

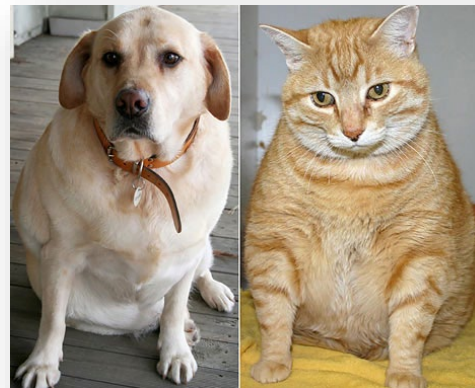


CHOLINE

Multiple functions in liver metabolism and obesity

Dr. Adronie Verbrugghe
DVM, PhD, DECVCN,
Associate Professor
Royal Canin Veterinary Diets Endowed Chair in Canine
and Feline Clinical Nutrition

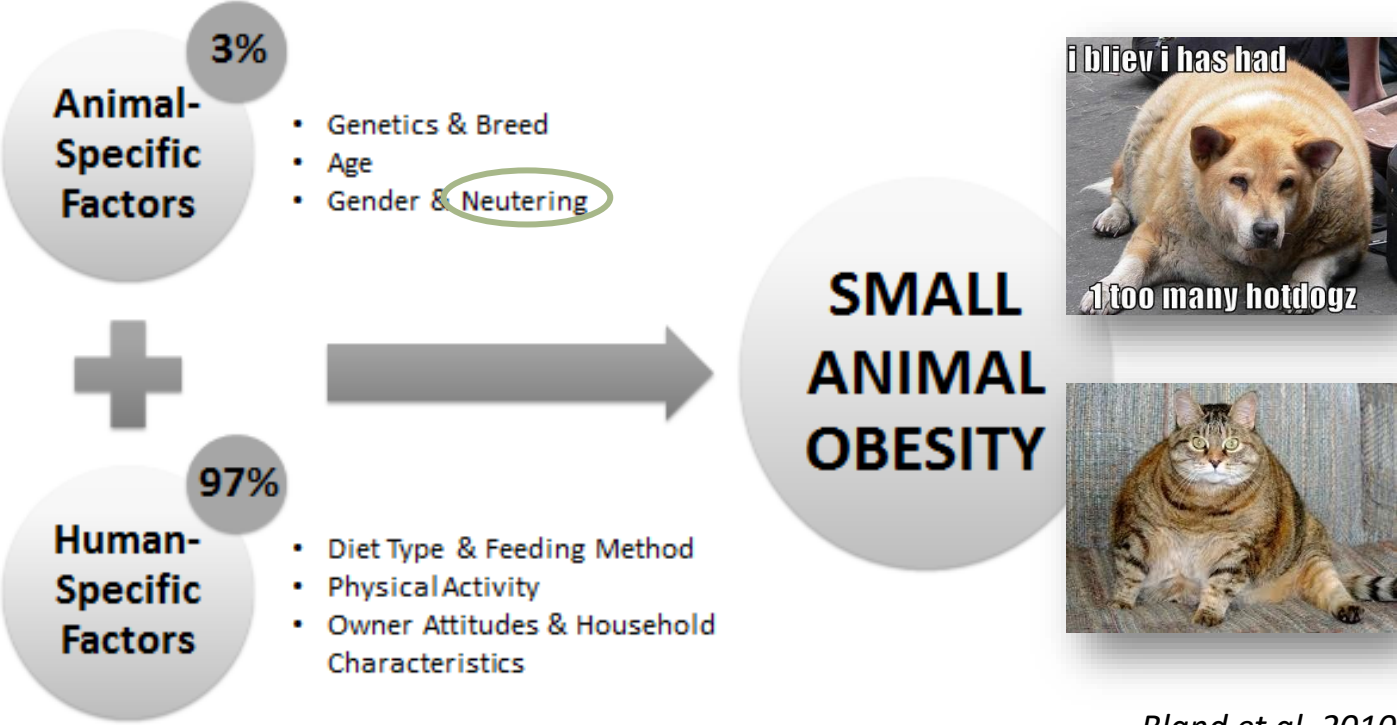
Pet Obesity



- Global problem, most common nutritional disorder
- Accumulation of excessive amounts of adipose tissue that is causing disease

energy intake >> energy needs

Factors Predisposing Pets To Obesity



Bland et al, 2010

Obesity Management Starts Early In Life!

