

Vitamin D in pregnancy: too much and too little

Claire Roberts

Discipline of Obstetrics and Gynaecology



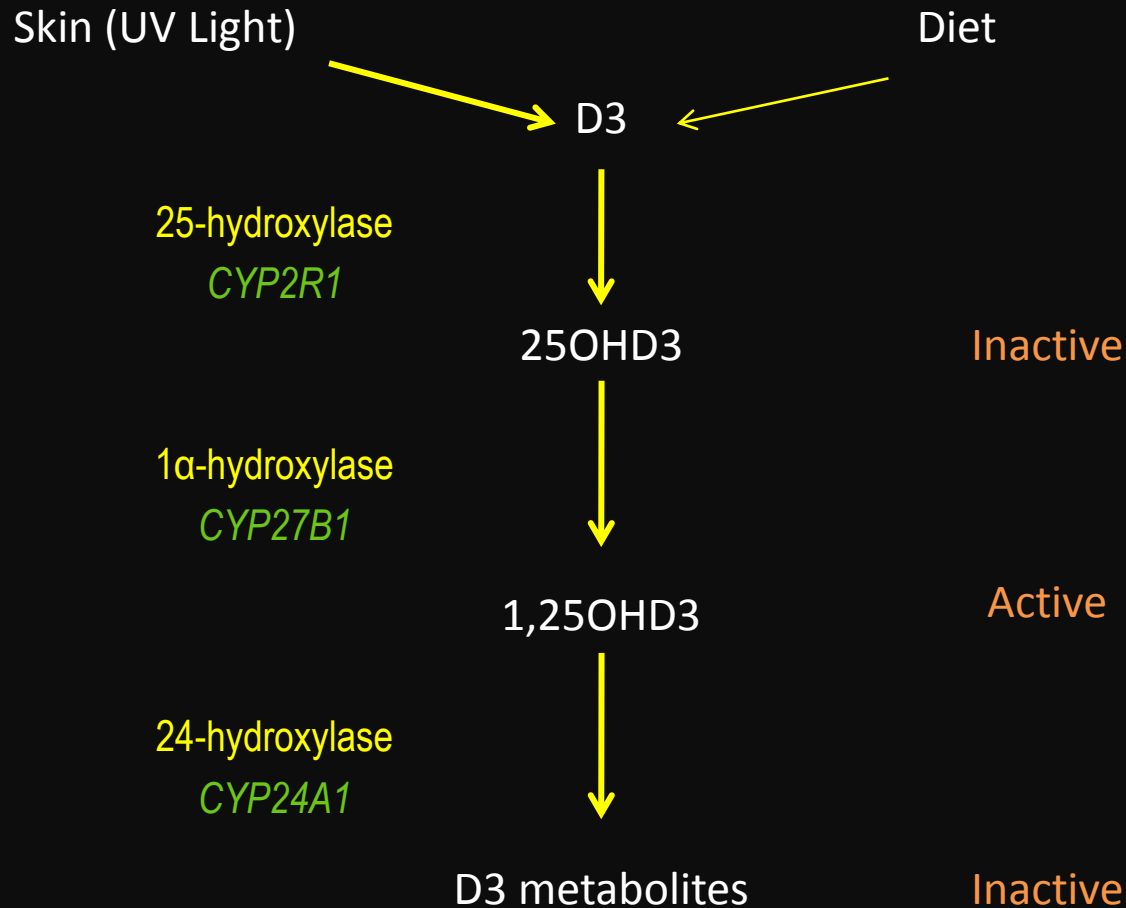
SCOPE Consortium

Vitamin D: a secosteroid hormone

- Vitamin D deficiency is associated with inflammatory diseases, various cancers, renin dependent hypertension, type 2 diabetes, bone diseases, CVD, multiple sclerosis, obesity, TB, influenza, depression, and others
- Emerging research shows that deficiency of Vitamin D is associated with pregnancy complications including preeclampsia, pre-term birth, IUGR and gestational diabetes
- Vitamin D increases hPL, hCG, oestrogen and progesterone synthesis in cultured term placenta



Vitamin D Synthesis





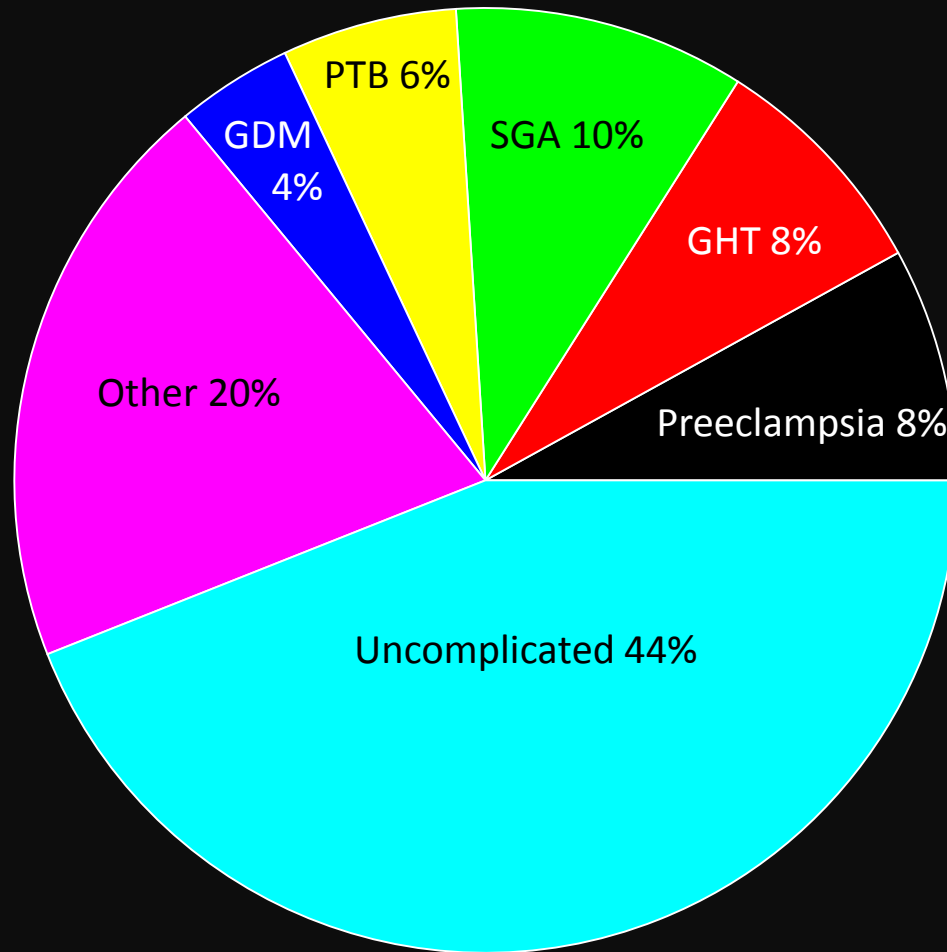
SCOPE

- **S**creening **f**Or **P**regnancy **E**ndpoints
- Adelaide 1380 women recruited at the Lyell McEwin Hospital between Sep 2005-Sep 2008, the last few of whom delivered in March 2009
- 1169 ongoing pregnancies from whom we have assembled a biobank of biological samples at various timepoints plus detailed family history, clinical, psycho-socio-economic & dietary information plus DNA and info from fathers and babies
- Plus SCOPE Auckland (2065 women), London, Manchester, Cork, Leeds (~2500 women)

