

Prevalence Of
Hyperhomocysteinemia
In Patients With
Predialysis Chronic Kidney Disease
After Folic Acid Food Fortification
Of The Canadian Food Supply

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Prevalence Of Predialysis Chronic Kidney Disease (CKD)

- An estimated 1.5 million Canadians have predialysis CKD.
Stigant C, 2003
- The prevalence of predialysis CKD is expected to increase as a result of the global pandemic of type 2 diabetes, which is a major cause of predialysis CKD.
Atkins RC, 2005

Stages Of CKD

5 to 10 times more likely to die than reach stage 5 CKD

Stage 1: GFR \geq 90

Stage 2: GFR = 60-89

Stage 3: GFR = 30-59

Stage 4: GFR = 15-29

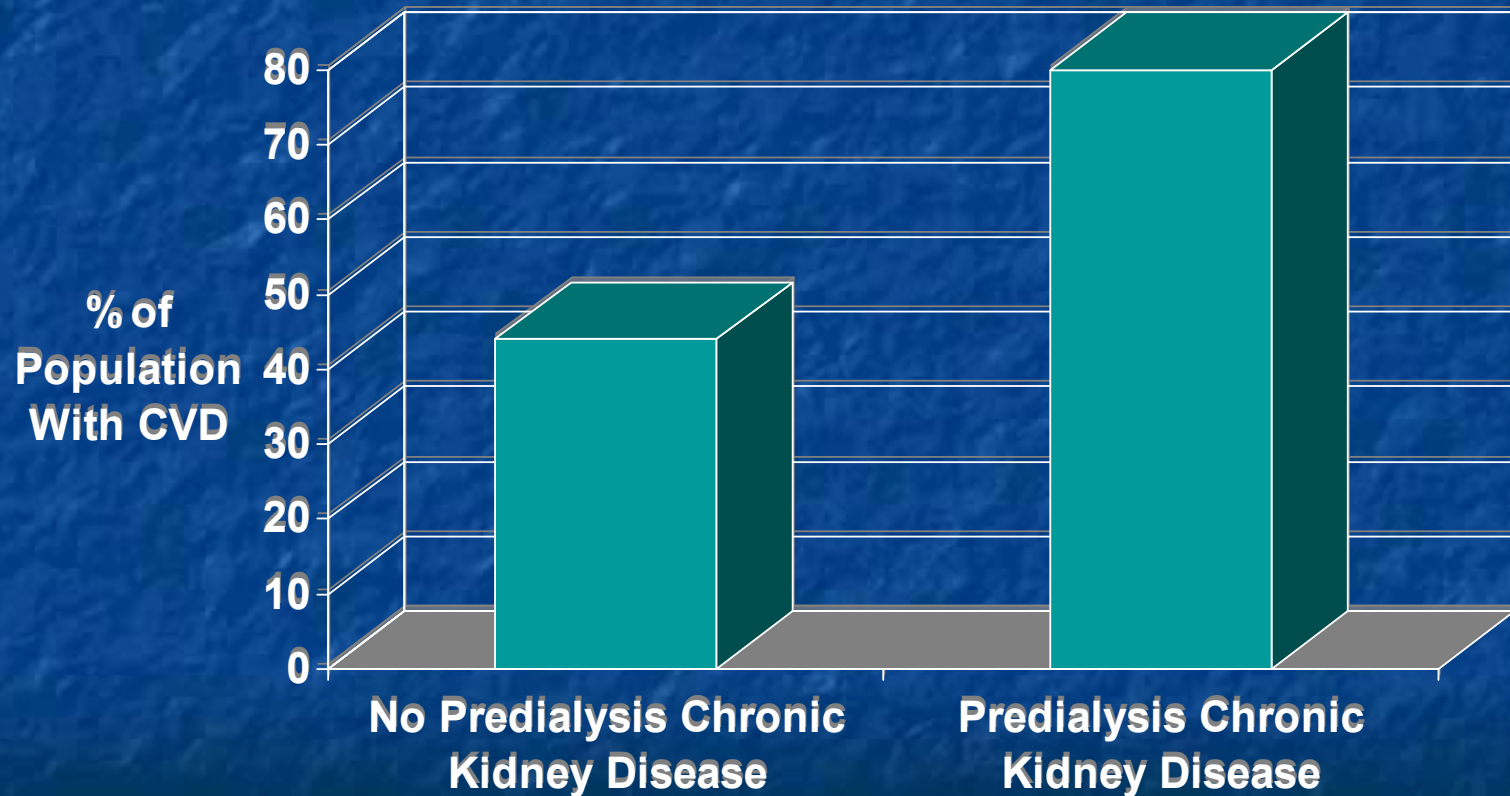
END STAGE RENAL DISEASE

Stage 5: GFR $<$ 15

GFR = ml/min/1.73m²

Collins AJ, 2003

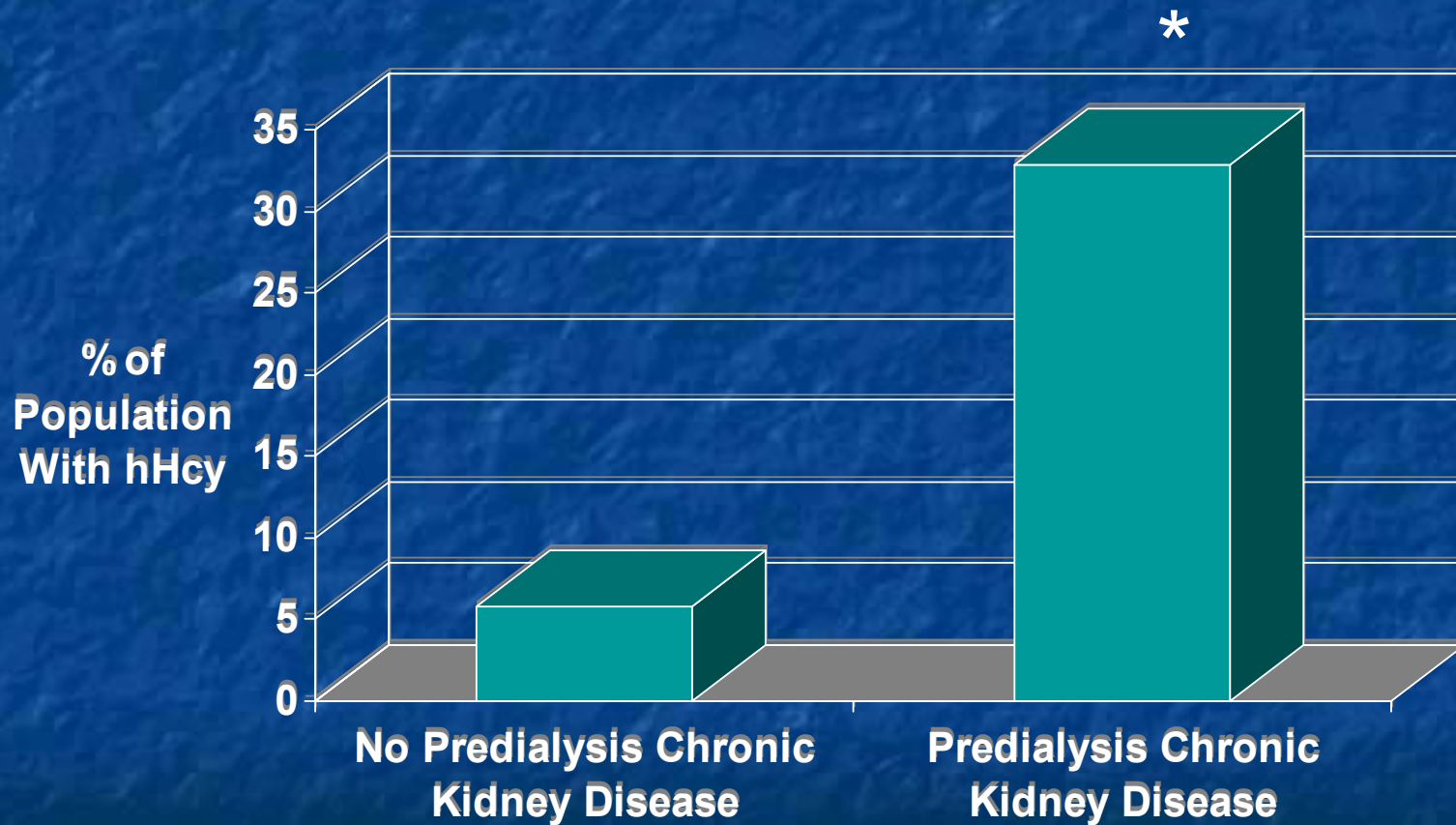
Prevalence Of Cardiovascular Disease - The General Population



Homocysteine And Risk For Cardiovascular Disease (CVD)

- Plasma total homocysteine may be an independent risk factor for CVD in both the general and predialysis chronic kidney disease populations.

Prevalence Of Hyperhomocysteinemia (hHcy) ($\geq 15\mu\text{mol/L}$)



* Significant Difference ($p < 0.01$)

Muntner P, 2004

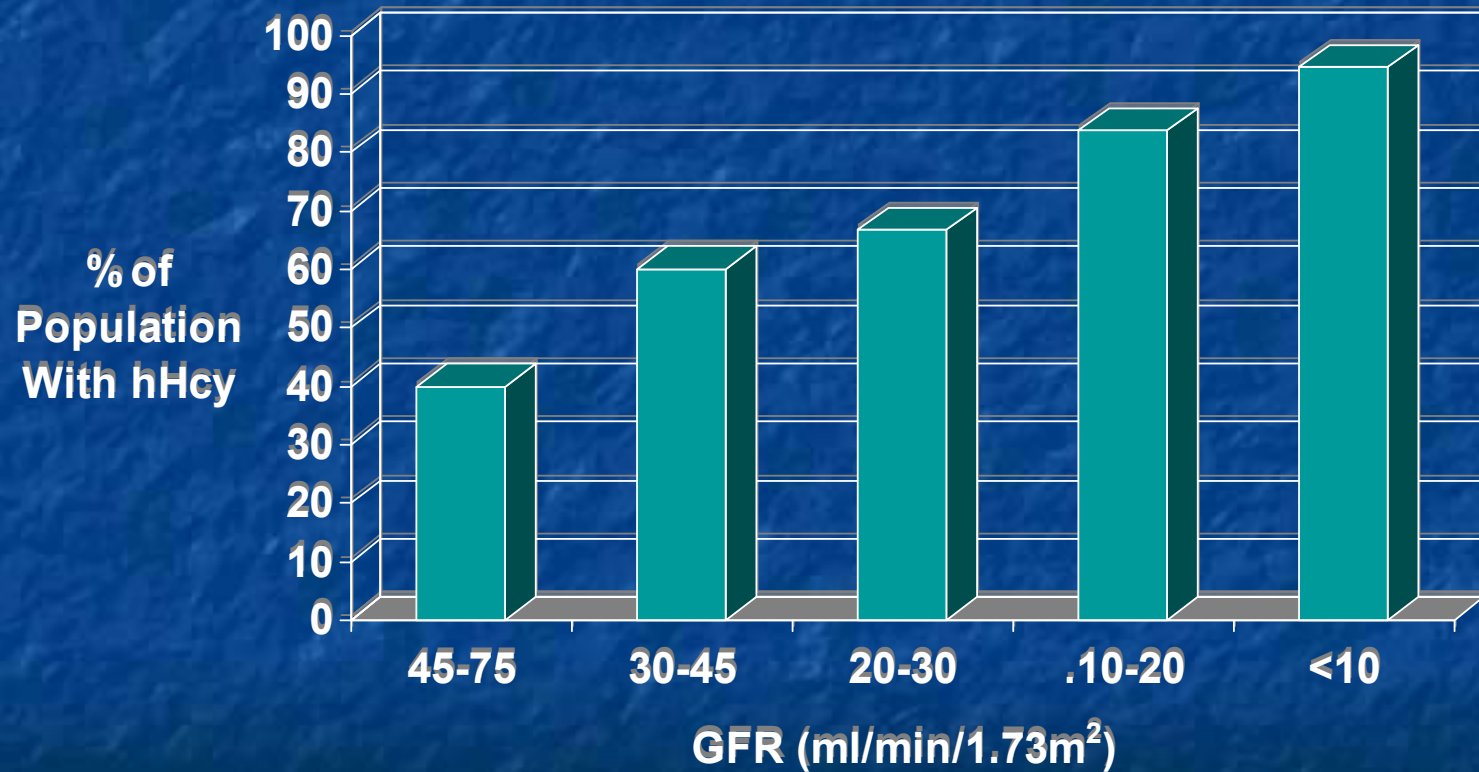
Severity Of Hyperhomocysteinemia In Various Populations