- Spay/neuter practices
 - Common ~80%
 - Benefits



Robertson, 2003; Courcier et al., 2012

Gonadectomy - Benefits

Aid Population Control

- Main driver for gonadectomy procedures
- Reduces likelihood of abandonment

Curb Behavioural Patterns

- Minimizes sexual behaviours
- Reduces territorial behaviour (i.e. territory marking via urination)

Disease Prevention

- Mammary gland neoplasia

Obesity Management Starts Early In Life!

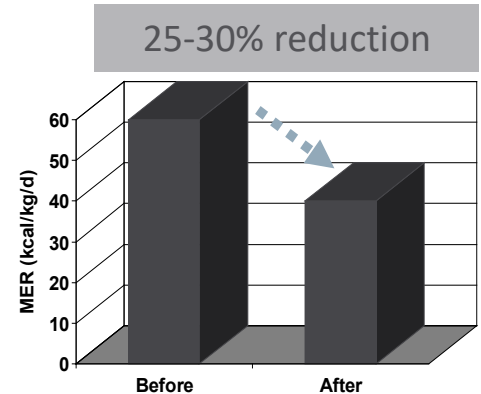
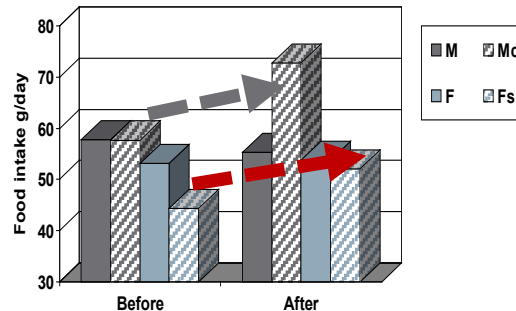
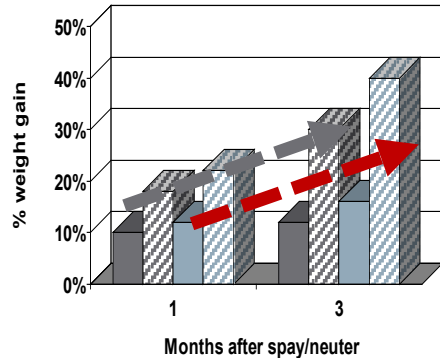
- Spay/neuter practices
 - Common ~80%
 - Benefits
- **Key link between neutering & obesity**
- Neutered **dogs 3.8 times, cats 2.6 times** more likely to be obese