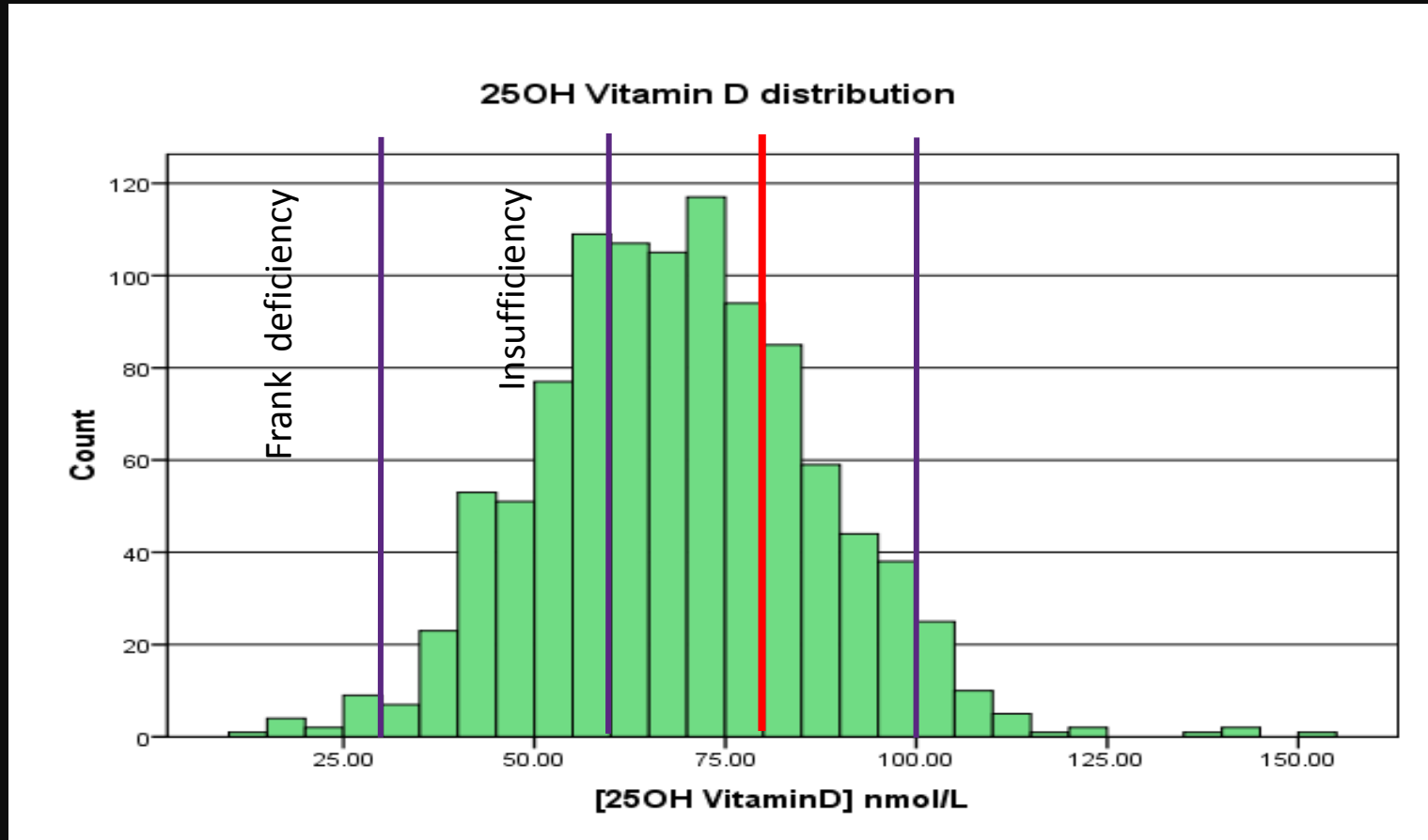


SCOPE Adelaide Outcomes

N=1169
Women
Partners
Babies



Serum 25OH D3 at 15 weeks gestation

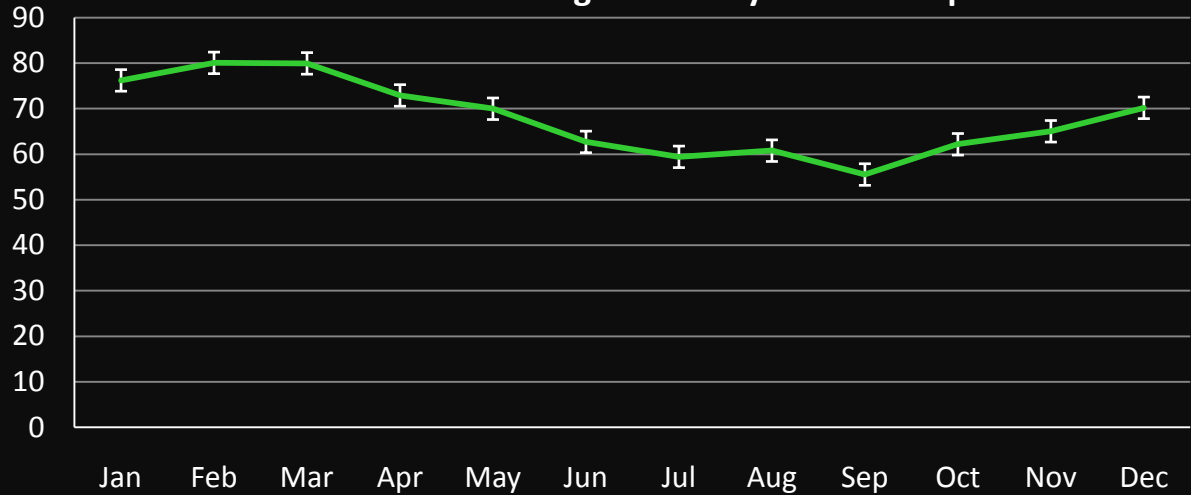


35% 75% 4%

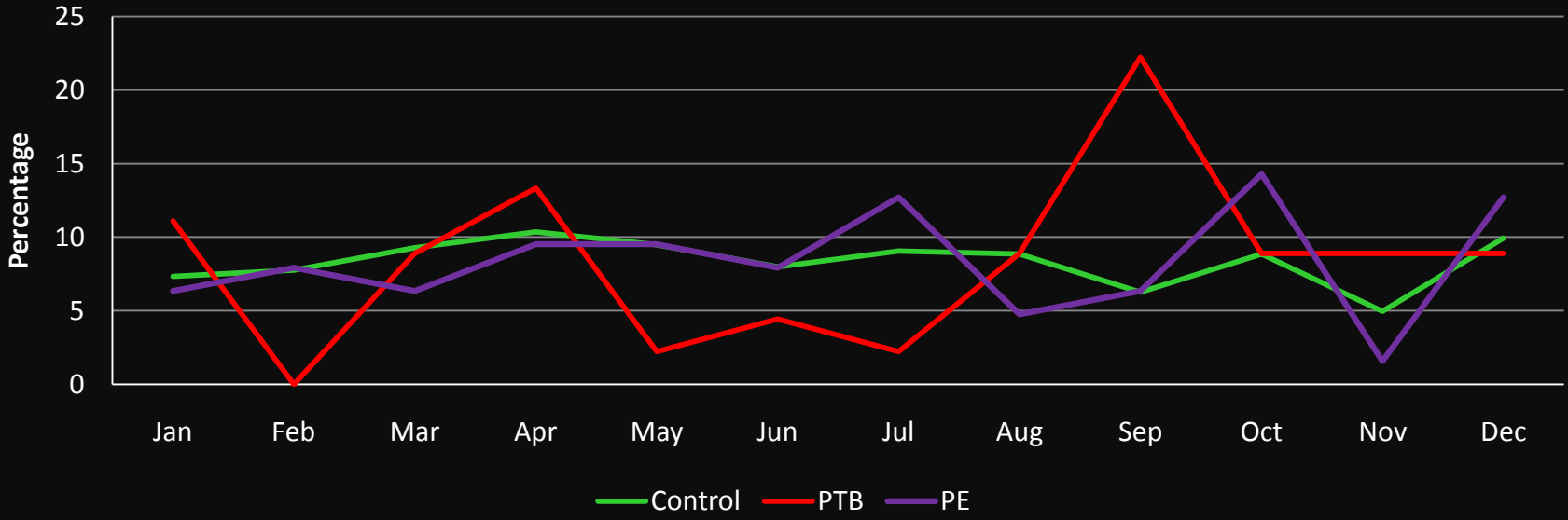
Mean: 68 nmol/L Min: 10 nmol/L Max: 152 nmol/L



