

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

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# Research Team

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# Prevalence Of Predialysis Chronic Kidney Disease (CKD)

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- 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

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**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**

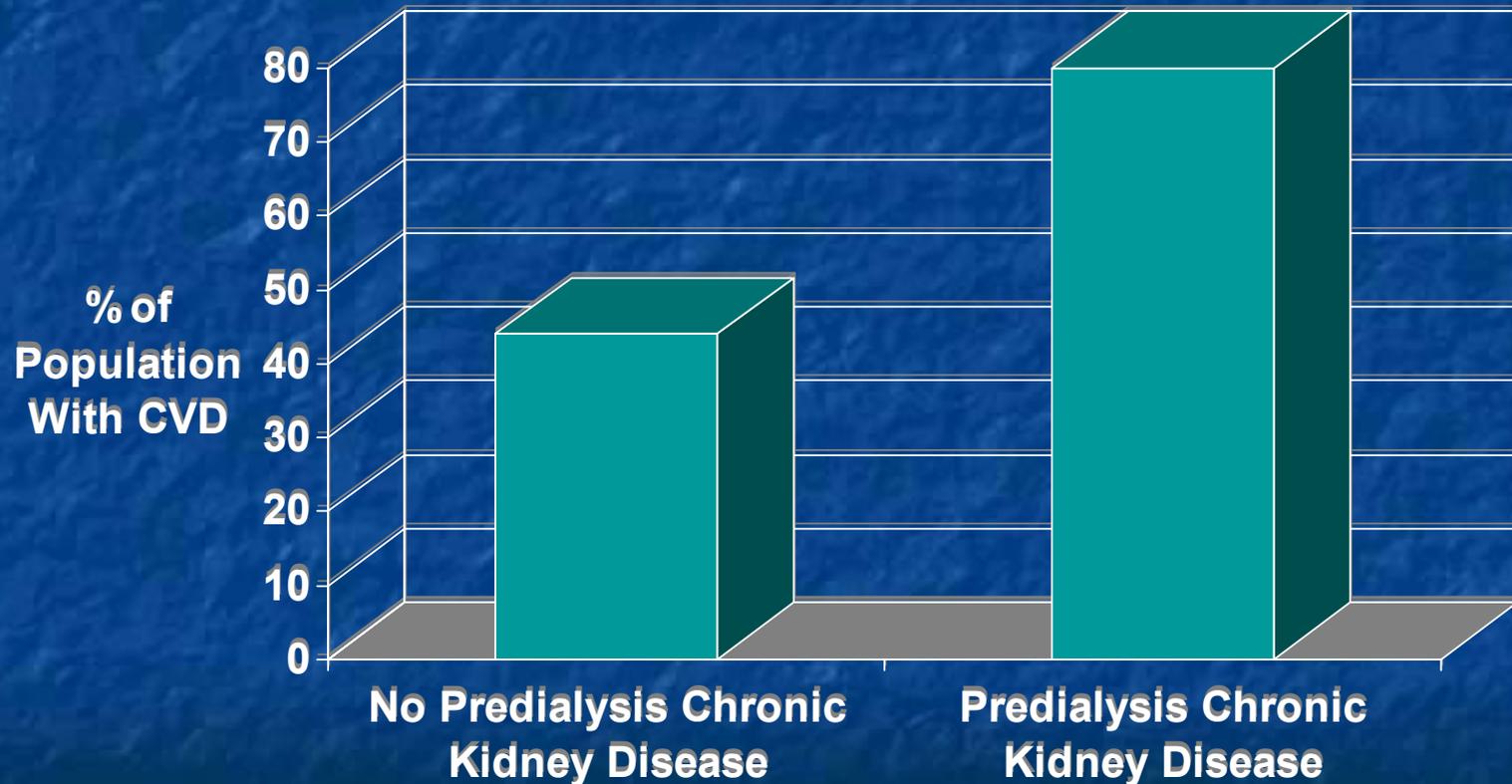
**Stage 5: GFR  $<$  15**

**GFR = ml/min/1.73m<sup>2</sup>**

Collins AJ, 2003