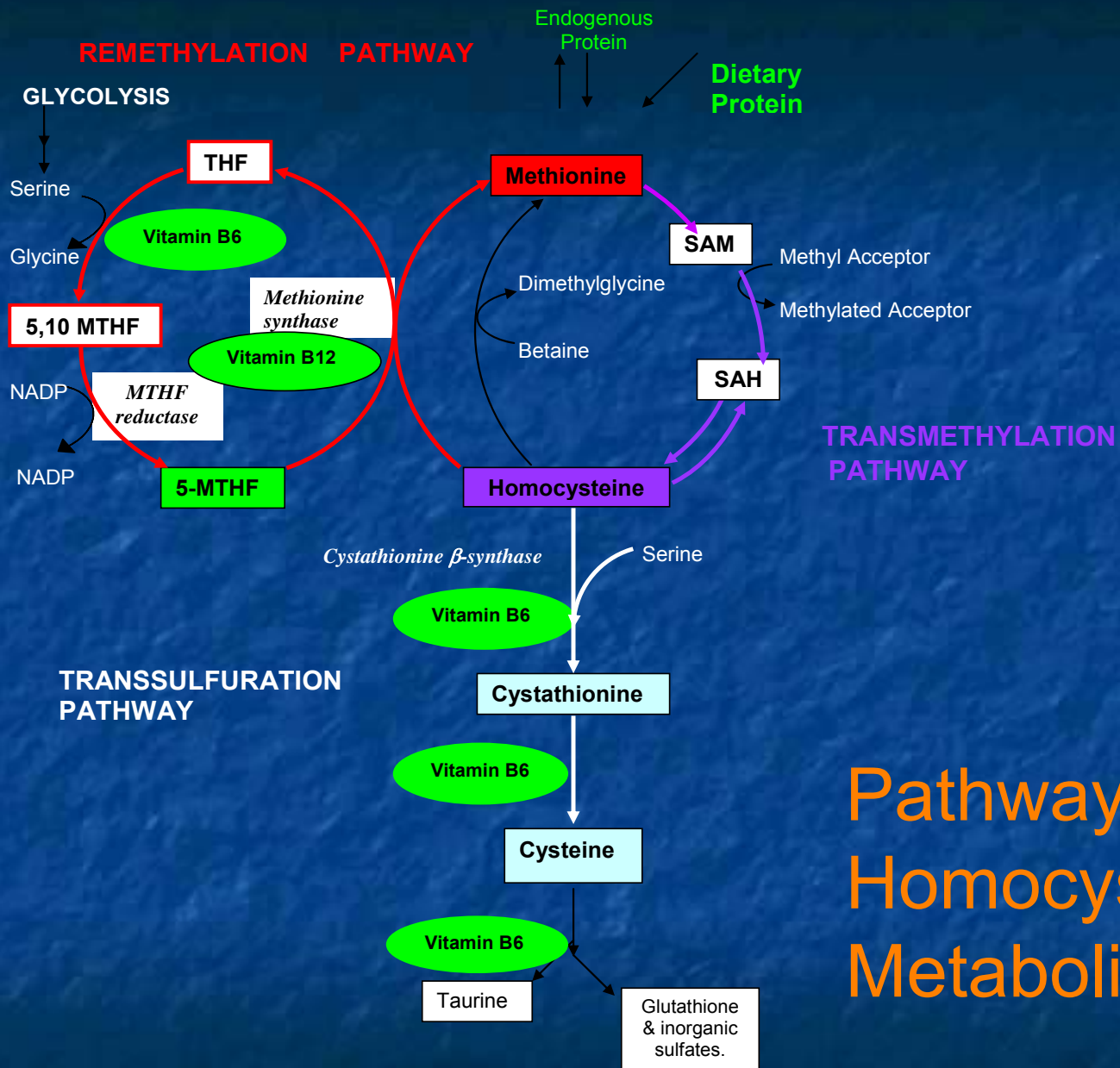
Population	Range Of Plasma Total Homocysteine (umol/L)
General	6 - 12 Friedman AN, 2002
Cardiovascular Disease	8 - 20 Gupta A, 1997
Predialysis CKD	6 – 50 Parsons DS, 2002
Classic Homocystinuria (Cystathionine β -synthase deficiency)	> 500 Gupta A, 1997

Glomerular Filtration Rate (GFR) Is A Determinant Of Plasma Total Homocysteine (P tHcy)

Plasma tHcy was found to be inversely associated with GFR ($r = -0.39$; $p < 0.0001$).