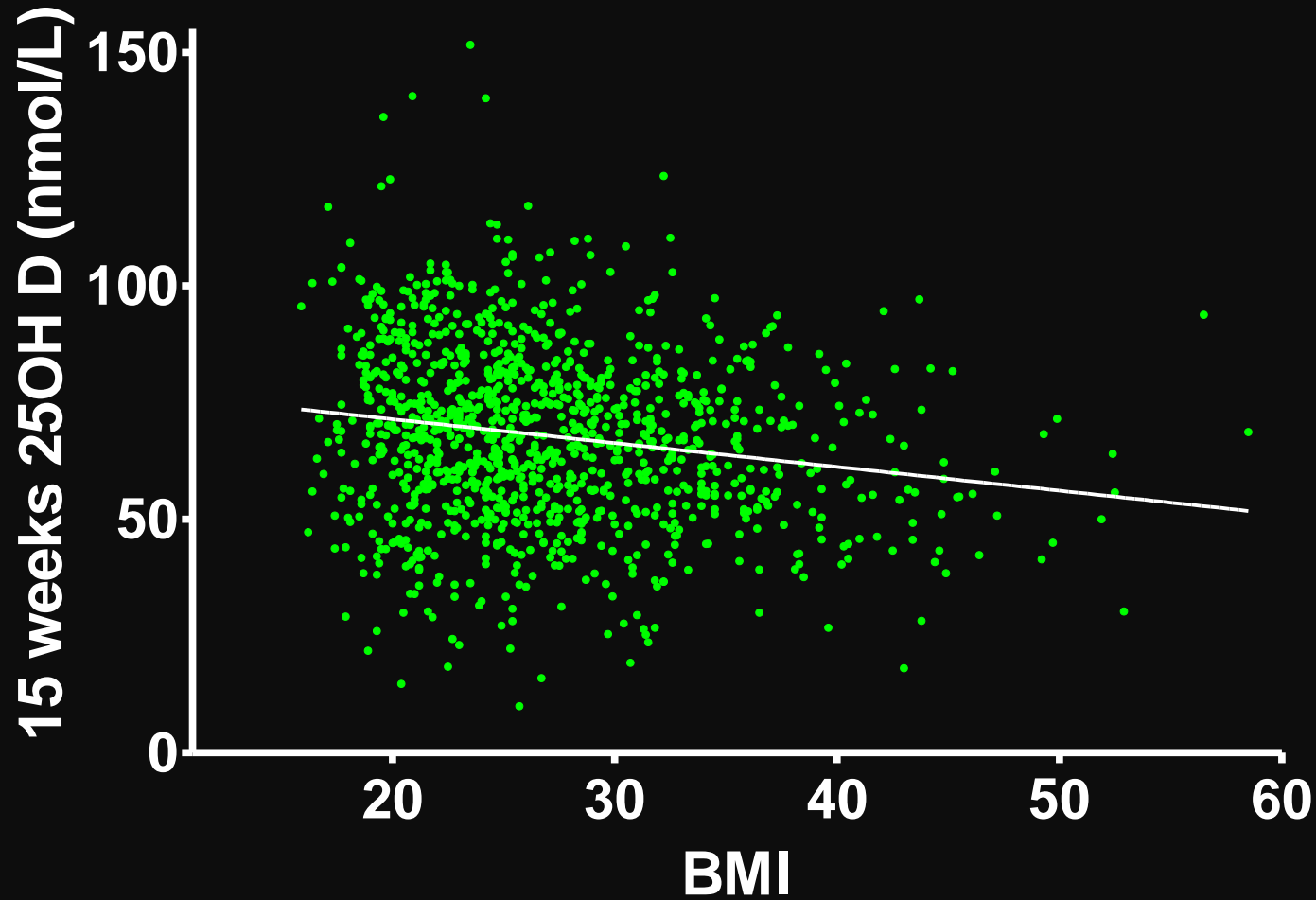
25OH Vitamin D3 15 weeks gestation by month sampled



