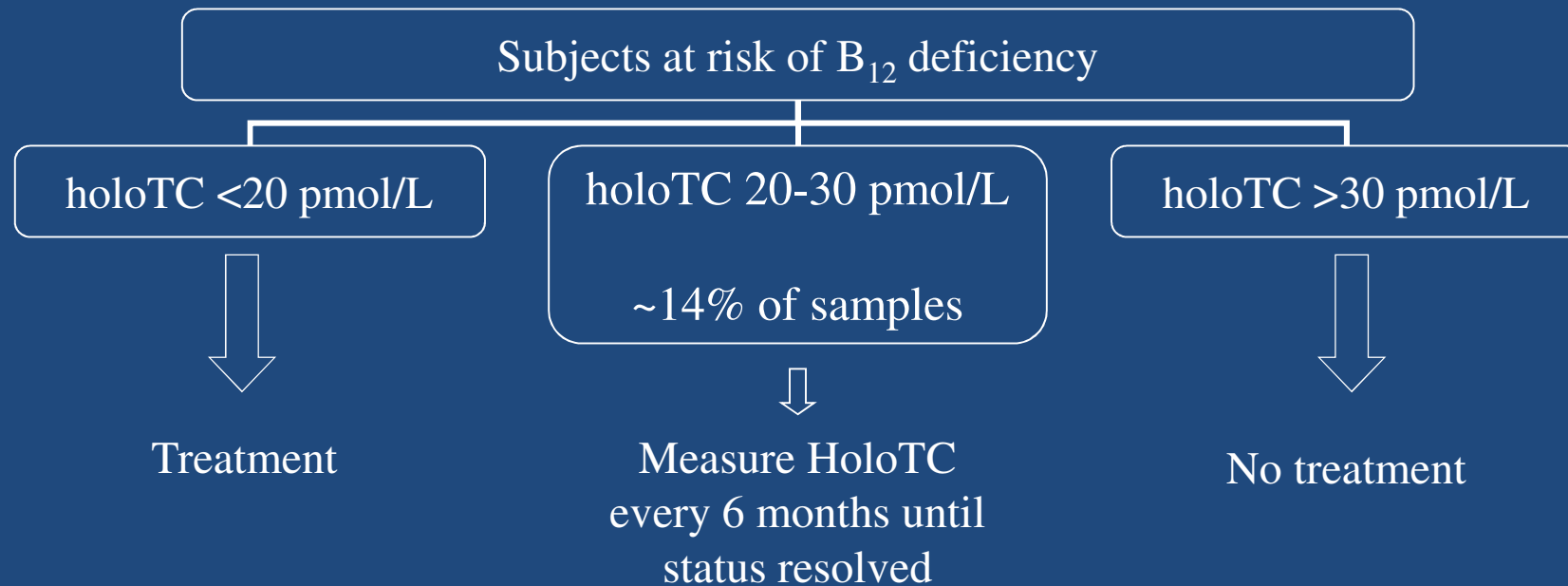
Performance of markers in relation to kidney function (glomerular filtration rate).



- HoloTC had highest PPV for diagnosing B12 deficiency even in most compromised patients with no relationship to renal function

- PPV of MMA shows a steady decline suggesting the diagnostic performance of MMA may be impacted by renal function

Suggested testing algorithm in holoTC screening



ACKNOWLEDGEMENTS

Diagnostic Accuracy of Holotranscobalamin, Methylmalonic Acid, Serum Cobalamin and other indicators of tissue vitamin B₁₂ status in the elderly

Edward Valente, John Scott, Per-Magne Ueland, Conal Cunningham, Miriam Casey and Anne Molloy
From *Clinical Chemistry* 57:6, 2011