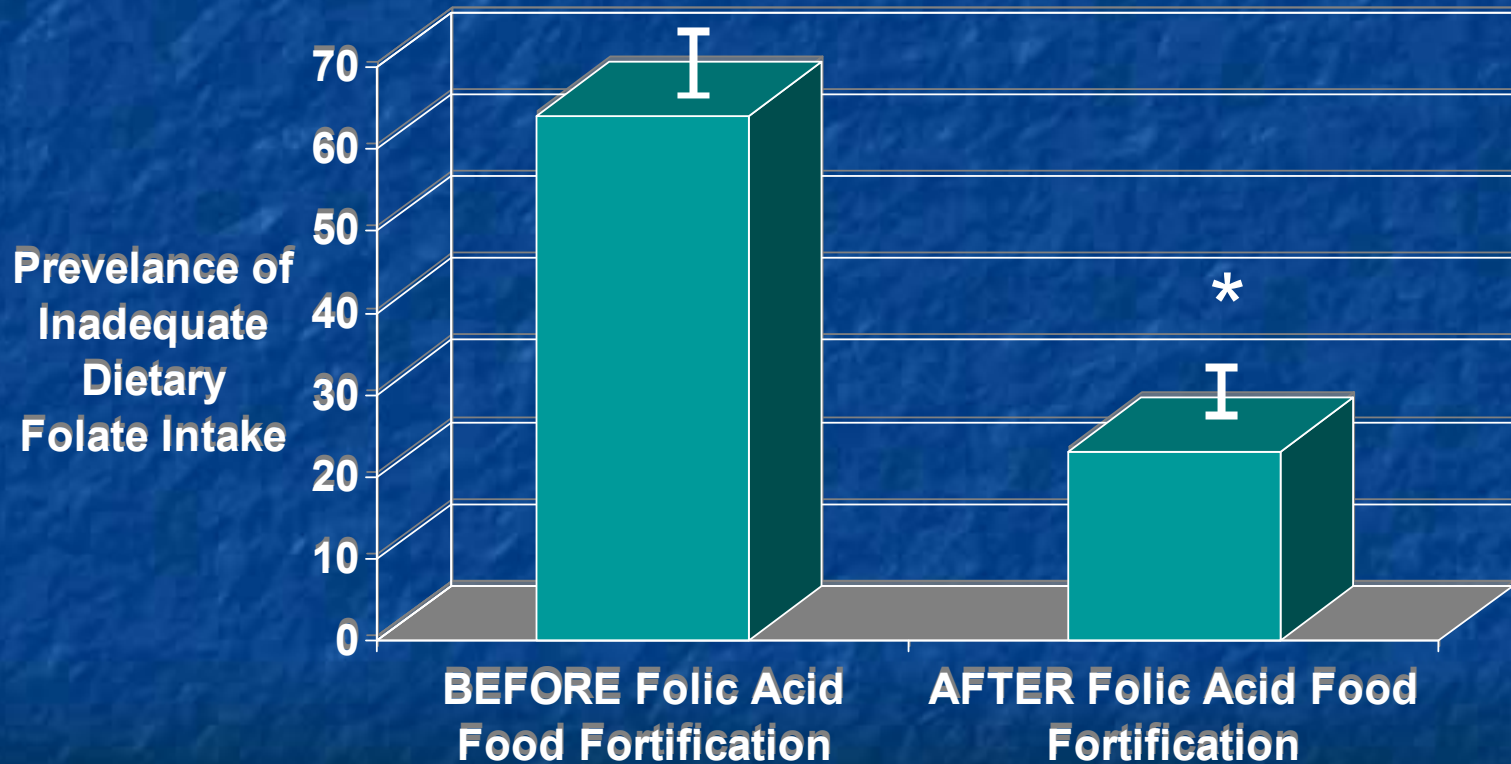
Prevalence Of Hyperhomocysteinemia (hHcy) By Glomerular Filtration Rate (GFR) In Predialysis Chronic Kidney Disease