Robertson, 2003; Courcier et al., 2012



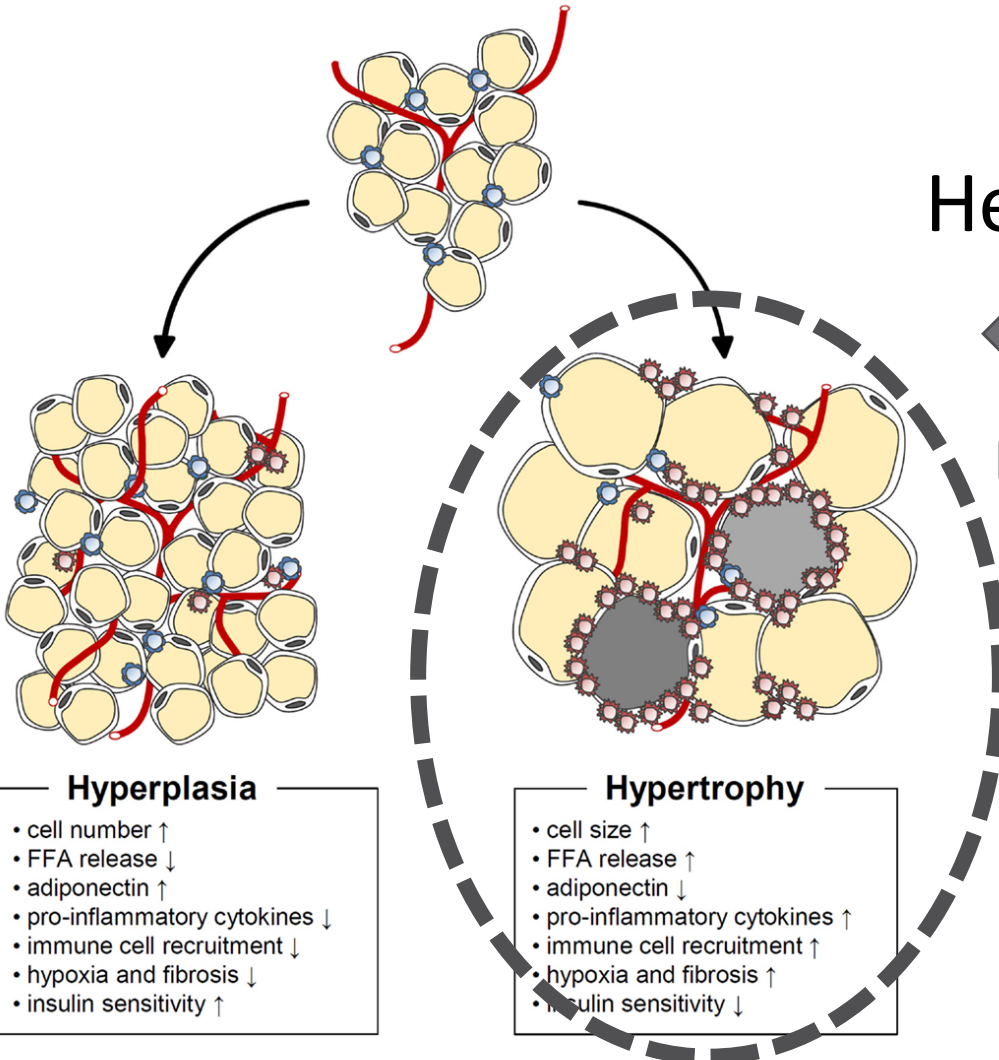
Gonadectomy - Consequences

- Removal of sex hormones → ex. estrogen causes appetite suppression
- Leads to:
 - Increased food intake and body weight post-gonadectomy
 - Substantial food restriction is needed to maintain ideal body weight
 - Resting energy requirement lower
 - Reduction of spontaneous activity



Fettman et al., 1997; Flynn et al., 1996

Obesity-related Health Consequences



OBESITY

CHRONIC LOW-GRADE
INFLAMMATION

Hyperplasia

- cell number ↑
- FFA release ↓
- adiponectin ↑
- pro-inflammatory cytokines ↓
- immune cell recruitment ↓
- hypoxia and fibrosis ↓
- insulin sensitivity ↑

Hypertrophy

- cell size ↑
- FFA release ↑
- adiponectin ↓
- pro-inflammatory cytokines ↑
- immune cell recruitment ↑
- hypoxia and fibrosis ↑
- insulin sensitivity ↓

- Joint problems, osteoarthritis
- Skin & coat disorders
- Difficulty breathing
- Heat intolerance
- Reduced activity
- Diabetes mellitus
- Heart disease
- Urinary tract disease
- Gastrointestinal problems

Reduced Quality Of Life



The Veterinary Journal 192 (2012) 428–434



Contents lists available at SciVerse ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl



Quality of life is reduced in obese dogs but improves after successful weight loss

A.J. German^{a,*}, S.L. Holden^a, M.L. Wiseman-Orr^b, J. Reid^b, A.M. Nolan^b, V. Biourge^c, P.J. Morris^d, E.M. Scott^b

^aDepartment of Obesity and Endocrinology, Institute of Ageing and Chronic Disease, University of Liverpool, Leahurst Campus, Chester High Road, Neston, Wirral CH64 7TE, United Kingdom

^bPain and Welfare Group, Faculty of Veterinary Medicine, University of Glasgow, Glasgow G12 8QW, United Kingdom

^cThe WALTHAM Centre for Pet Nutrition, Freaby Lane, Waltham-on-the-Wolds, Melton Mowbray LE14 4RT, United Kingdom

^dRoyal Canin Research Center, B.P.4 – 650 Avenue de la Petite Camargue, 30470 Aimargues, France