# Prevalence Of Cardiovascular Disease - The General Population

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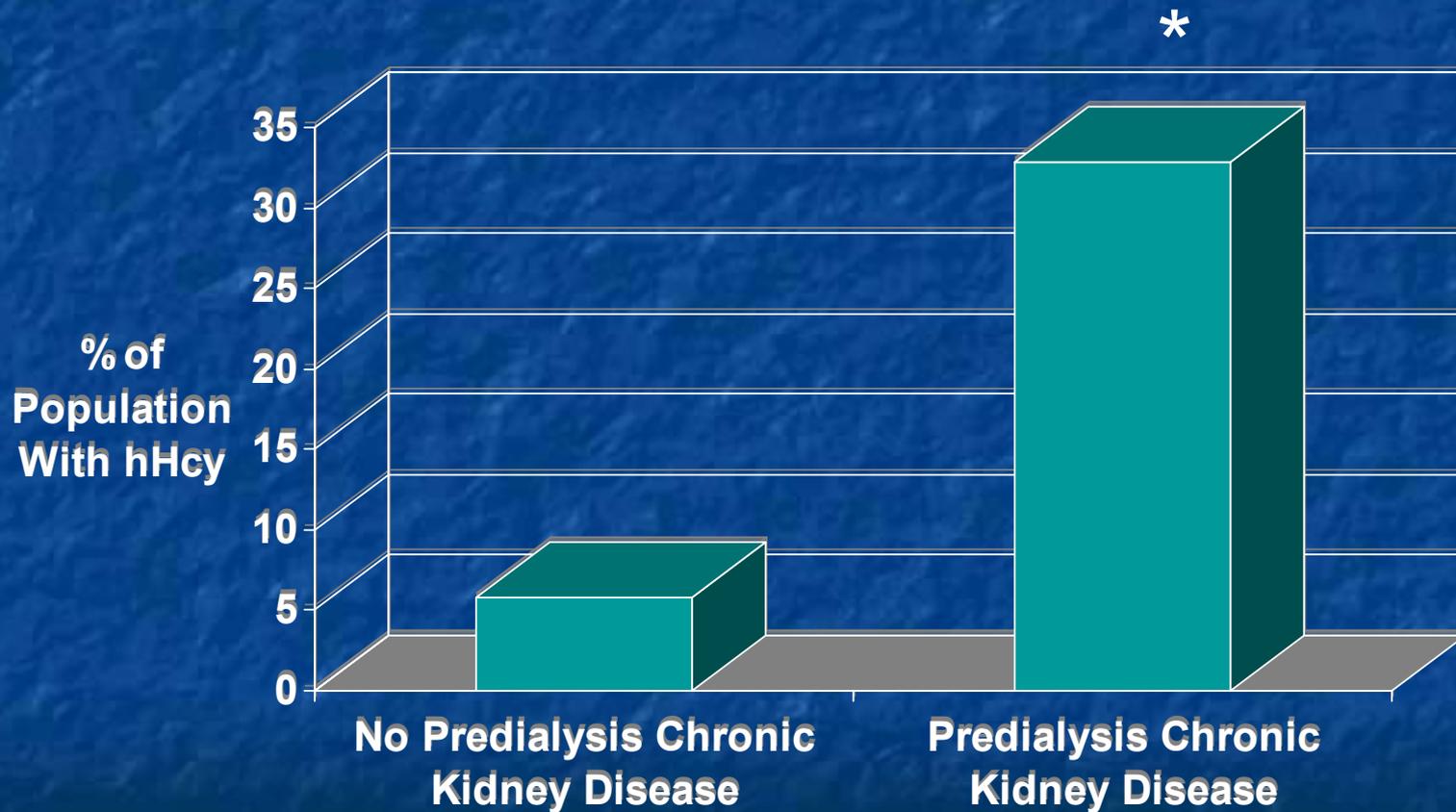


# Homocysteine And Risk For Cardiovascular Disease (CVD)

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- 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

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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 $\beta$ -synthase deficiency)	> 500 Gupta A, 1997

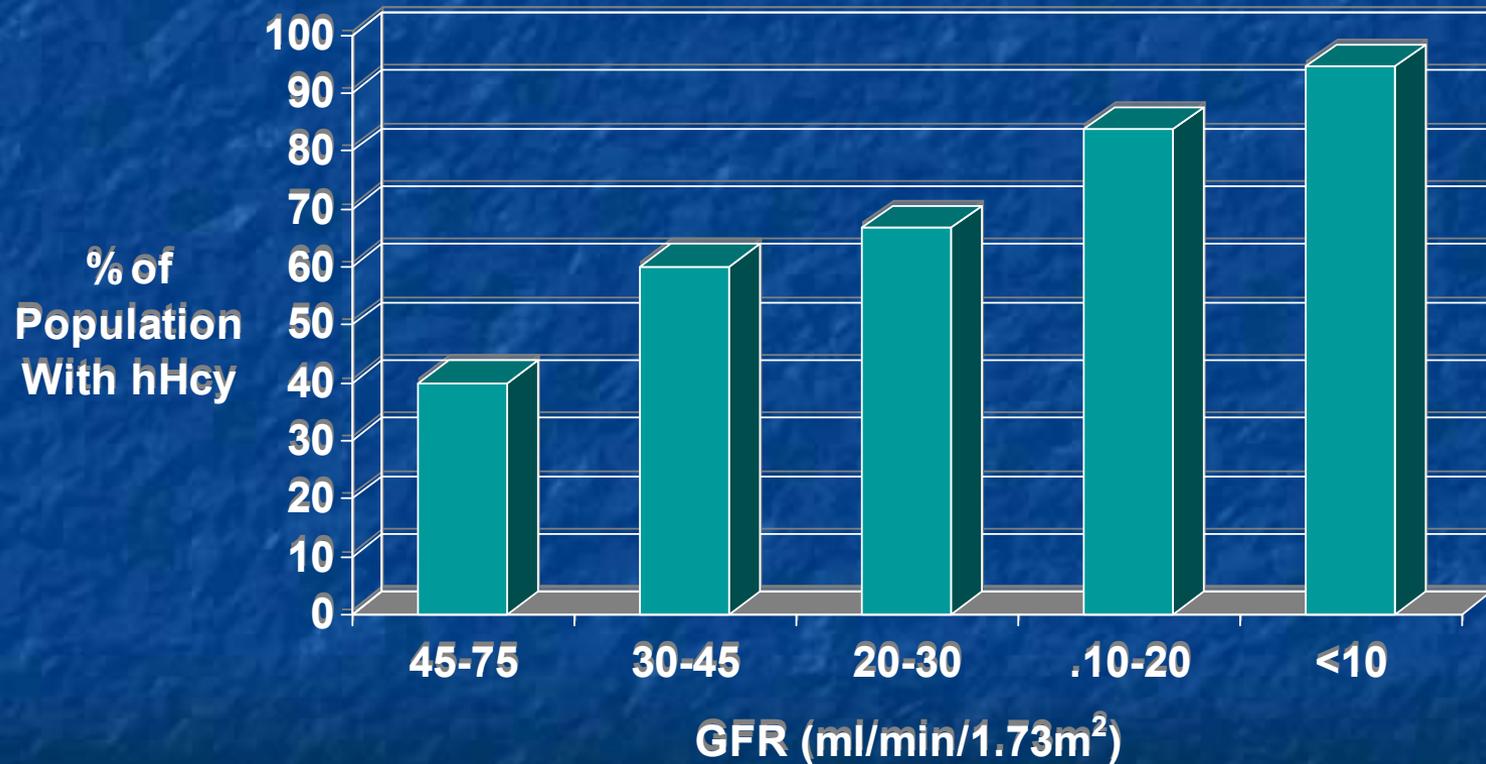
# Glomerular Filtration Rate (GFR) Is A Determinant Of Plasma Total Homocysteine (P tHcy)