Percentage of Pregnancies by month of EDD



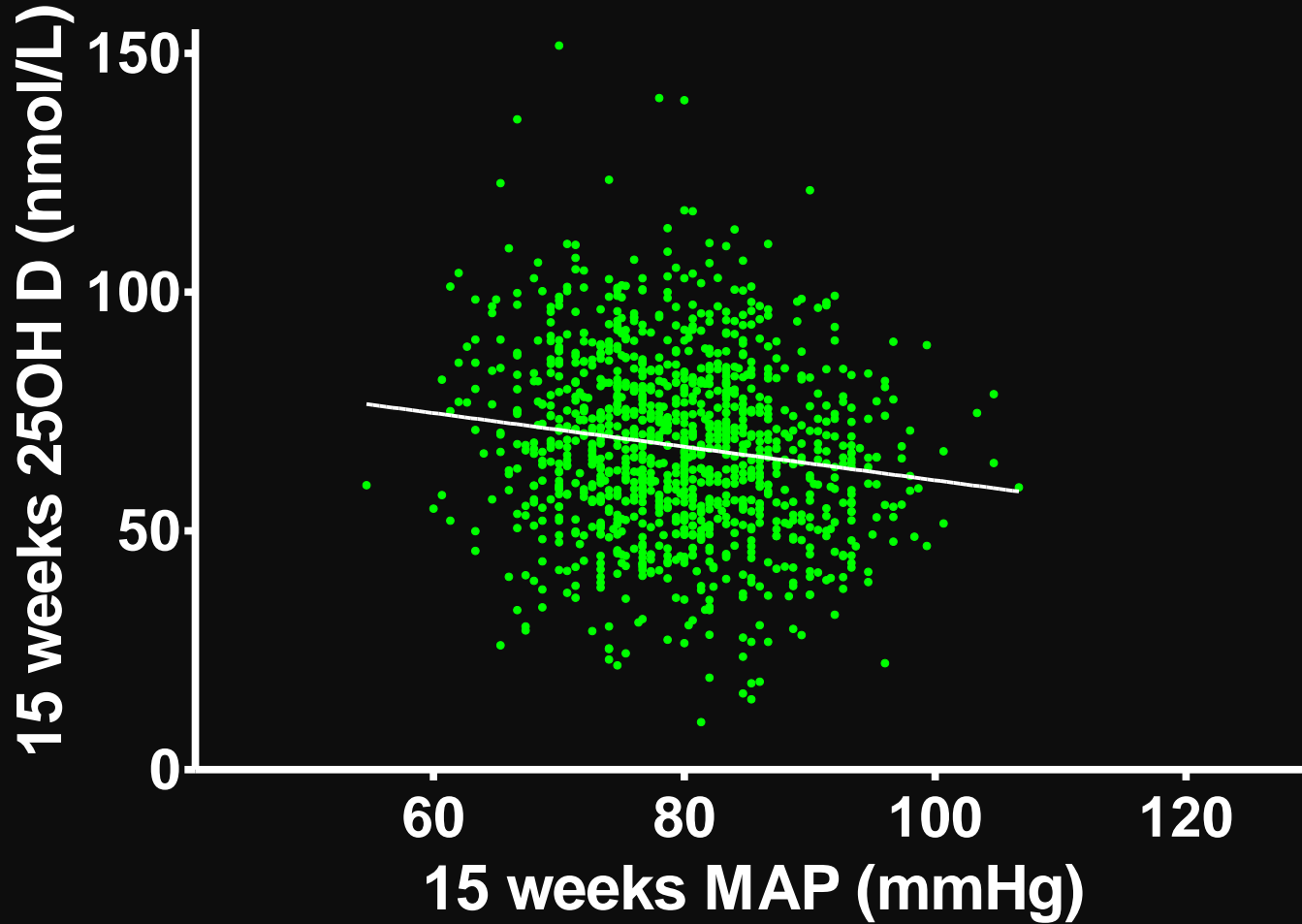
15 weeks 25OH D vs BMI



N=1156 $R^2=0.03$ $P<0.0001$



15 weeks 25OH D vs MAP



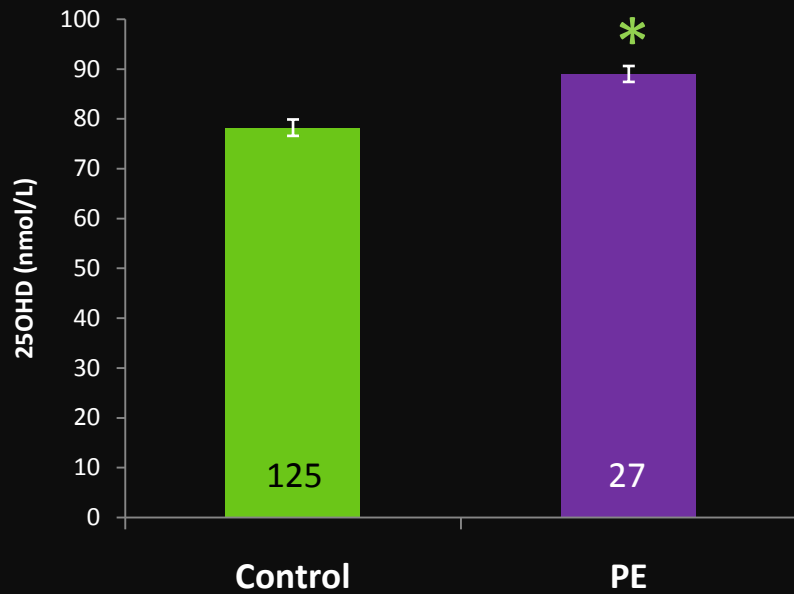
N=1156 R²=0.02 P<0.0001



15 weeks

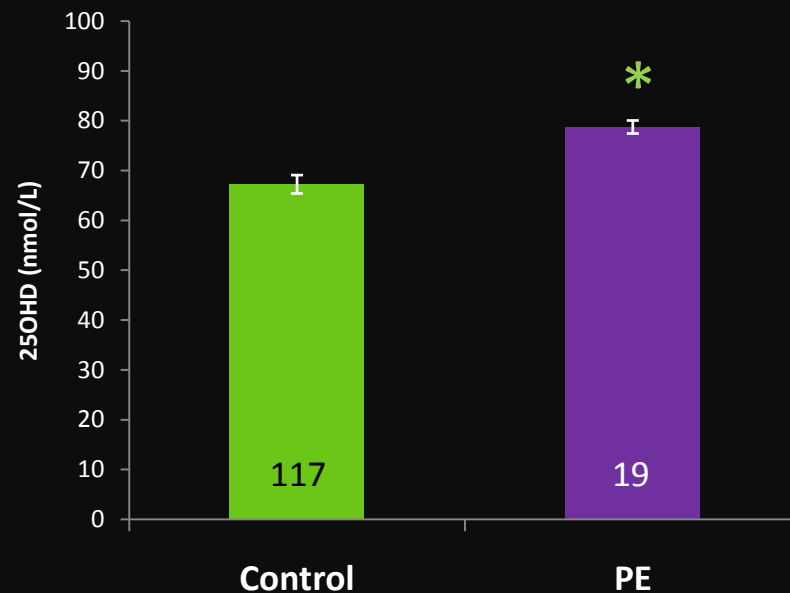
Summer

p<0.02

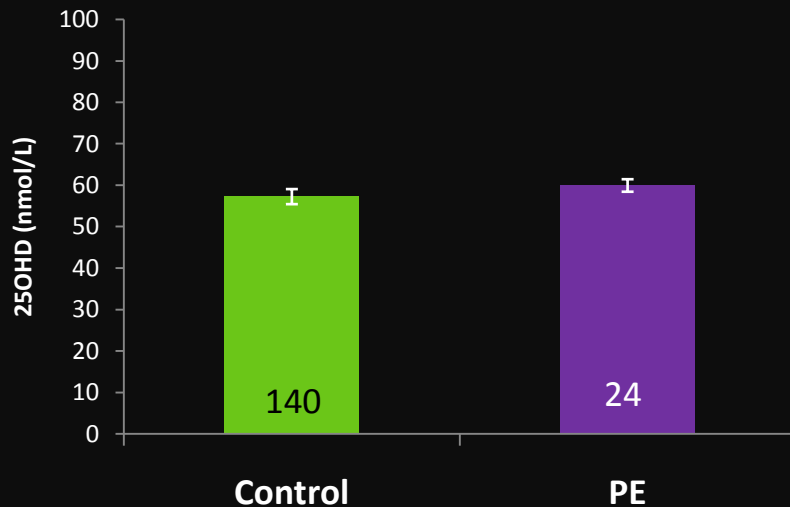


Autumn