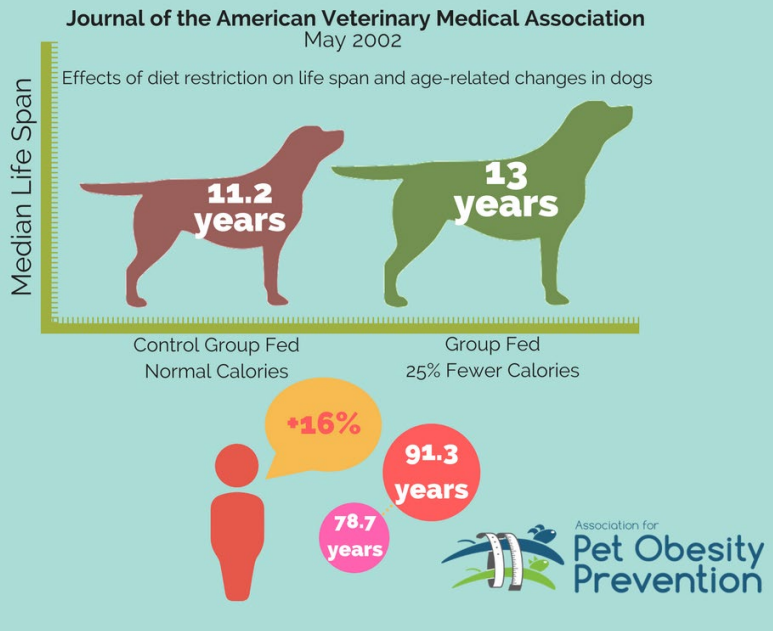


Brief Report

Impact of Obesity on Quality of Life and Owner's Perception of Weight Loss Programs in Cats

Rachel Hanford and Deborah E. Linder *^b

Shortened Lifespan



Effects of diet restriction on life span and age-related changes in dogs

Richard D. Kealy, PhD; Dennis F. Lawler, DVM; Joan M. Ballam, MS; Sandra L. Mantz; Darryl N. Biery, DVM, DACVR; Elizabeth H. Greeley, PhD; George Lust, PhD; Mariangela Segre, DSc; Gail K. Smith, DVM, PhD, DACVS; Howard D. Stowe, DVM, PhD



The Weight Loss Challenge

- Enrollment in weight loss plan recommended

55% stop prematurely

Not always successful

Struggle to maintain weight loss long-term



The Weight Loss Challenge

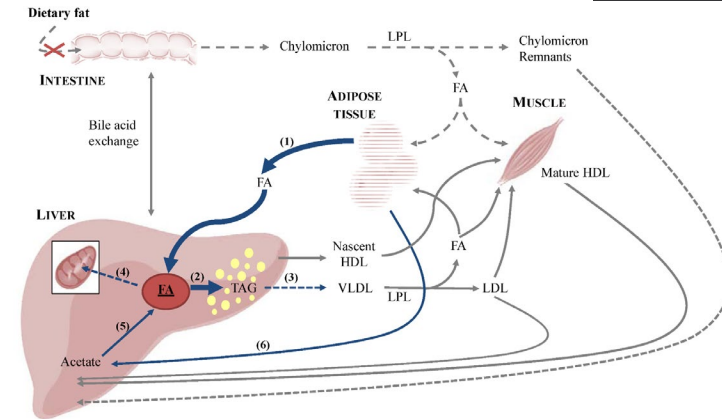
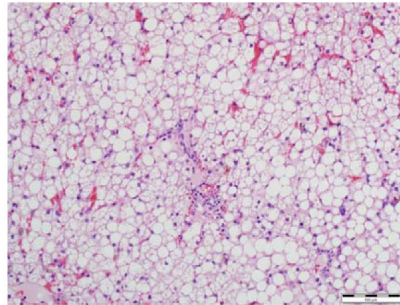
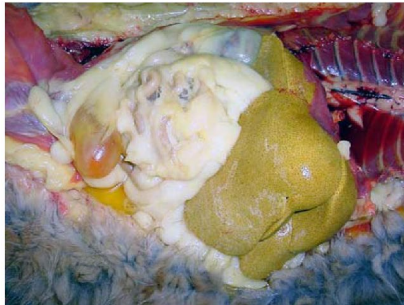
- Safe weight loss = losing 0.5-2% initial weight/week

Fast weight loss and drastic energy restriction
→ Feline Hepatic Lipidosis



Fatty Liver In Cats

- Most common liver disease affecting cats in North America
- Most commonly affects overweight & obese cats
- Most commonly caused by complete or partial anorexia
- Can be fatal if untreated



Armstrong et al. 2009; Gagne et al. 1996; Crawford et al. 2010; Valtolina et al. 2005, Verbrugge & Bakovic 2013