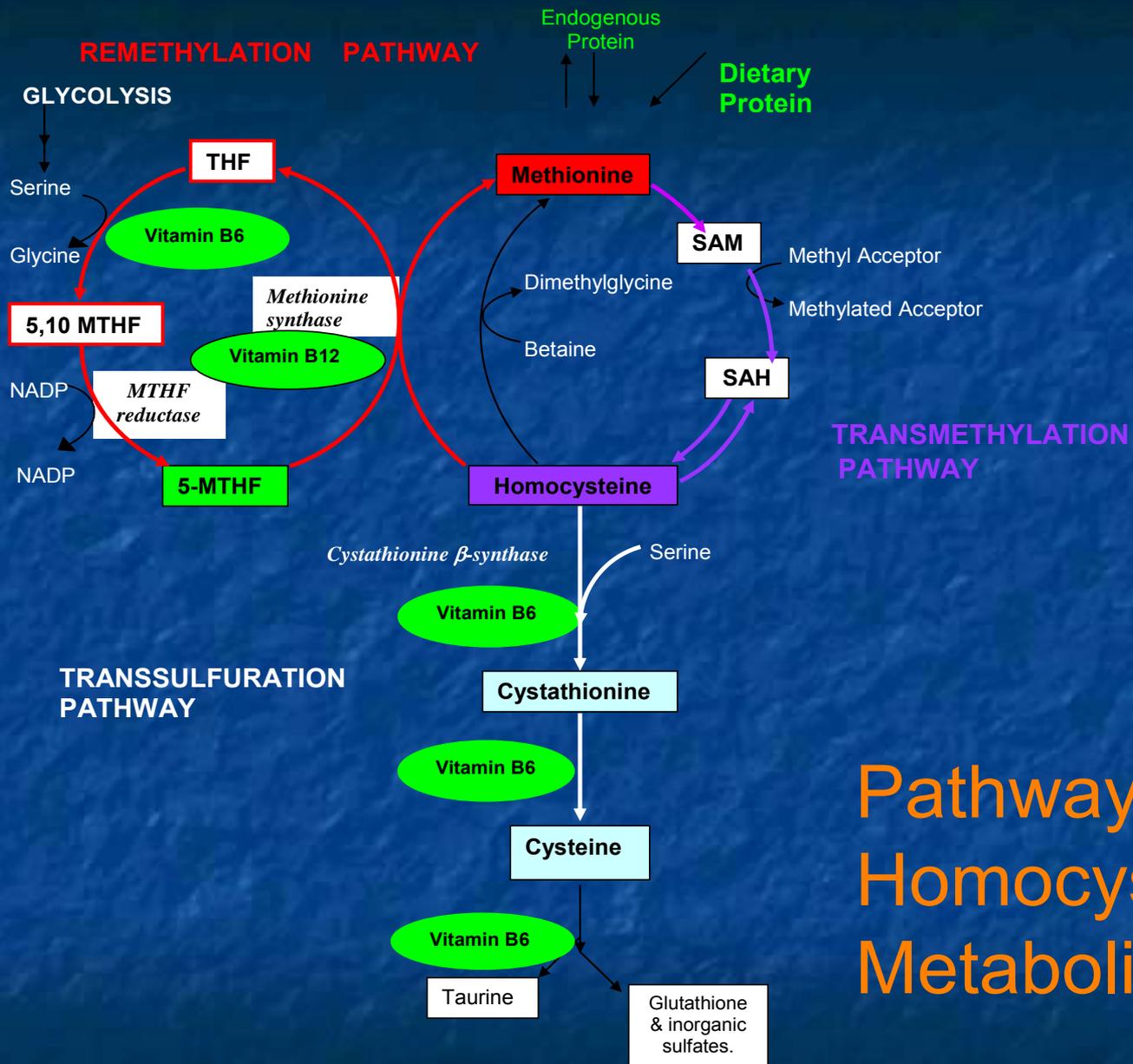
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Plasma tHcy was found to be inversely associated with GFR ( $r = -0.39$ ;  $p < 0.0001$ ).