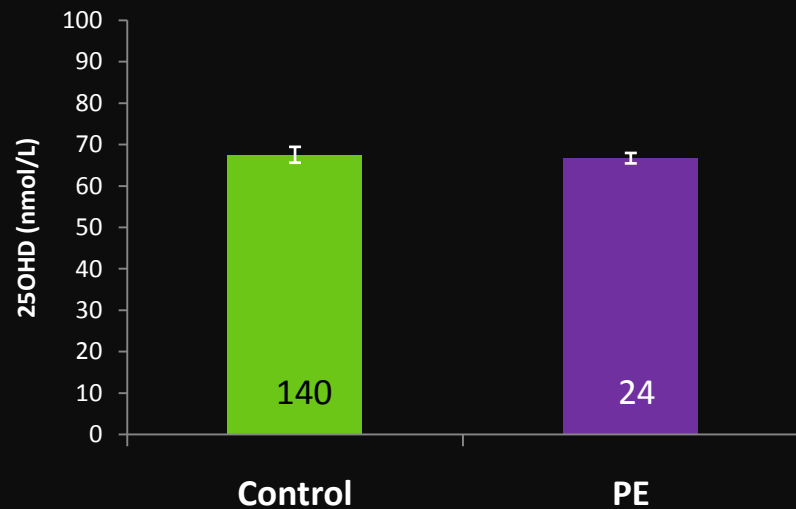
p<0.007



Winter



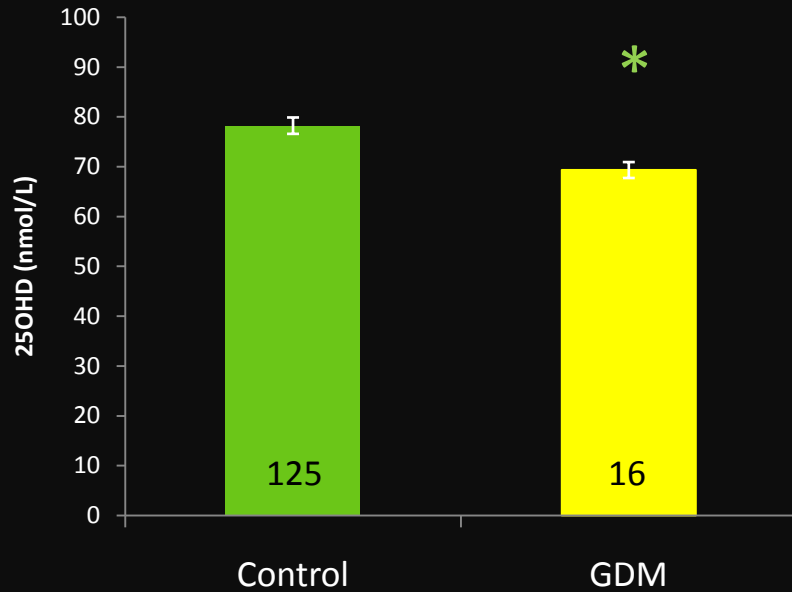
Spring



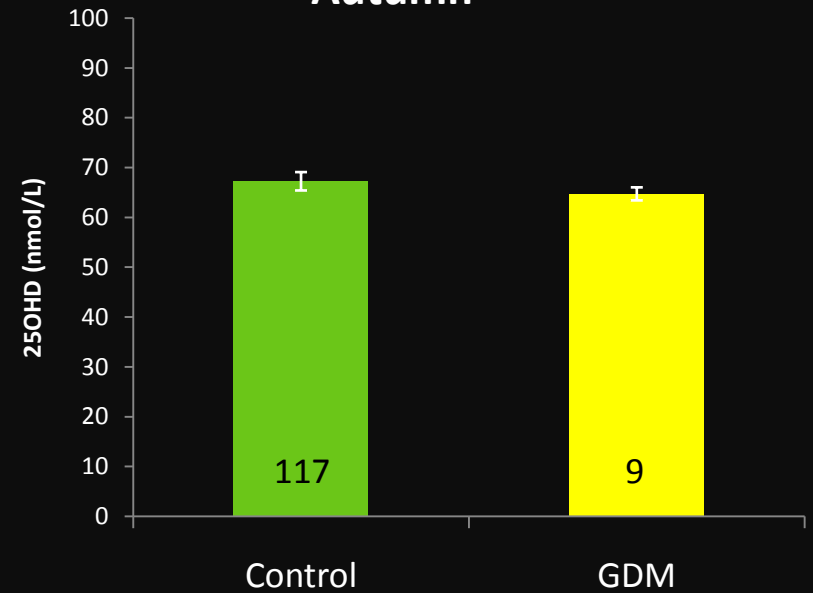
15 weeks

Summer

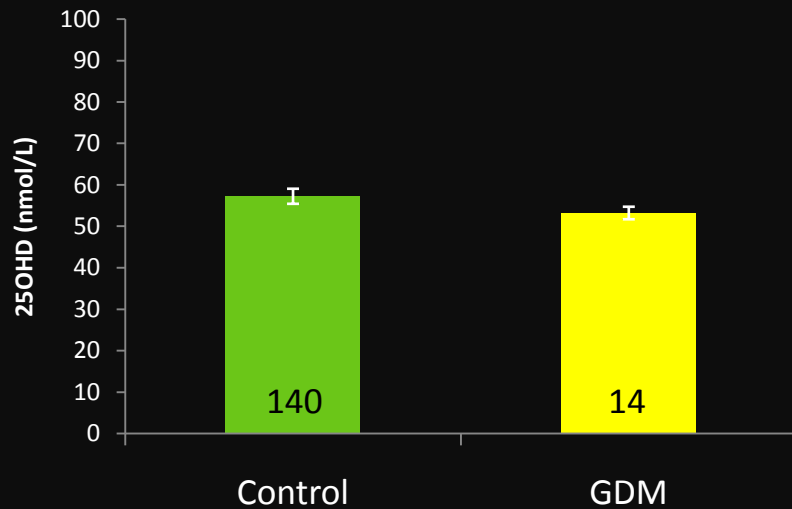
$p < 0.024$



Autumn

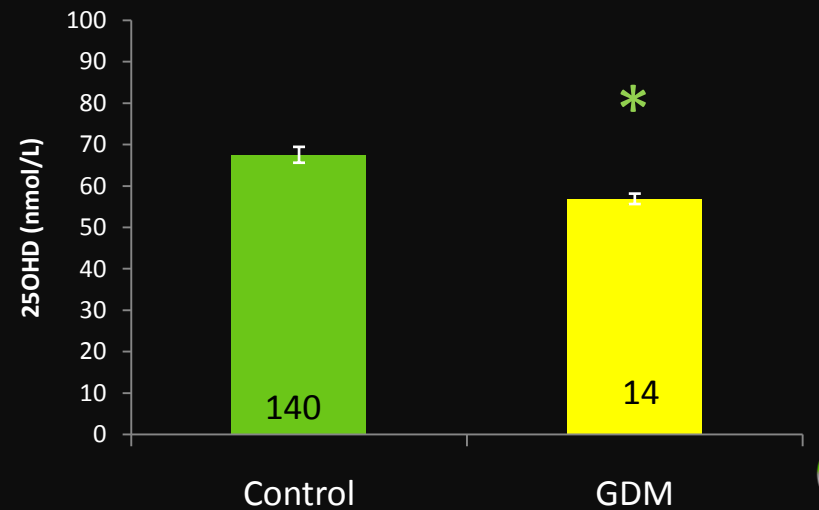


Winter

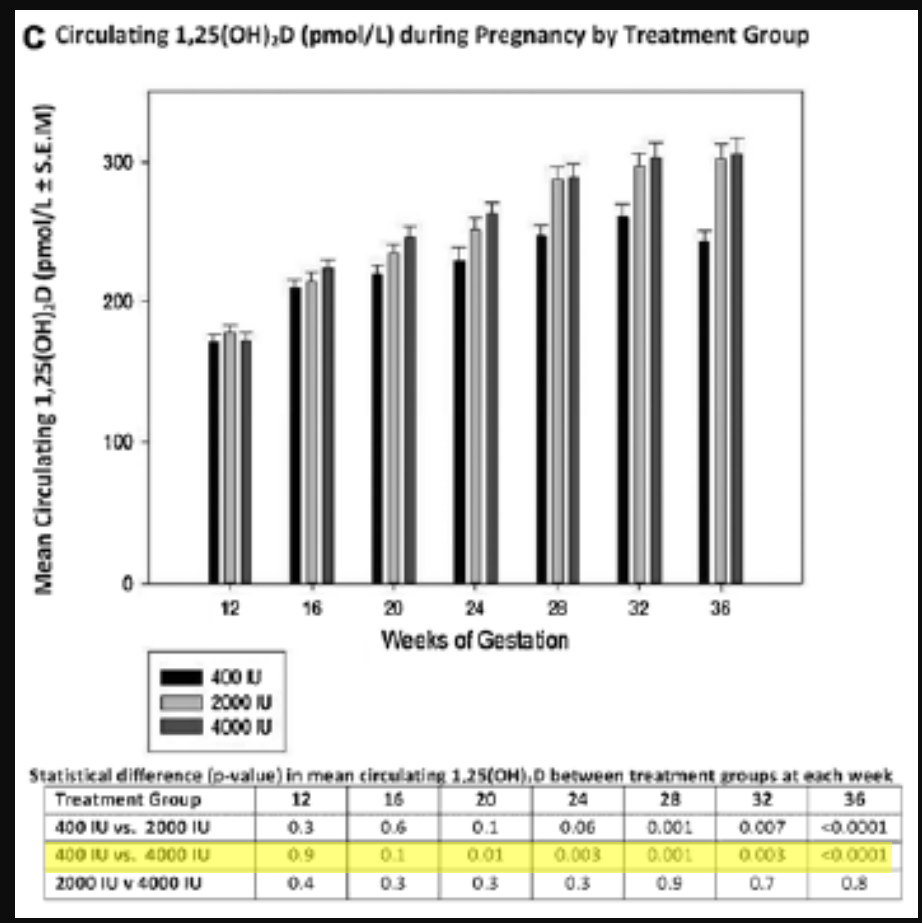
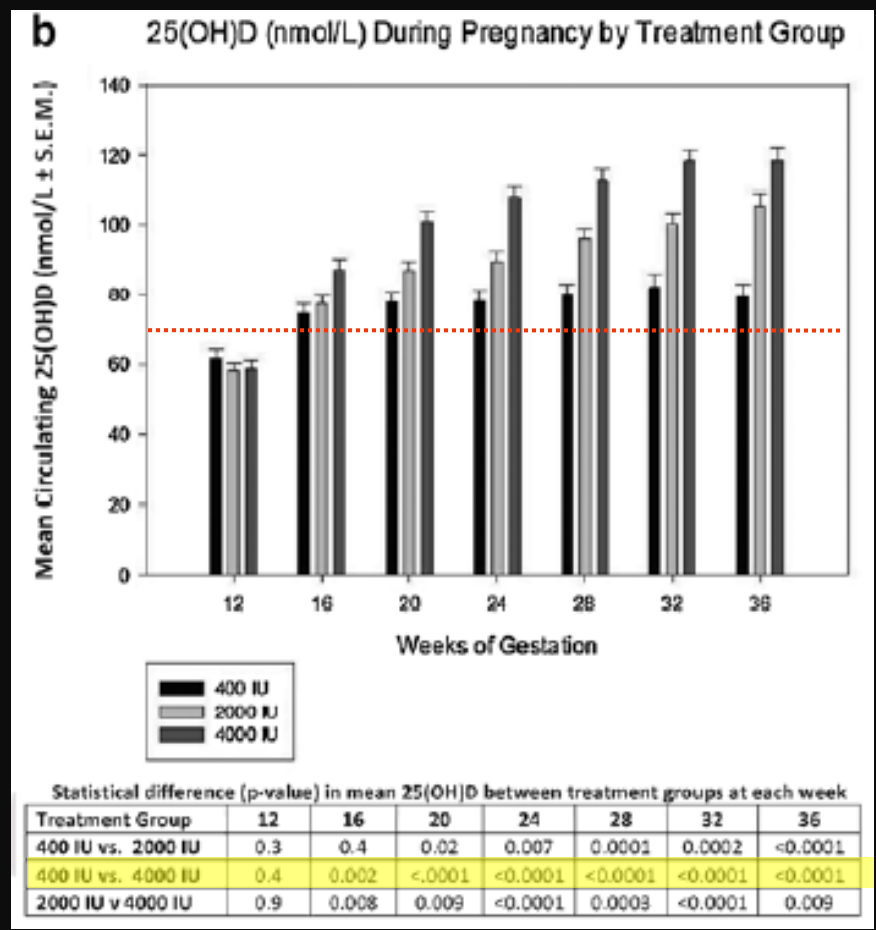