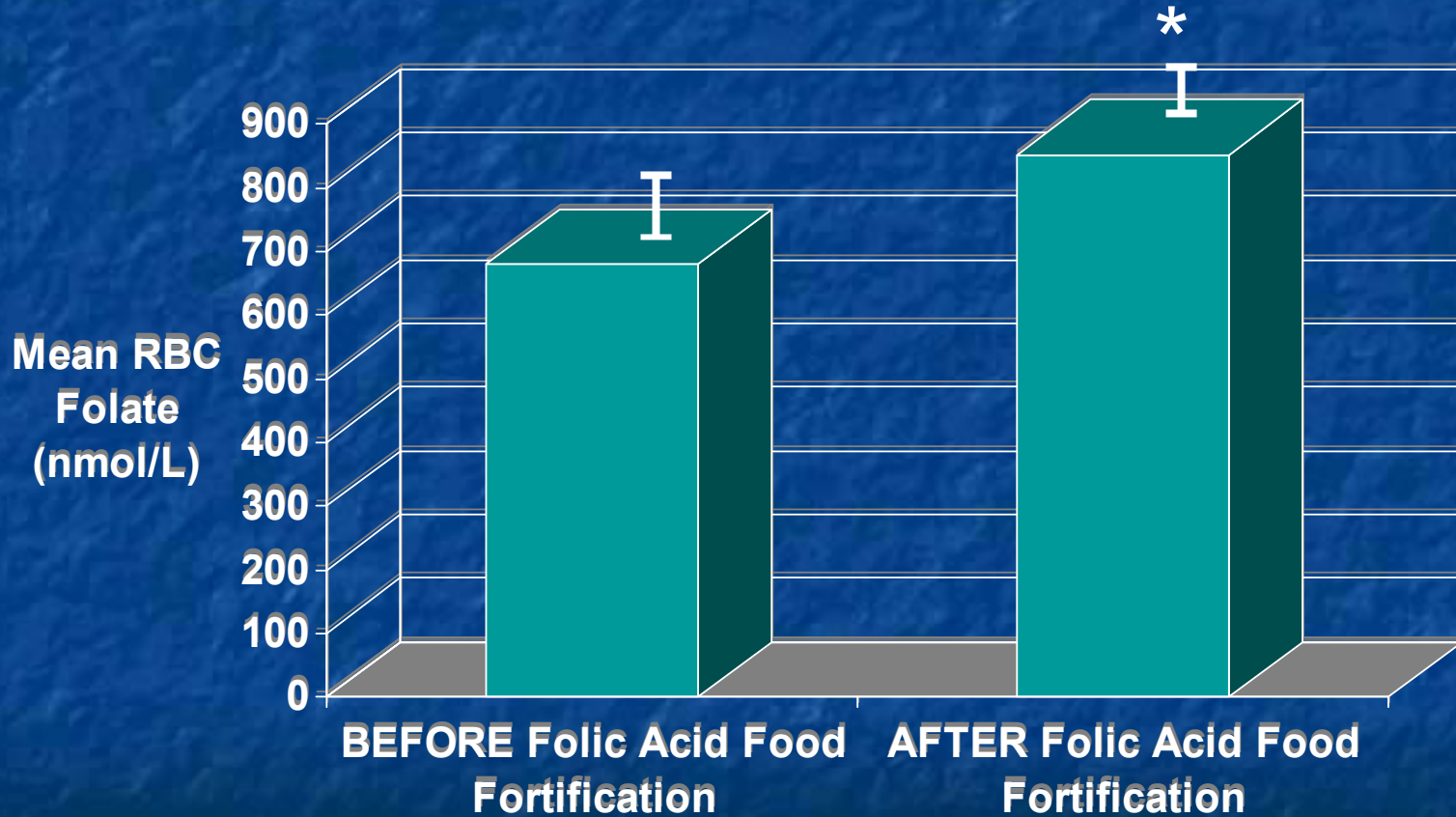
Pathway Of Homocysteine Metabolism

Prevalence Of Inadequate Dietary Folate Intake In The General Population



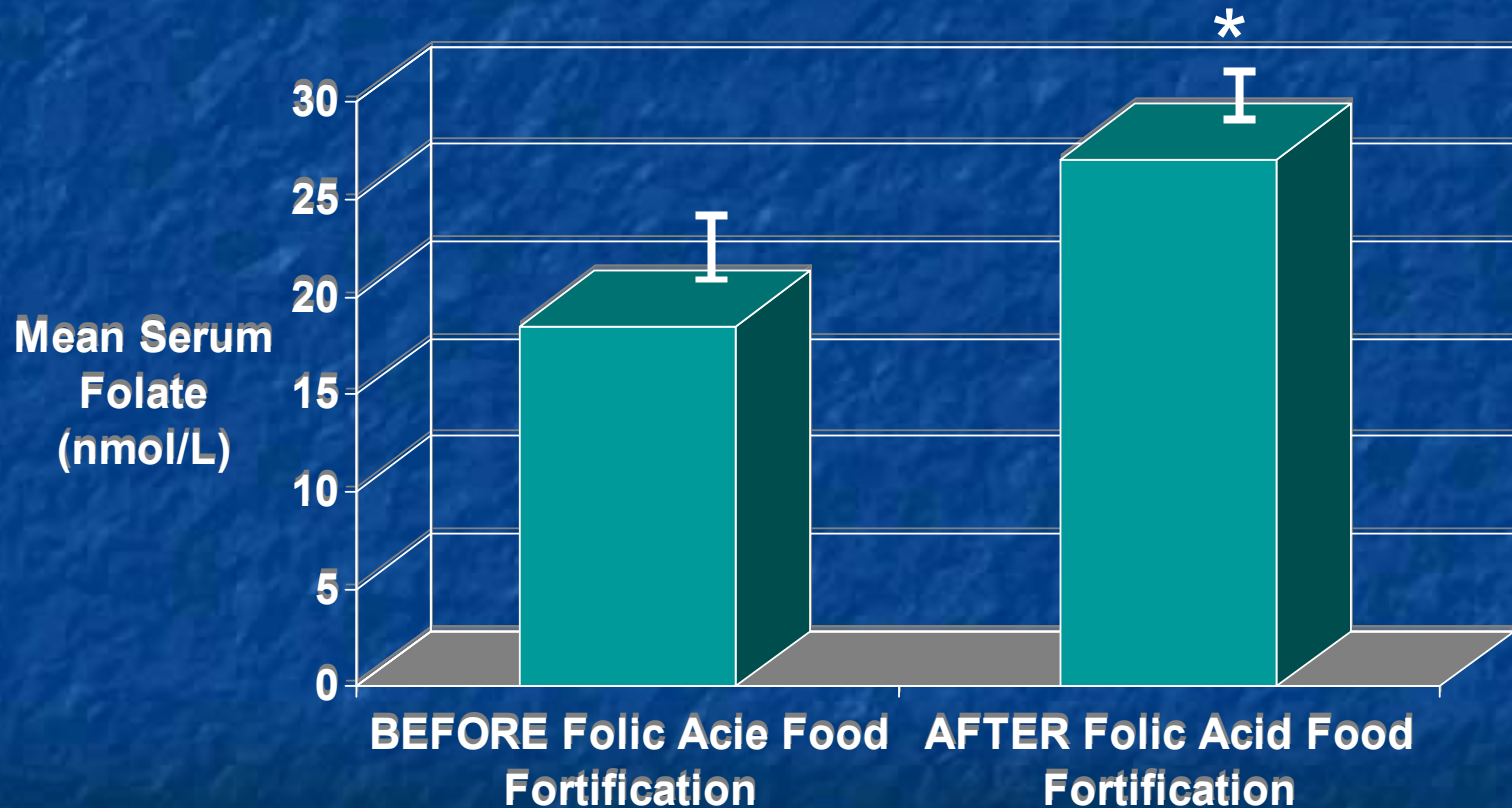
* Significant Difference ($p < 0.001$)