The Weight Loss Challenge

- Nutrient deficiencies

Dependent on restriction level and diet choice



Nutrient Deficiencies



Grant et al. BMC Veterinary Research (2020) 16:426
https://doi.org/10.1186/s12917-020-02649-0

BMC Veterinary Research

RESEARCH ARTICLE

Open Access

Dietary intake of amino acids and vitamins compared to NRC requirements in obese cats undergoing energy restriction for weight loss



Caitlin E. Grant¹, Anna K. Shoveller², Shauna Blois¹, Marica Bakovic³, Gabrielle Monteith¹ and Adronie Verbrugge^{1*}

- **Weight loss trial** with VTD
 - Intake of majority of indispensable amino acids and vitamins greater than NRC recommended allowance
 - Except **arginine, choline, crude protein, phenylalanine plus tyrosine and threonine**

Grant et al, 2023 – submitted PlosONE

- **Theoretical estimation** of amino acid and vitamin intake during energy restriction
 - Fewer nutrient intakes below NRC recommended allowance with VTD compared to OTC maintenance and low-calorie diets
 - Higher number of nutrients below NRC recommended allowance with increasing level of restriction
 - Nutrients of concern: **crude protein, phenylalanine plus tyrosine, choline**


Nutrient Deficiencies

German et al. BMC Veterinary Research (2015) 11:253
DOI 10.1186/s12917-015-0570-y



RESEARCH ARTICLE

Open Access

Assessing the adequacy of essential nutrient intake in obese dogs undergoing energy restriction for weight loss: a cohort study 

Alexander J. German^{1,2*}, Shelley L. Holden^{1,2}, Samuel Serisier^{1,2}, Yann Queau^{1,2} and Vincent Biourge^{1,2}

- **Weight loss trial** with VTD
 - Intake of majority of nutrients greater than NRC recommended allowance
 - Some nutrients lower than NRC recommended allowance
 - **Total fat, tryptophan, methionine and cysteine, magnesium, potassium, selenium, choline**



Veterinary Quarterly
Vol. 32, Nos. 3–4, September–December 2012, 123–129

RESEARCH ARTICLE

Theoretical evaluation of risk for nutritional deficiency with caloric restriction in dogs
Deborah E. Linder^a, Lisa M. Freeman^{a*}, Penelope Morris^b, Alexander J. German^c, Vincent Biourge^d,
Caitlin Heinze^a and Lucille Alexander^b

- **Theoretical** estimation of nutrient intake during energy restriction → VTD and OTC diets
 - All diets → at least one nutrient below NRC recommended allowance when restricted minimally
 - Number of nutrients deficient increased with increased degree of restriction
 - Most common were **selenium and choline**

Nutrient Deficiencies

Grant et al. BMC Veterinary Research (2020) 16:426
https://doi.org/10.1186/s12917-020-02649-0

BMC Veterinary Research

RESEARCH ARTICLE

Open Access

Dietary intake of amino acids and vitamins compared to NRC requirements in obese cats undergoing energy restriction for weight loss



Caitlin E. Grant¹, Anna K. Shoveller², Shauna Blois¹, Marica Bakovic³, Gabrielle Monteith¹ and Adronie Verbrugghe¹

- **Weight loss trial** with VTD
 - Intake of majority of indispensable amino acids and vitamins greater than NRC recommended allowance
 - Except **arginine, choline, crude protein, phenylalanine plus tyrosine and threonine**



Grant et al, 2023 – Submitted PlosONE

- **Theoretical** estimation of amino acid and vitamin intake during energy restriction
 - Fewer nutrient intakes below NRC recommended allowance with VTD compared to OTC maintenance and low-calorie diets
 - Higher number of nutrients below NRC recommended allowance with increasing level of restriction
 - Nutrients of concern: **crude protein, phenylalanine plus tyrosine, choline**


Nutrient Deficiencies

German et al. BMC Veterinary Research (2015) 11:253
DOI 10.1186/s12917-015-0570-y



RESEARCH ARTICLE

Open Access

Assessing the adequacy of essential nutrient intake in obese dogs undergoing energy restriction for weight loss: a cohort study 

Alexander J. German^{1,2}, Shelley L. Holden^{1,2}, Samuel Serisier^{1,2}, Yann Queau^{1,2} and Vincent Biourge^{1,2}