Spring

$p < 0.026$

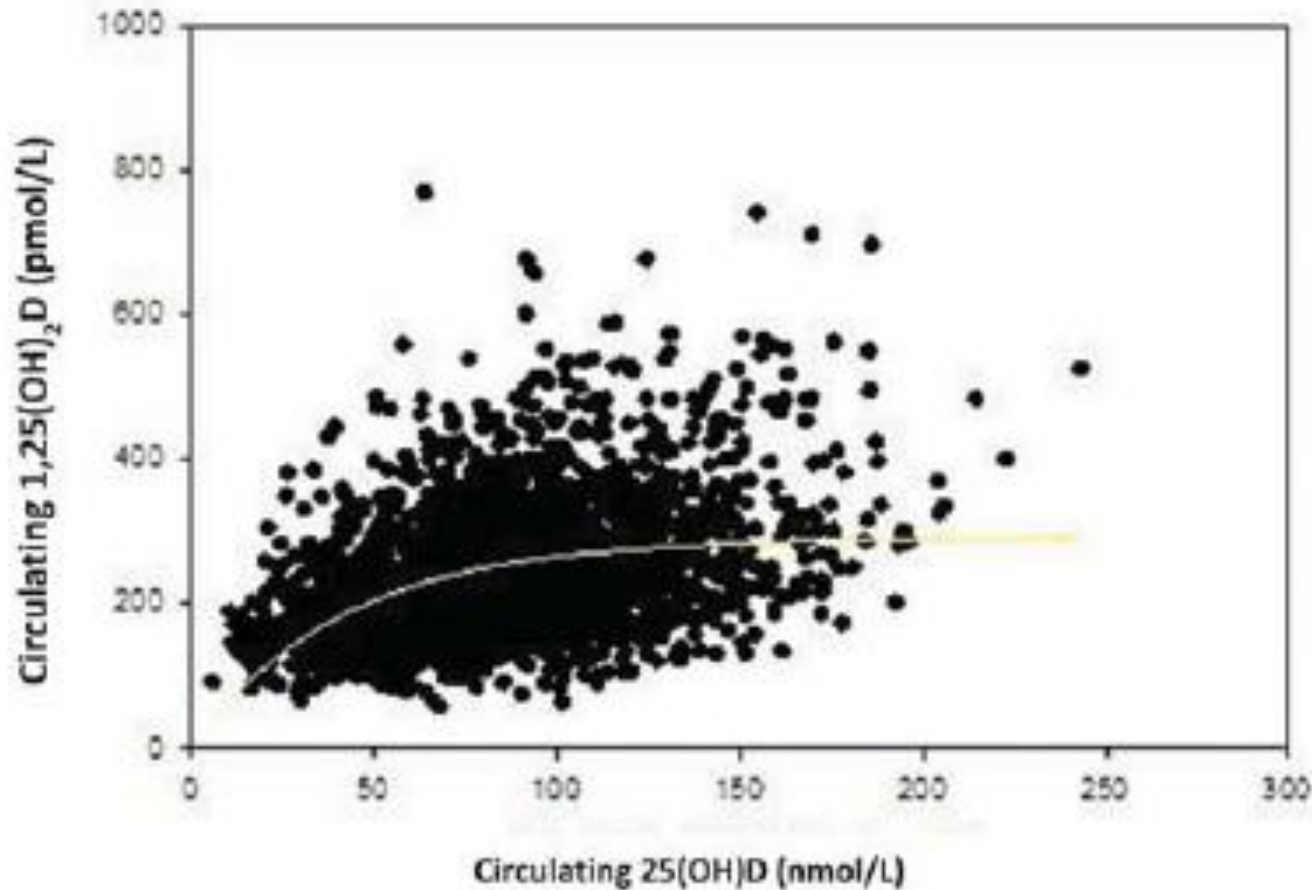


Vitamin D Supplementation Study



Vitamin D Supplementation Study

Relationship of Circulating 25(OH)D on Circulating 1,25(OH)₂D during Pregnancy

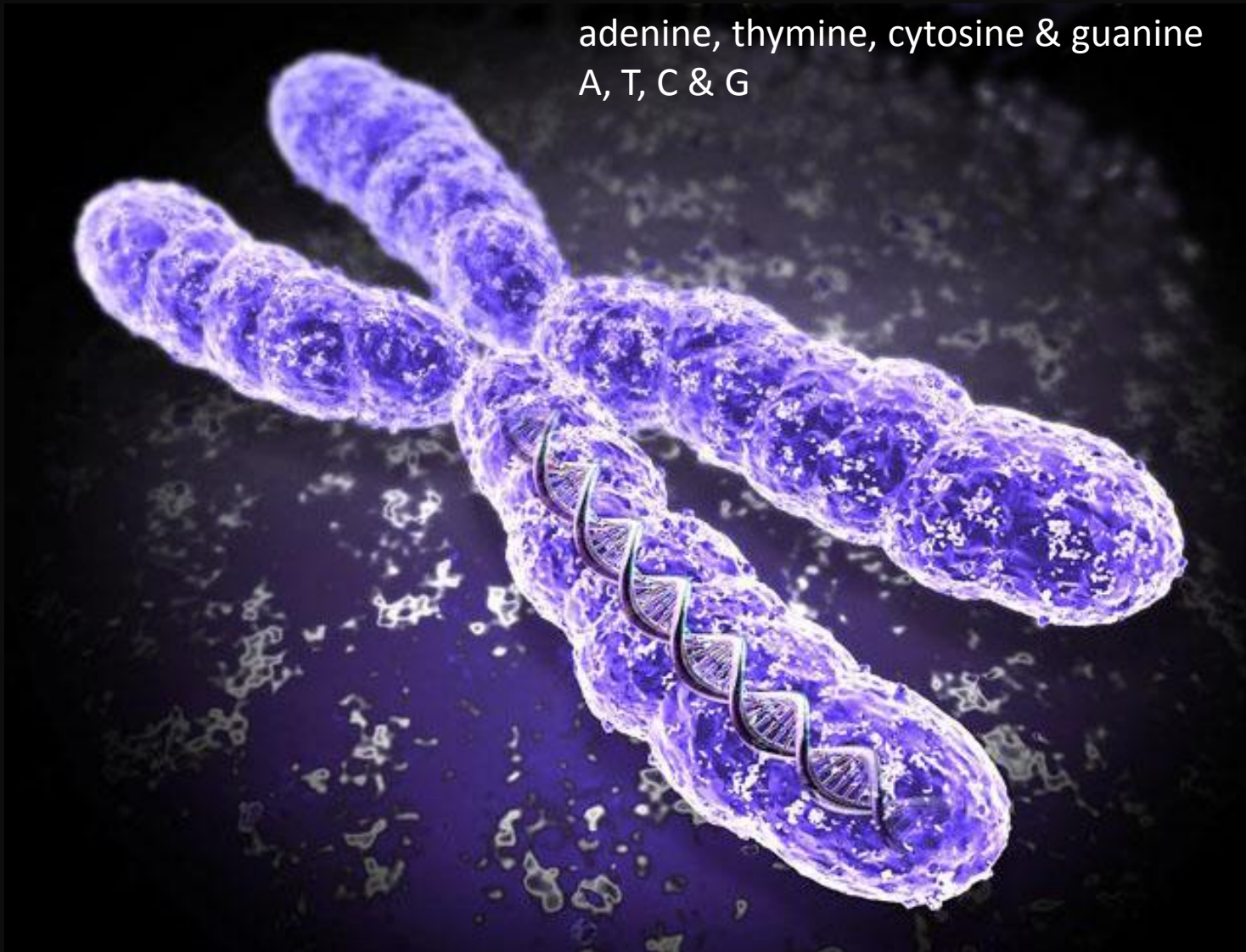


$$1,25(\text{OH})_2\text{D} = 291.23 * (1 - \exp(-0.0243 * 25(\text{OH})\text{D}))$$