Red Blood Cell (RBC) Folate In The General Population



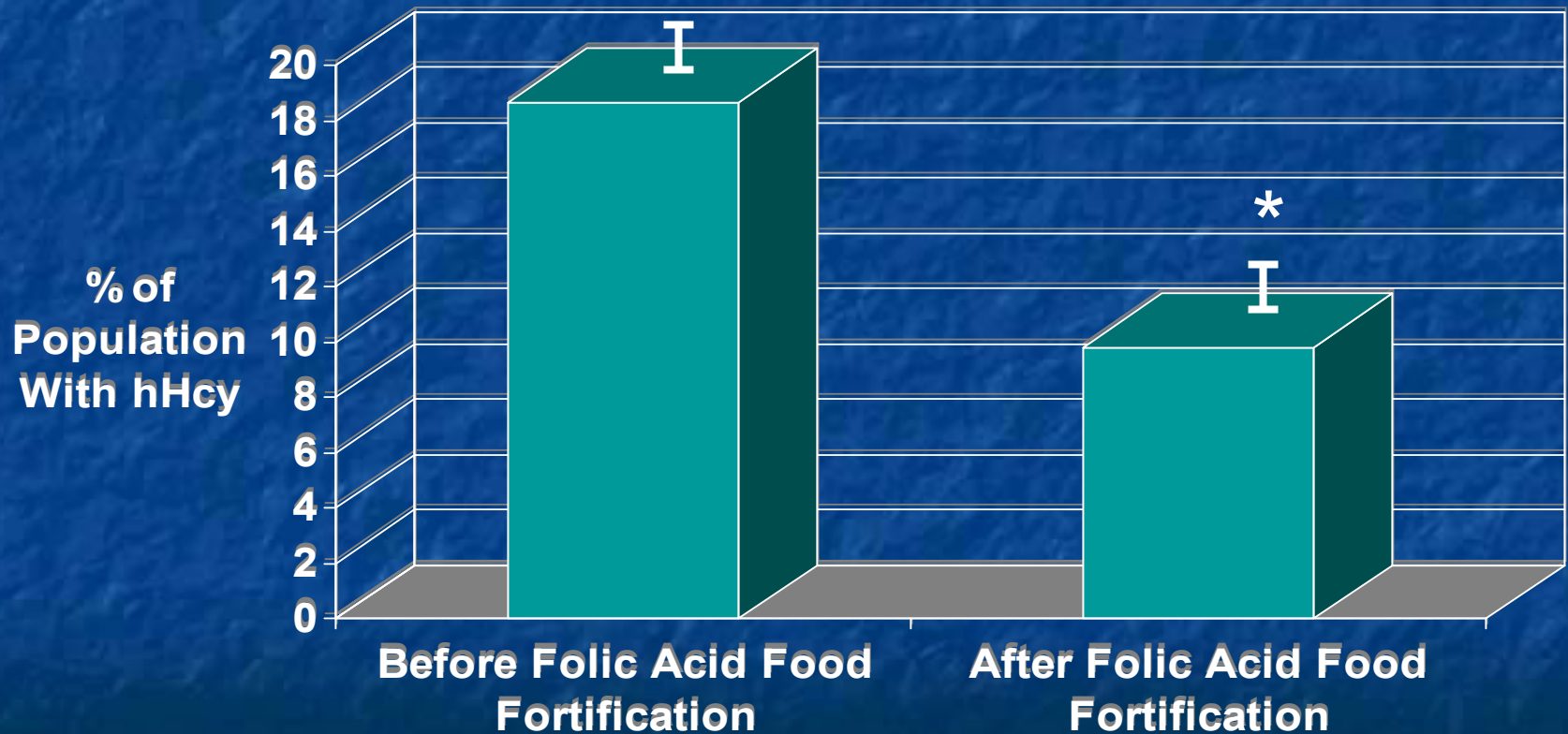
* Significant Difference ($p < 0.001$)

Serum Folate In The General Population



* Significant Difference ($p < 0.001$)

Prevalence Of Hyperhomocysteinemia (hHcy) ($\geq 13\mu\text{mol/L}$) In The General Population



* Significant Difference ($p < 0.001$)