- **Weight loss trial** with VTD
 - Intake of majority of nutrients greater than NRC recommended allowance
 - Some nutrients lower than NRC recommended allowance
 - **Total fat, tryptophan, methionine and cysteine, magnesium, potassium, selenium, choline**



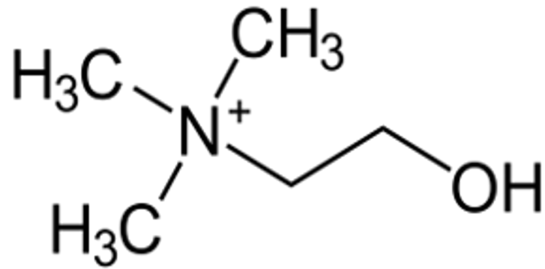
Veterinary Quarterly
Vol. 32, Nos. 3-4, September-December 2012, 123-129

RESEARCH ARTICLE

Theoretical evaluation of risk for nutritional deficiency with caloric restriction in dogs
Deborah E. Linder^a, Lisa M. Freeman^{a,b}, Penelope Morris^b, Alexander J. German^c, Vincent Biourge^d, Cailin Heinze^a and Lucille Alexander^b

- **Theoretical** estimation of nutrient intake during energy restriction → VTD and OTC diets
 - All diets → at least one nutrient below NRC recommended allowance when restricted minimally
 - Number of nutrients deficient increased with increased degree of restriction
 - Most common were **selenium and choline**