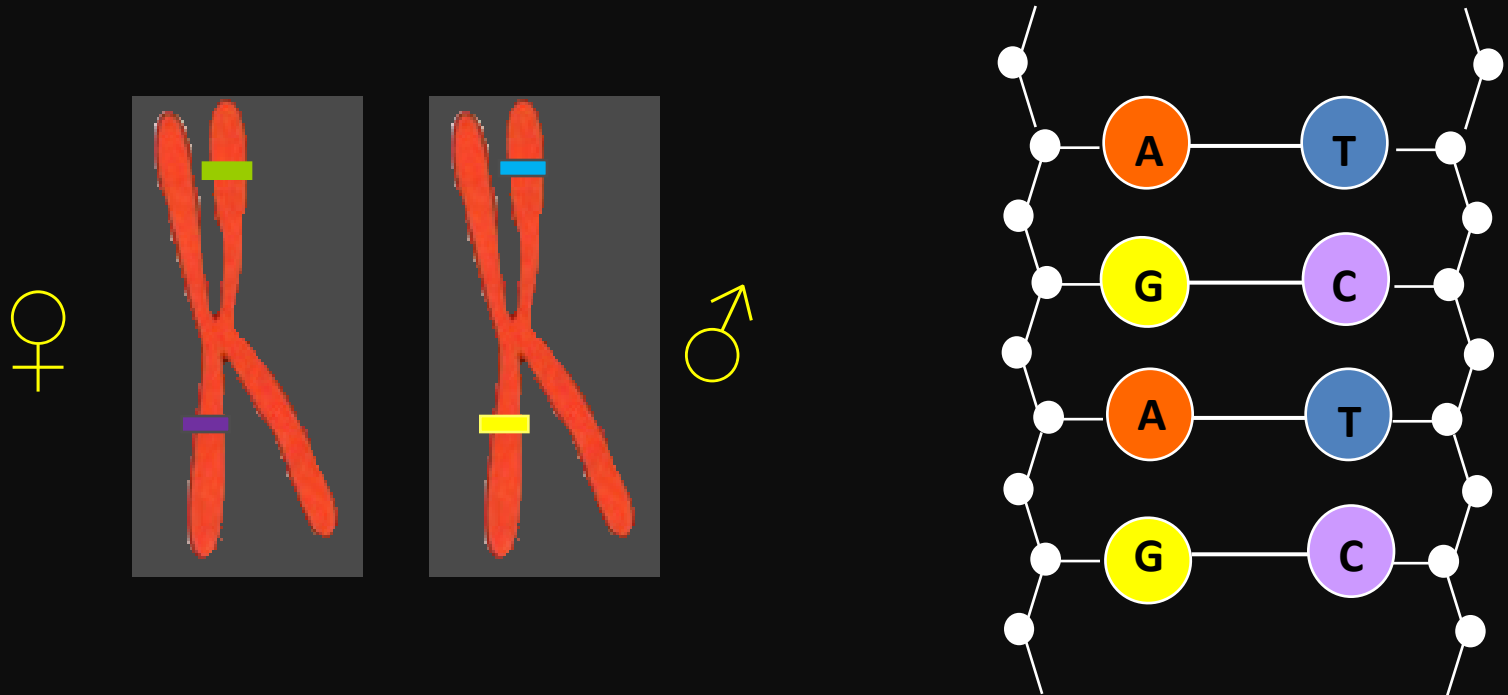


DNA provides the sequence of our genes

adenine, thymine, cytosine & guanine
A, T, C & G



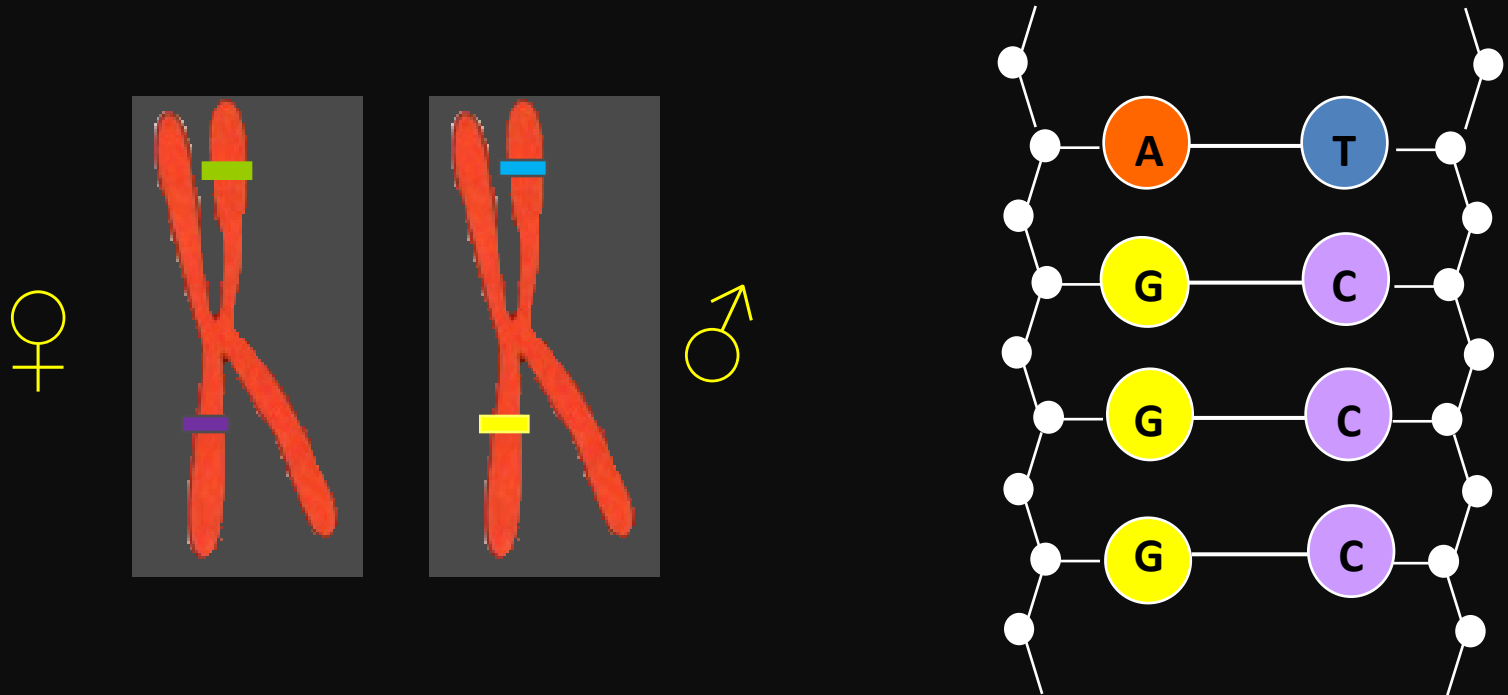
1 copy of each chromosome from each parent



The DNA sequence from each copy of each gene may be slightly different between individuals and is said to be polymorphic



1 copy of each chromosome from each parent

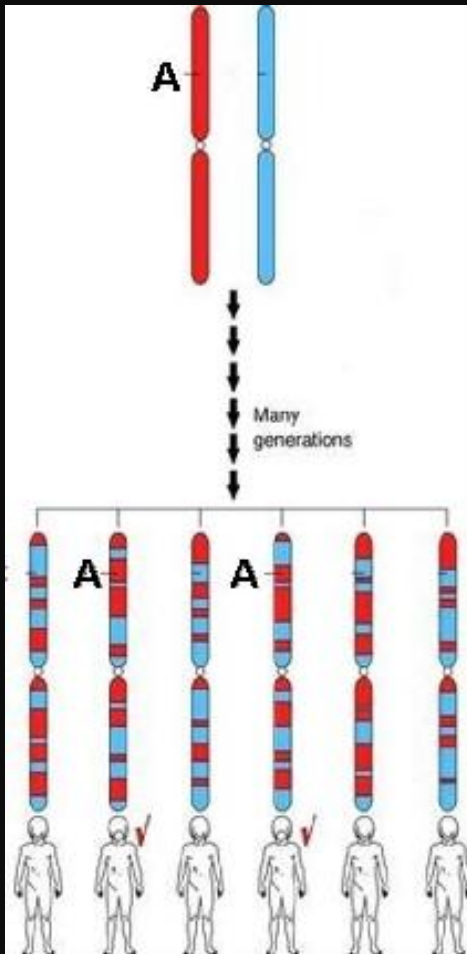


The DNA sequence from each copy of each gene may be slightly different between individuals and is said to be polymorphic

Some polymorphisms are single nucleotide polymorphisms or SNPs



Single Nucleotide Polymorphisms (SNPs)

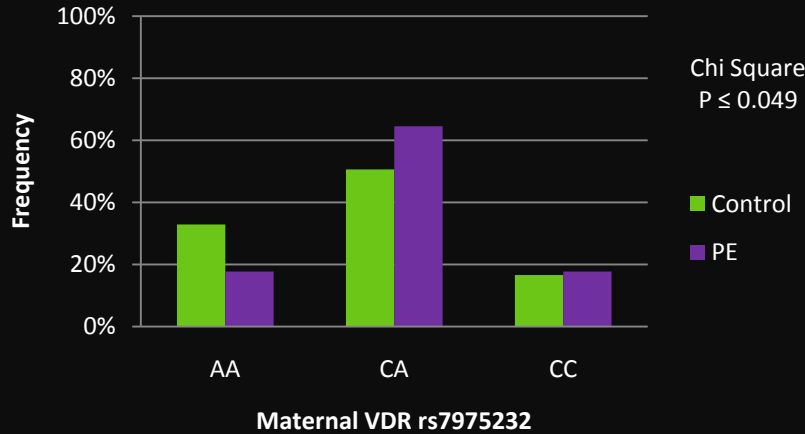


AAAGCAAAGTATTA AAAACGAATTGGCTGAGAAACAATTGGCAAA
ATAAAGGAATTTGGCACTCCCCACCAGCCACTCTTTG/ACTCTTCTC
CCTTGGACTTTGAGTCAAATTGGCCTGGACTTGAGTCCCTGAACCA
GCAAAGAGAAAAGAAGGCCCCAGAAATCACAGGTGGGCACGTGC
CTGCTACCGCCATCTCGCTTCTCACGGGAATGTTTCAGGGTAAACTG
GCCATCCGAAAATAGCAACAACCCAGACTGGCTCCTCACTCCCTTA
GTCCATCACTAAAGATCACAGAGCAGTCAGAGATGCAATTACGG/C
CCTAATAGC