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

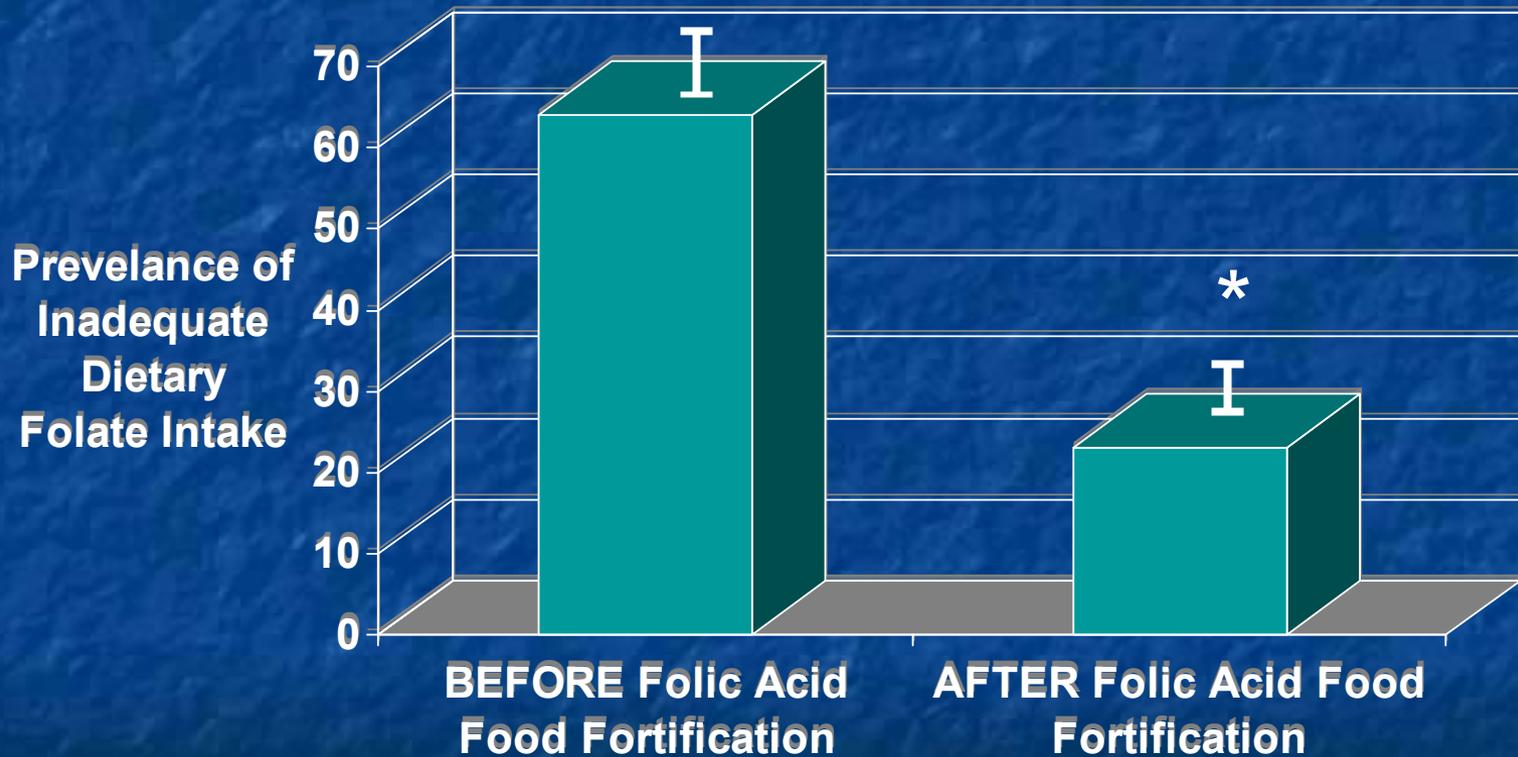
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# Pathway Of Homocysteine Metabolism