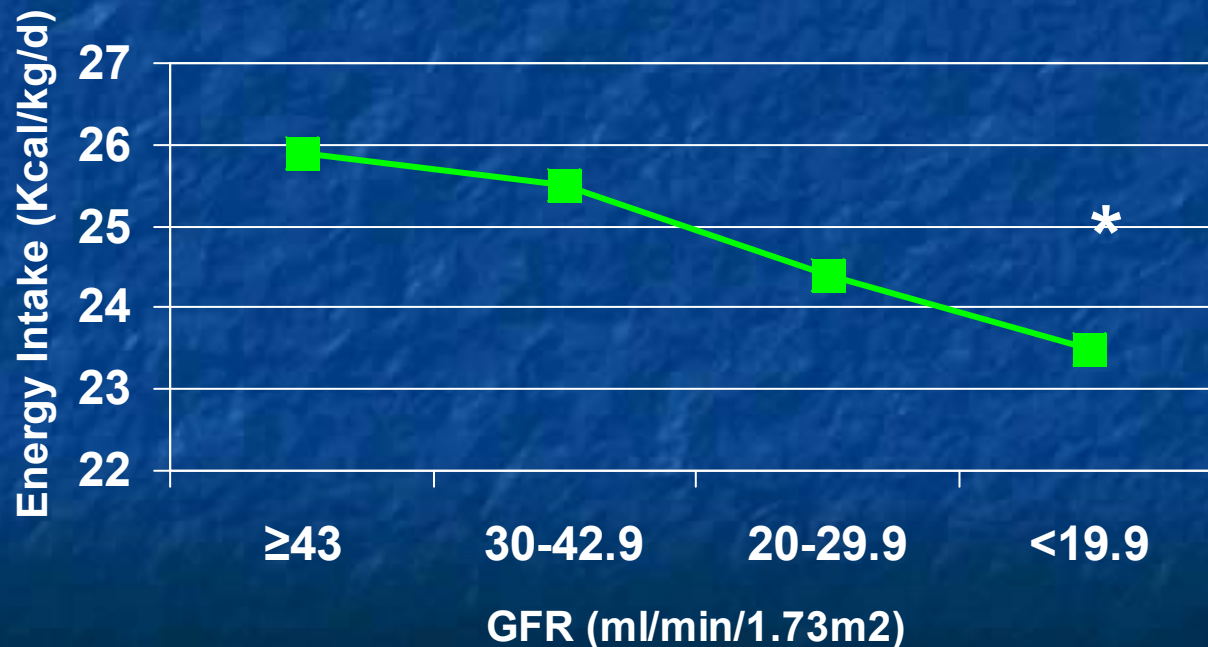
Jacques P, 1999

Prevalence Of Hyperhomocysteinemia (hHcy)
($\geq 12\mu\text{mol/L}$) in people with predialysis CKD
after Folic Acid Fortification of the Food Supply



Energy Intake By Glomerular Filtration Rate (GFR) In Predialysis Chronic Kidney Disease

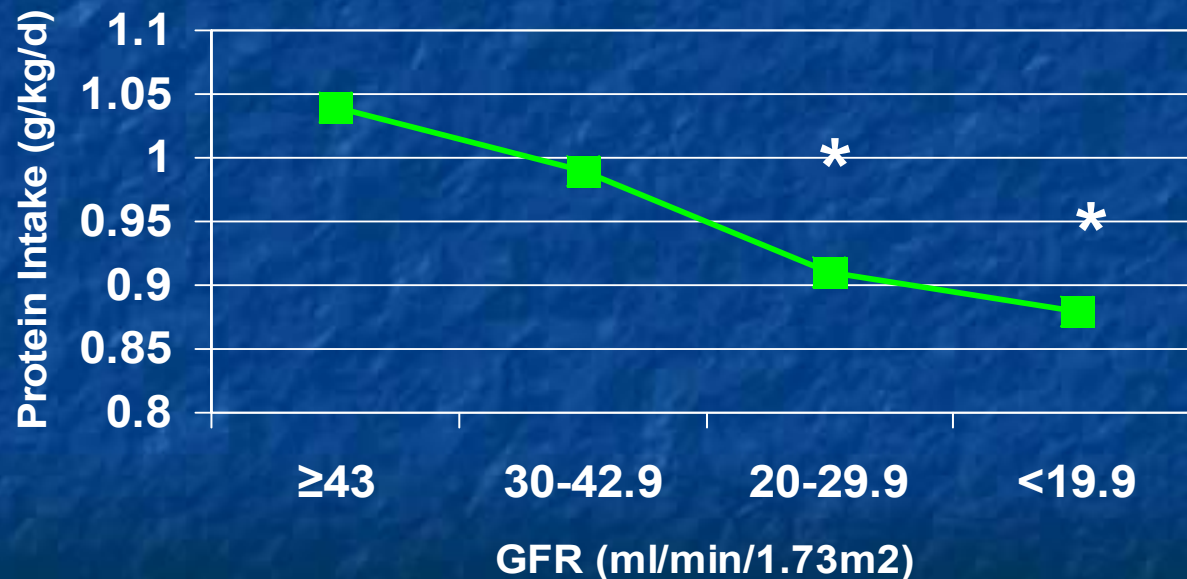
Energy Intake By GFR Quartile



* P<0.05 as compared with a GFR of ≥ 43

Protein Intake And Glomerular Filtration Rate (GFR) In Predialysis Chronic Kidney Disease

Protein Intake By GFR Quartile



* P<0.05 as compared with a GFR ≥ 43

Rationale

In the predialysis CKD population:

- The prevalence of hyperhomocysteinemia has not been described after folic acid food fortification
- The prevalence of inadequate intakes of folate, vitamins B12 and B6, energy and protein have never been described and
- There is uncertainty as to the need for the supplementation of the vitamins folate, B12 and B6

Primary Objectives

In the pCKD population:

- To estimate the prevalence and severity of hyperhomocysteinemia
- To measure intake of folate, vitamins B12 and B6, protein and energy from food and supplements and estimate the prevalence of inadequate intake of these nutrients from food alone

Secondary Objectives

In the pCKD population:

1. To describe the associations between:

Fasting plasma total homocysteine and

- dietary and supplemental intakes of folate, vitamins B₁₂ and B₆, protein and energy.
- vitamin status as measured by RBC folate and serums folate, B₁₂ and B₆.
- glomerular filtration rate.
- energy-protein status.

Secondary Objectives

2. To describe the associations between:

Dietary intakes of folate, vitamins B₁₂ and B₆, protein, energy and

- Gastrointestinal symptoms of uremia
- Glomerular filtration rate

Hypothesis

In the pCKD population:

- The prevalence of hyperhomocysteinemia (tHcy > 12 $\mu\text{mol/L}$), after folic acid food fortification, will be 75%.
- The majority of these patients will have inadequate intakes of folate, vitamins B₁₂ and B₆, protein and energy from food.

Methodology

Study Design

Prospective cross-sectional descriptive

Subjects

All new patient referrals to the predialysis clinics at St. Michael's Hospital and the University Health Network.

Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none">■ ≥ 18 years old■ $\text{GFR} < 60 \text{ mL/min/1.73m}^2$■ Able to read and understand English■ Able to provide informed consent	<ul style="list-style-type: none">■ Liver or kidney transplant■ Cancer or liver disease■ Vitamin B₁₂ deficiency■ Taking an antibiotic 7 days prior to blood sample■ In another study that interferes with Hcy metabolism

Data Collection

1ST
visit

Fasting blood samples

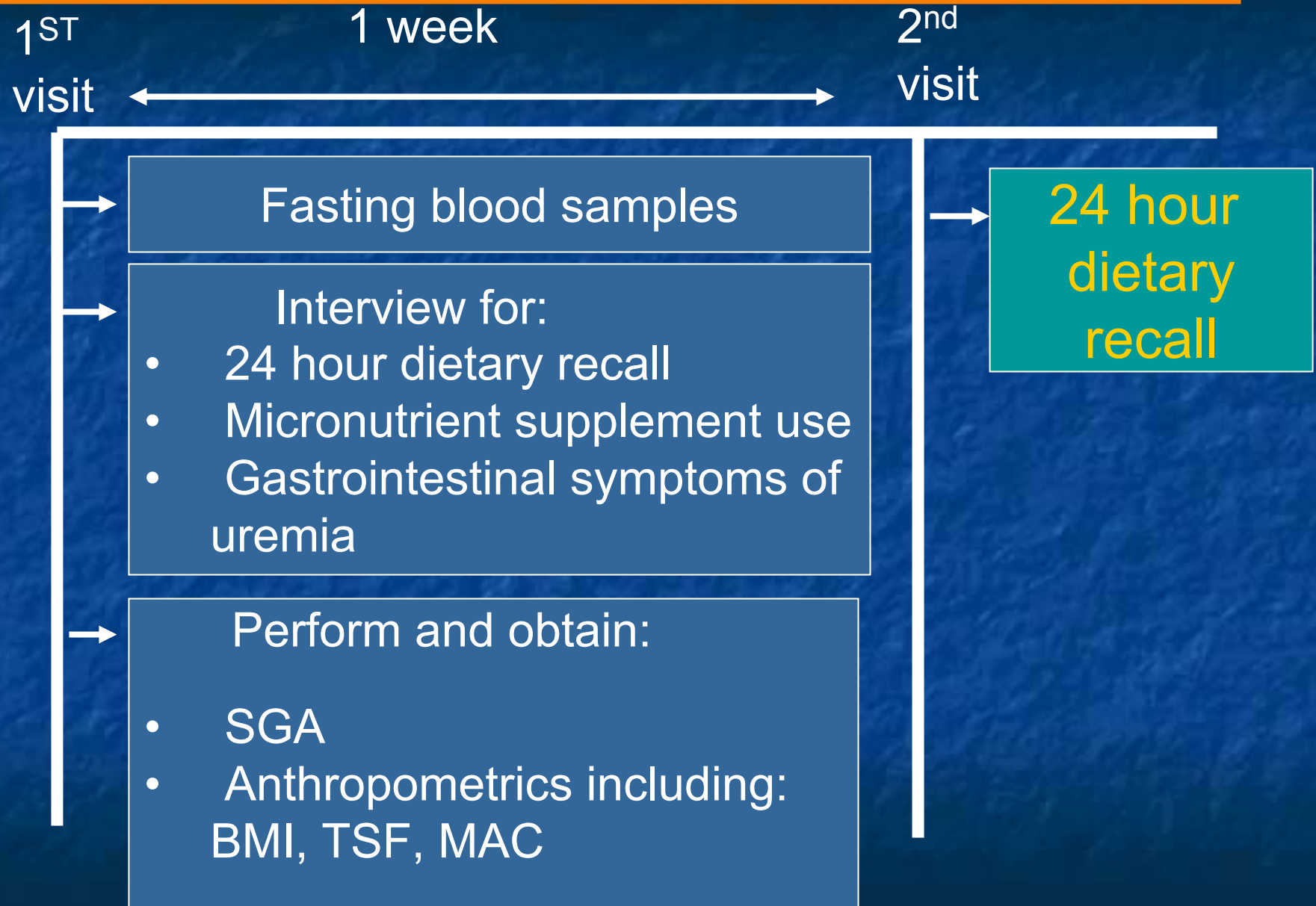
Interview For:

- 24 hour dietary recall
- Micronutrient supplement use
- Gastrointestinal symptoms of uremia

Perform & Obtain Information For:

1. Subjective Global Assessment (SGA)
2. Anthropometrics including: height, weight, triceps skinfold (TSF), mid upper arm circumference (MAC)

Data Collection



Biochemical Analysis

Sample	Analytical Method
Plasma total homocysteine	Competitive immunoassay
Serum B ₁₂	Competitive immunoassay
RBC folate	Microbiological assay
Serum Folate	Microbiological assay
Serum pyridoxal 5 phosphate	Tyrosine decarboxylase assay

Sample Size

- Sample size calculation $n = 72$ subjects
- Sample size estimate based on:
 1. A predicted prevalence of hyperhomocysteinemia of 75%
 2. A 95% confidence level
 3. A 20% confidence interval

Clinical Implications Of Our Research

- This will be the first study to describe the prevalence of hHcy in a pCKD population in the era of Folic Acid Fortification, and will elucidate if elevated plasma tHcy is still a health concern in the Canadian pCKD population.

Clinical Implications Of Our Research

This will be the first study to describe the prevalence of inadequate dietary intake of the vitamins involved in homocysteine metabolism the CKD population in the era of Folic Acid Fortification.

This information, considered in conjunction with vitamin status and p tHcy, may provide evidence to guide dietetic practice regarding whether or not dietitians should be prescribing vitamin supplements to people with pCKD.