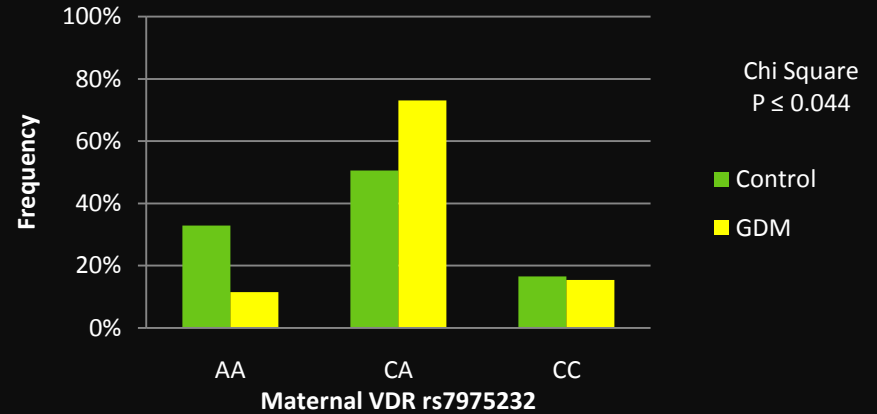
Vitamin D related genes

Maternal VDR rs7975232 vs PE

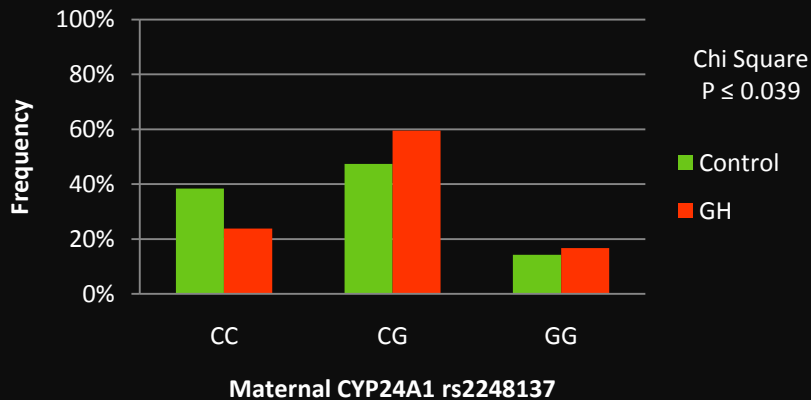


C allele also associated with asthma

Maternal VDR rs7975232 vs GDM

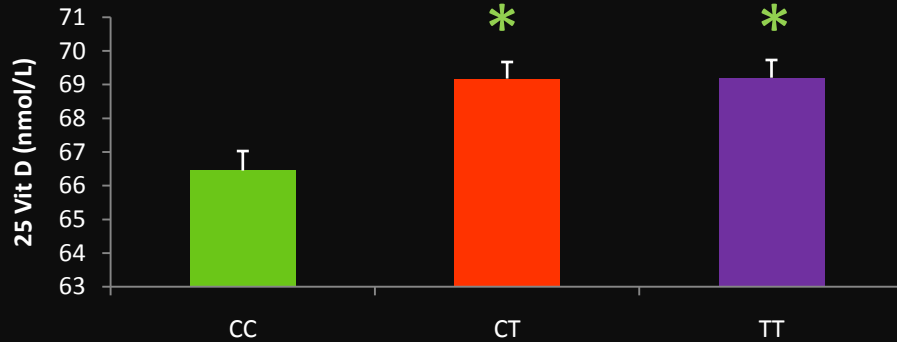


Maternal CYP24A1 rs2248137 vs GH



Effect of genotype on 25OH Vitamin D at 15 weeks gestation

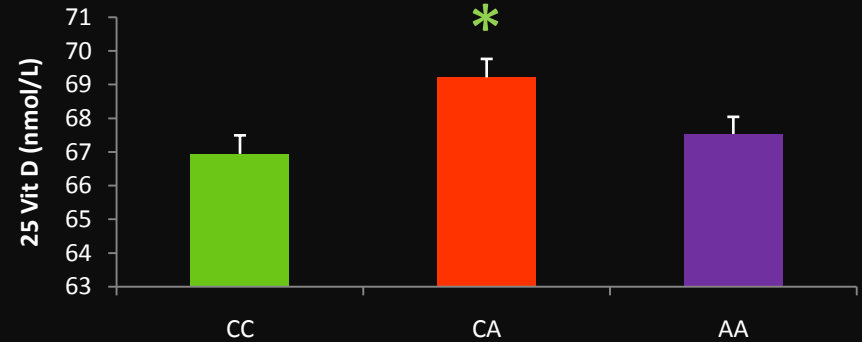
Baby VDR RS2228570



Baby VDR RS2228570 genotype

Baby VDR RS7975232

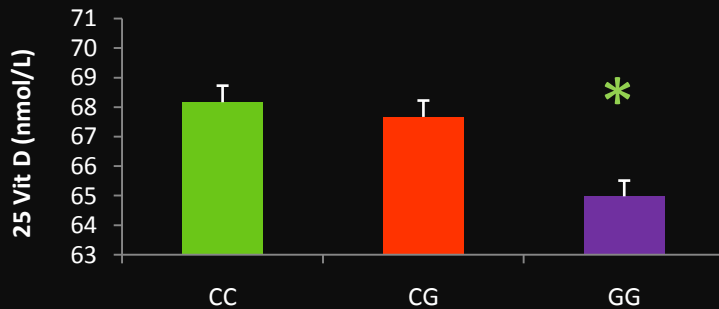
In ♀ assoc PE & GDM



Baby VDR RS7975232 genotype

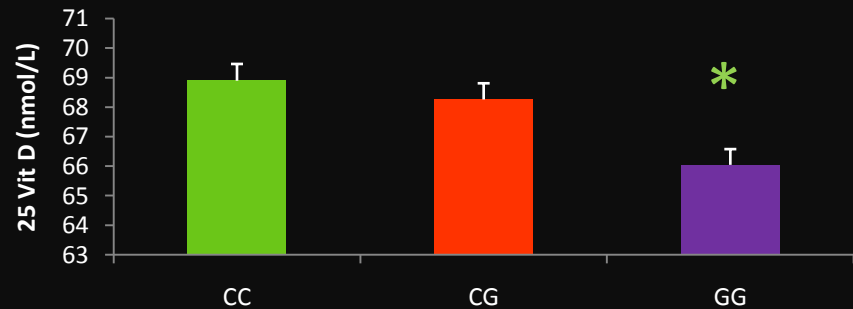
In ♀ assoc GH

Maternal CYP24A1 RS2248137



Maternal CYP24A1 RS2248137 genotype

Baby CYP24A1 RS2248137

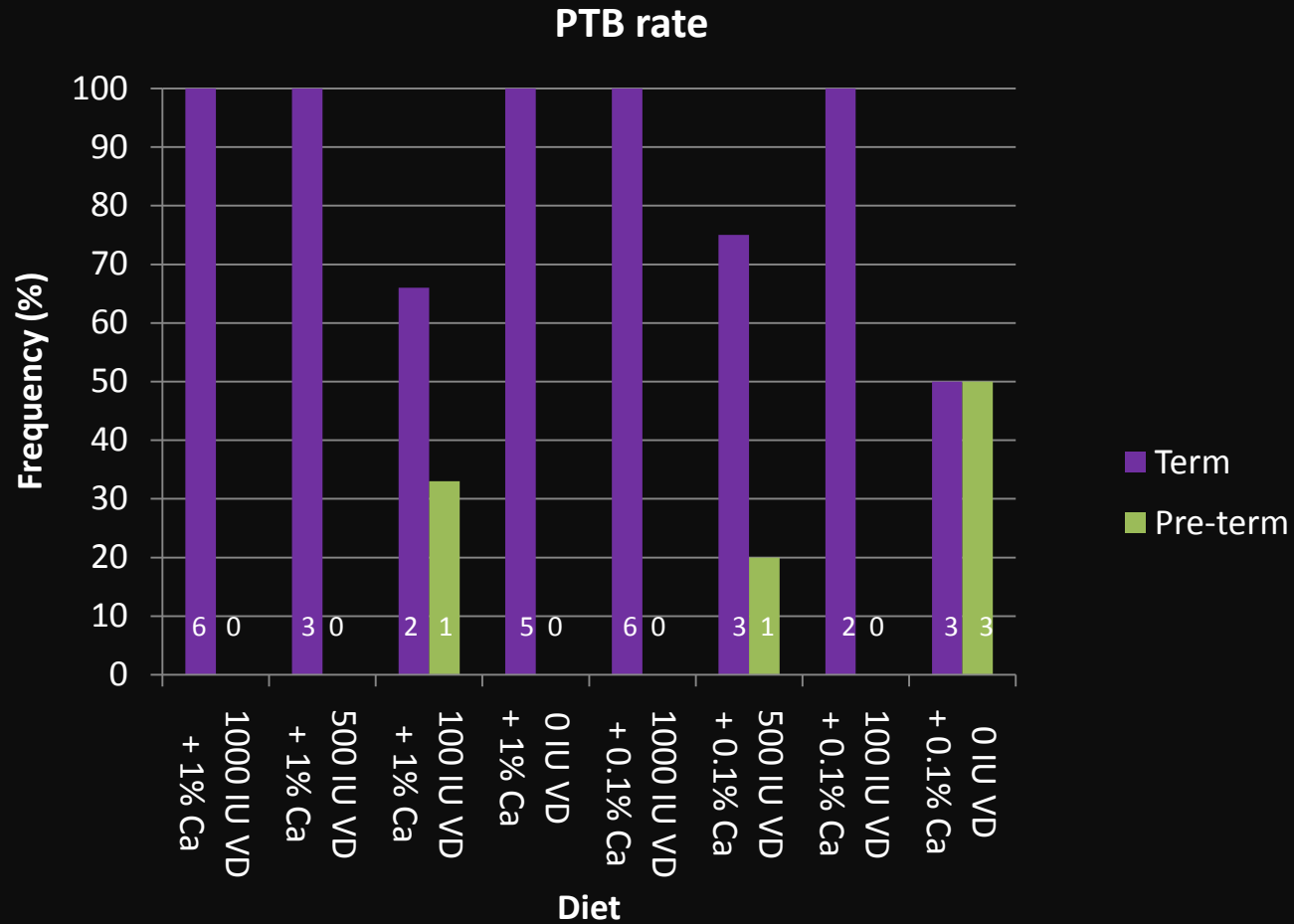


Baby CYP24A1 RS2248137 genotype

N=1163 * P<0.05



Preterm Birth Rate in Mice



Conclusions

- Vitamin D may have important roles in pregnancy
- SNPs in vitamin D related genes may confer risk for complications
- SNPs in vitamin D related genes affect circulating levels of 25OH D at 15 weeks gestation
- Serum 25OH D is negatively correlated with maternal BMI and MAP at 15 weeks gestation
- Ongoing functional studies in first trimester and term placenta and trophoblast cell lines as well as mouse



Acknowledgments

- PSRF South Australia
- University of Adelaide
- Adelaide Research and Innovation Pty Ltd
- Paul Anderson
- Howard Morris



- SCOPE Consortium
- SCOPE families who provided samples

- Gus Dekker
- Denise Healy
- Karen Rivers
- Lynda Shearer
- Denise Furness
- Amanda Highet
- Tina Bianco-Miotto
- Steven Thompson
- Jamie Zhang
- Gary Heinemann
- Dylan McCullough
- Ang Zhou
- Prabha Andraweera
- Dee McCormack
- Jessica Laurence
- Shalem Lee