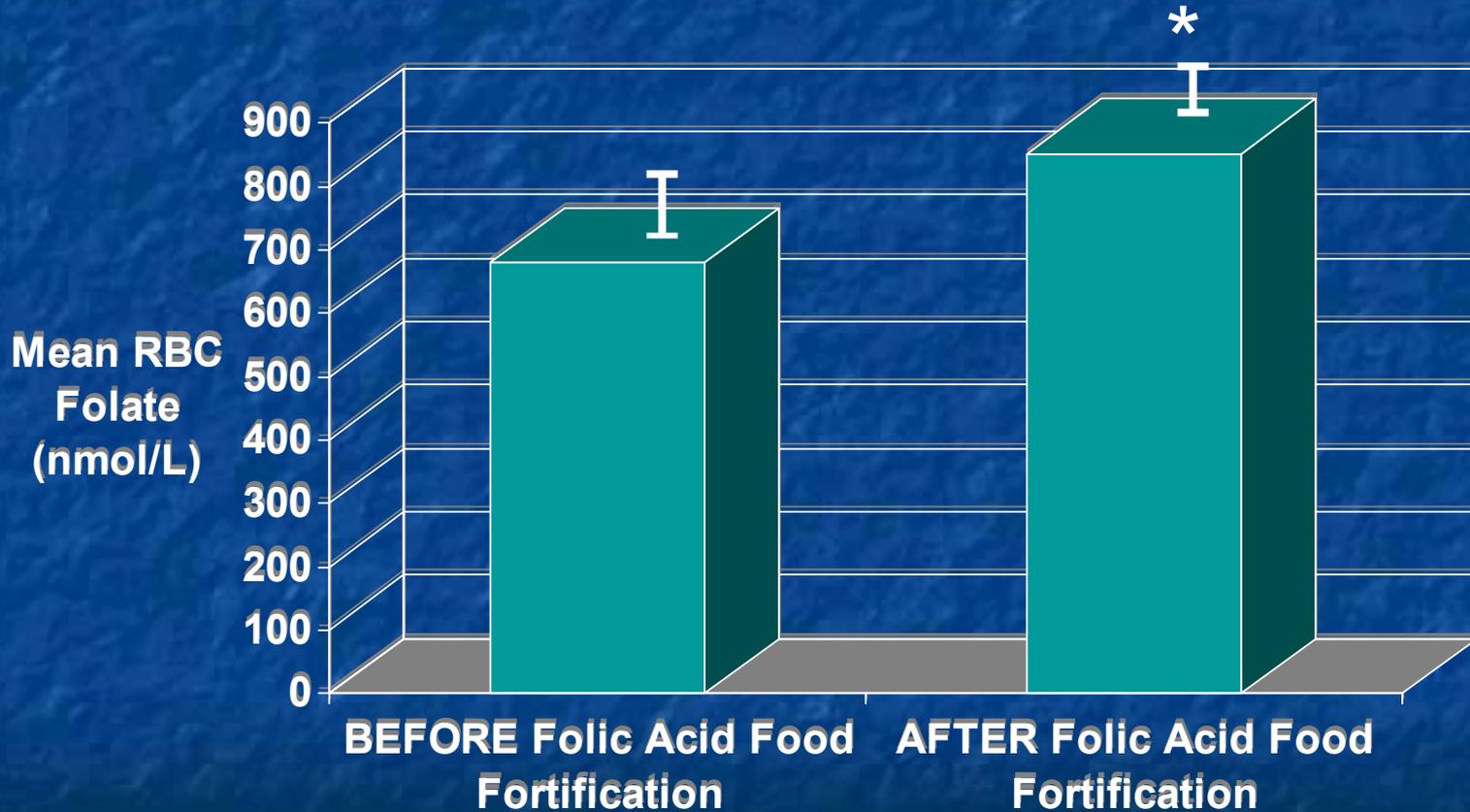
# Prevalence Of Inadequate Dietary Folate Intake In The General Population



\* Significant Difference ( $p < 0.001$ )

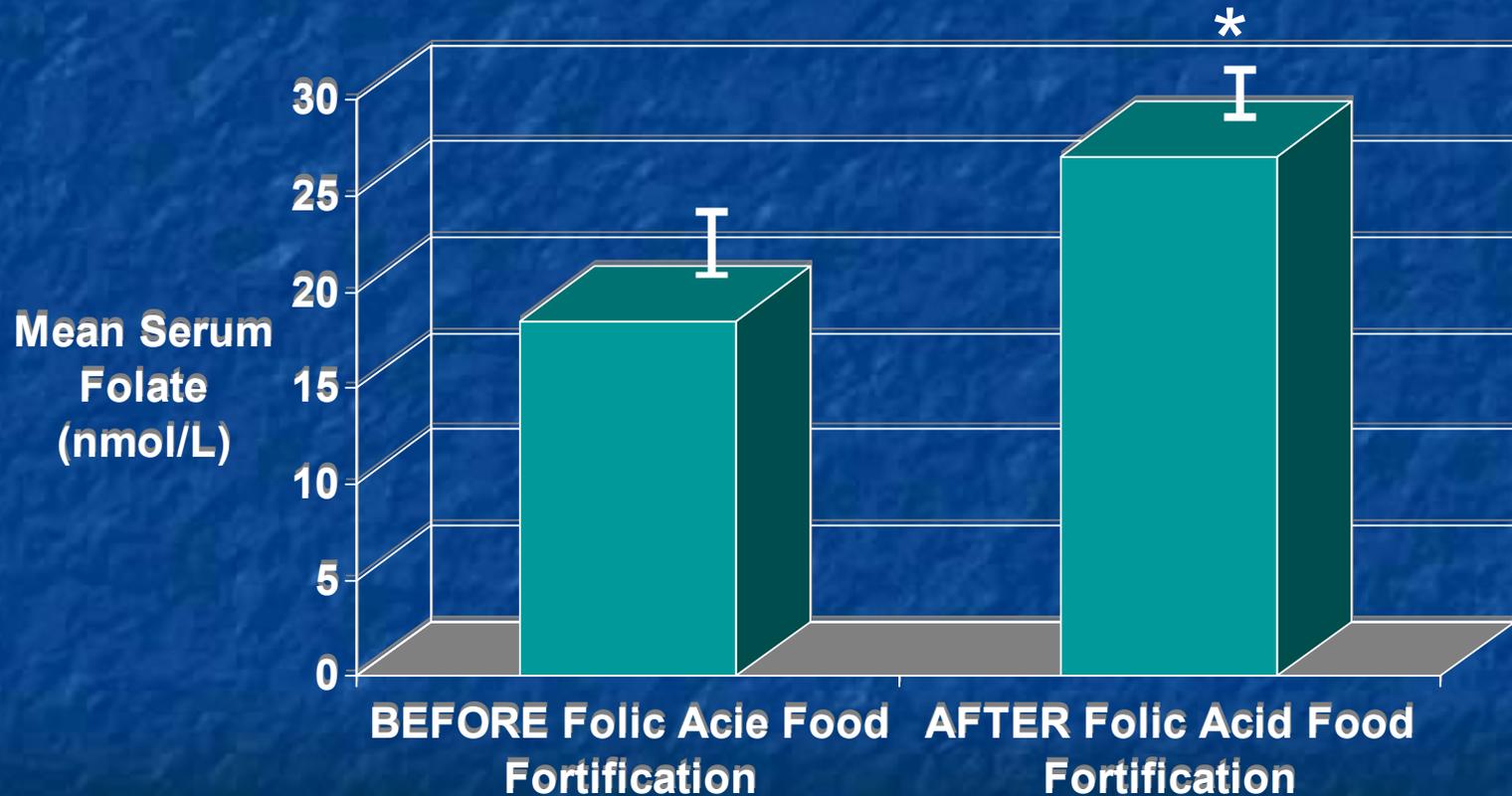
# Red Blood Cell (RBC) Folate In The General Population

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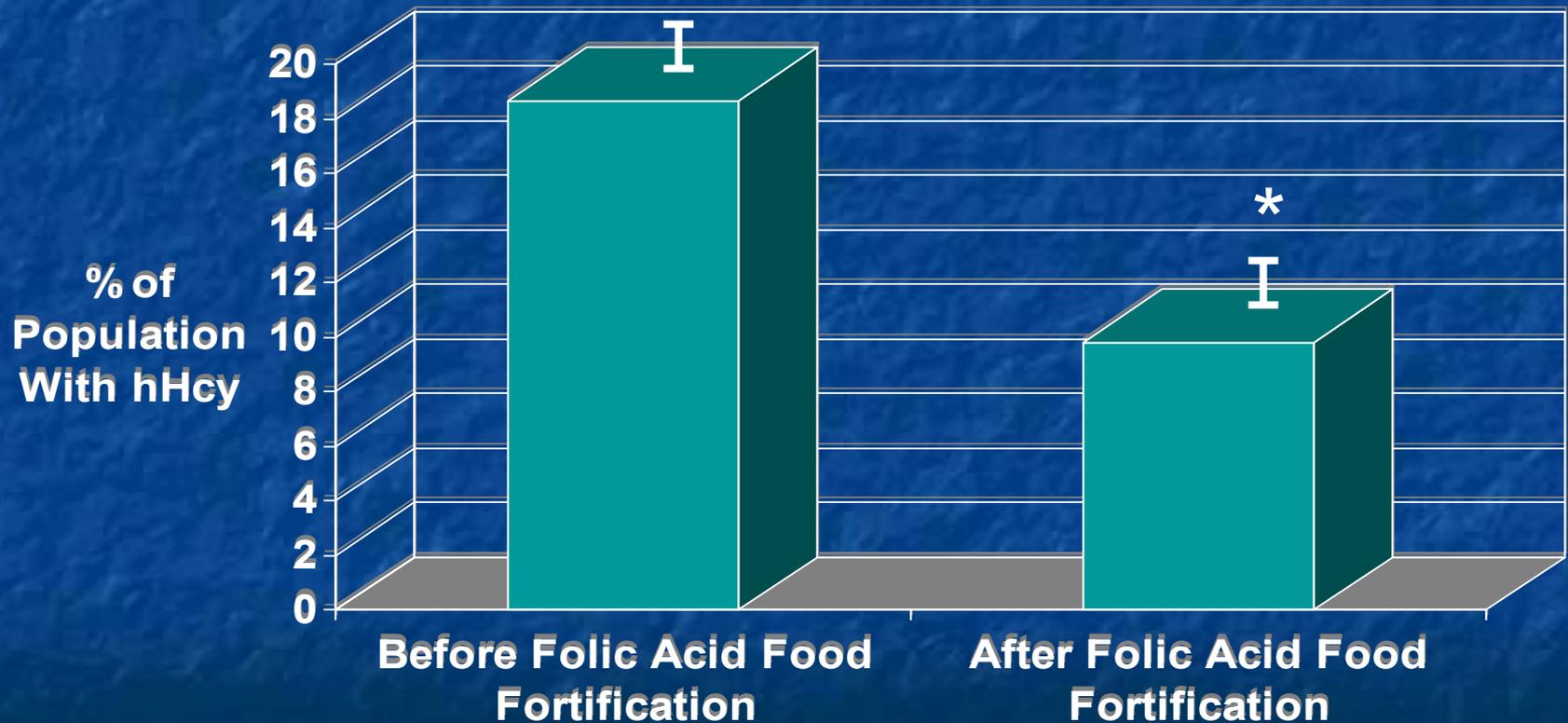
\* Significant Difference ( $p < 0.001$ )

# 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

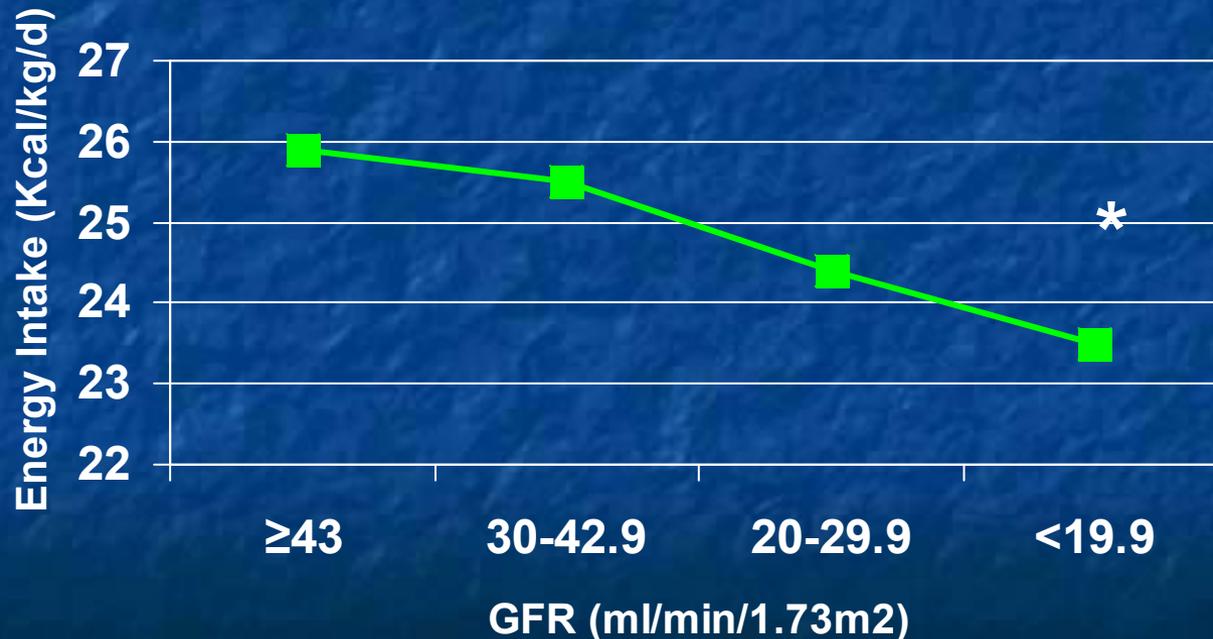
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# Energy Intake By Glomerular Filtration Rate (GFR) In Predialysis Chronic Kidney Disease

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Energy Intake By GFR Quartile

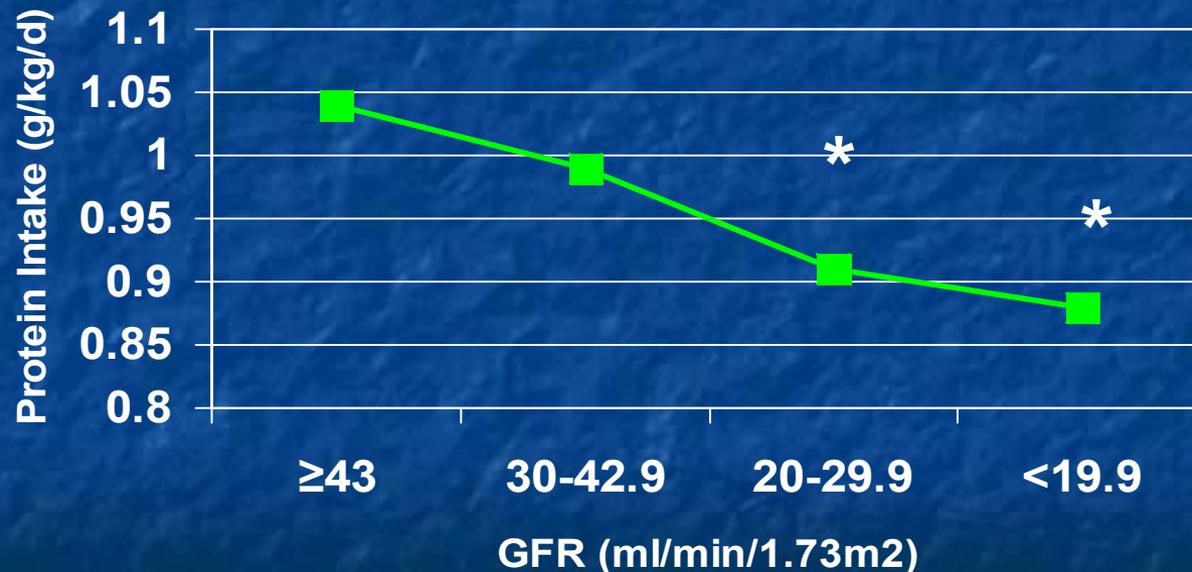


\* P<0.05 as compared with a GFR of ≥ 43

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

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Protein Intake By GFR Quartile



\* P<0.05 as compared with a GFR ≥ 43

# Rationale

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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

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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

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In the pCKD population:

1. To describe the associations between:

Fasting plasma total homocysteine and

- dietary and supplemental intakes of folate, vitamins B<sub>12</sub> and B<sub>6</sub>, protein and energy.
- vitamin status as measured by RBC folate and serums folate, B<sub>12</sub> and B<sub>6</sub>.
- glomerular filtration rate.
- energy-protein status.

# Secondary Objectives

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2. To describe the associations between:

Dietary intakes of folate, vitamins B<sub>12</sub> and B<sub>6</sub>, protein, energy and

- Gastrointestinal symptoms of uremia
- Glomerular filtration rate

# Hypothesis

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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 B<sub>12</sub> and B<sub>6</sub>, protein and energy from food.

# Methodology

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## 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

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Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"><li>■ <math>\geq 18</math> years old</li><li>■ <math>\text{GFR} &lt; 60 \text{ mL/min/1.73m}^2</math></li><li>■ Able to read and understand English</li><li>■ Able to provide informed consent</li></ul>	<ul style="list-style-type: none"><li>■ Liver or kidney transplant</li><li>■ Cancer or liver disease</li><li>■ Vitamin B<sub>12</sub> deficiency</li><li>■ Taking an antibiotic 7 days prior to blood sample</li><li>■ In another study that interferes with Hcy metabolism</li></ul>

# Data Collection

1<sup>ST</sup>  
visit

Fasting blood samples

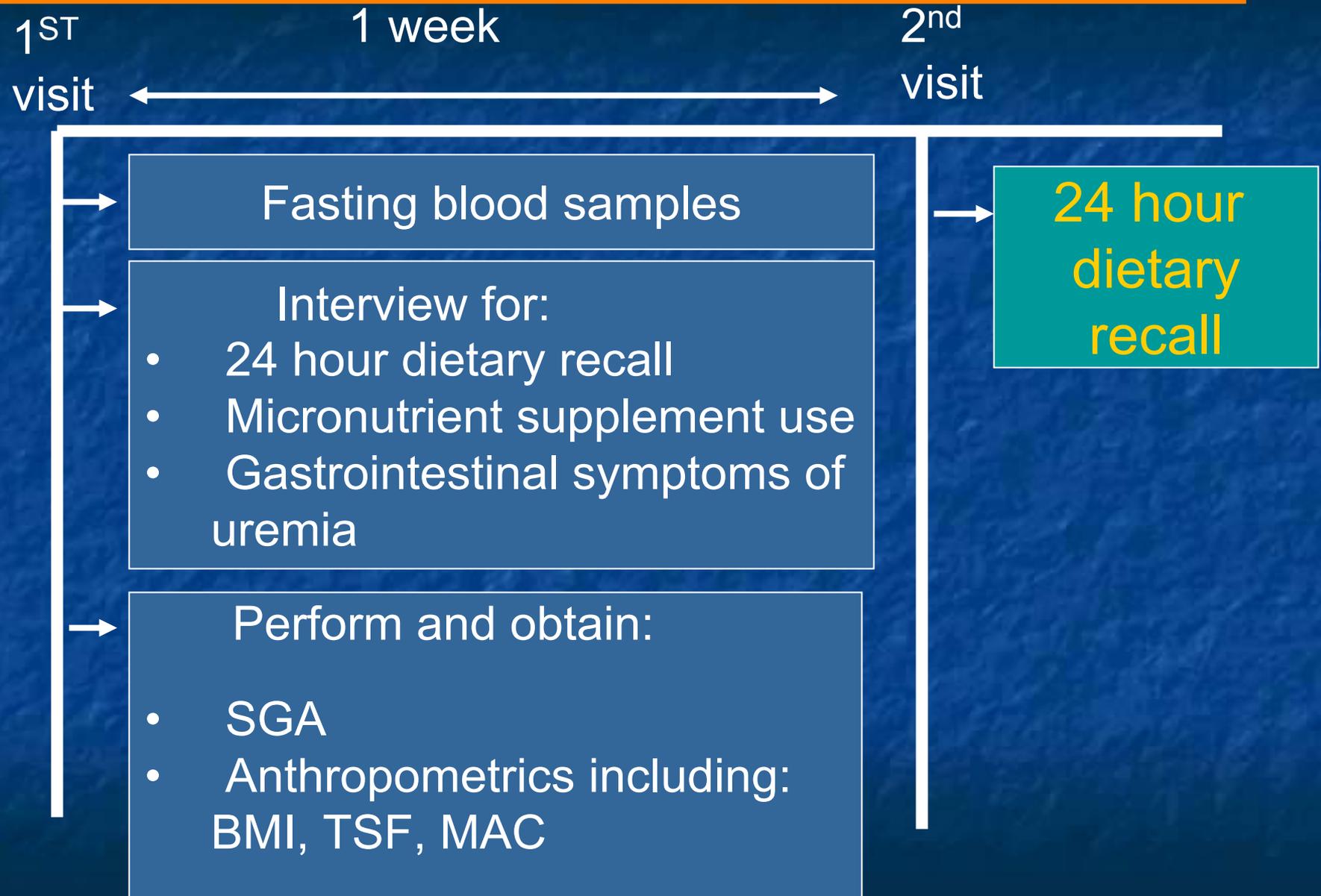
Interview For:

- 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

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

# Sample Size

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- 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

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- 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

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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.