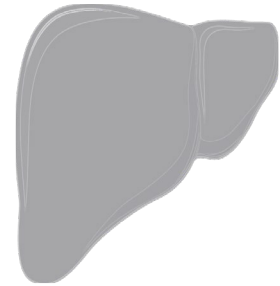
Choline, Essential Nutrient



Found
Commonly in
eggs, wheat
germ, organ
meats

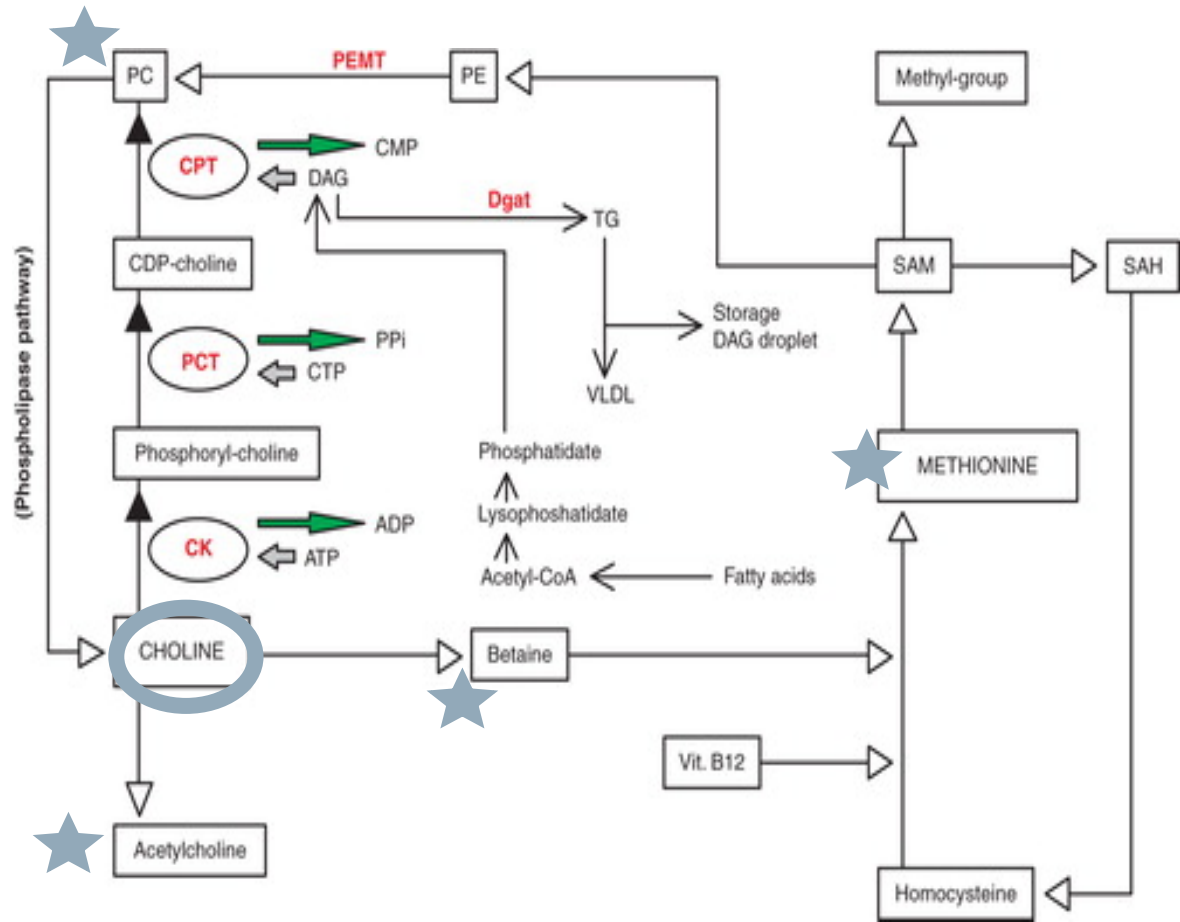


NRC 2006
Growth
133 mg/kg^{0.67}
Maintenance
63 mg/kg^{0.67}



Important for
normal liver
and body
functions

Choline Functions



Potential for Choline Supplementation



Increased markers of one-carbon metabolism, fatty acid oxidation, and protein synthesis



Improved Carcass Composition
↓ FAS; ↑ HSL



↓ Average Daily FI
↑ Feed Conversion Ratios
↓ Liver Fat Accumulation









↓ Plasma NEFA
↓ Hepatic TAG Accumulation
↑ Lipid Mobilization & Oxidation



CHOLINE SUPPLEMENTATION

RESEARCH ARTICLE

Dietary choline in gonadectomized kittens improved food intake and body composition but not satiety, serum lipids, or energy expenditure

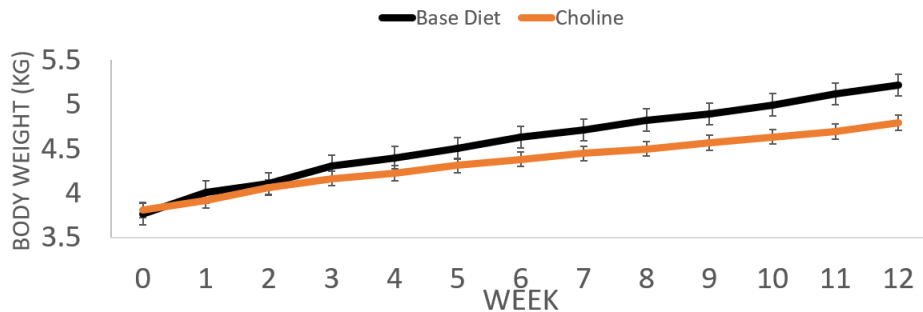
Hannah Godfrey¹ , Alexandra Rankovic² , Caitlin E. Grant¹ , Anna Kate Shoveller³ ,
Marica Bakovic⁴, Sarah K. Abood¹ , Adronie Verbrugghe¹ *



Kittens

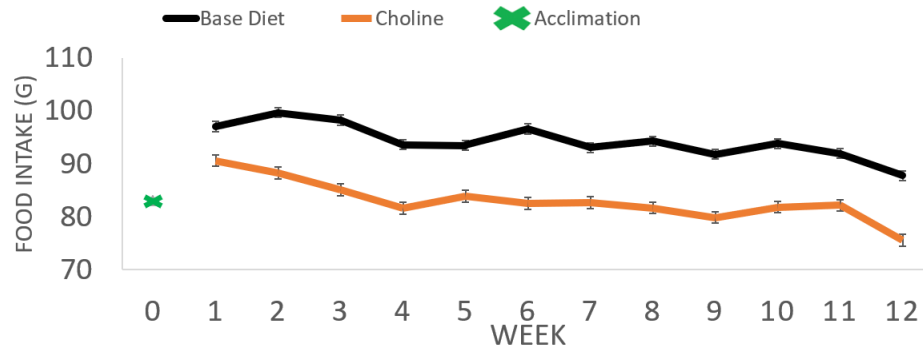
N=16

Post-gonadectomy
3 x DER to mimic ad lib
Choline vs. control
Choline @ 3 x NRC RA
12 weeks



Body Weight

Treatment: P=0.0209
Time: P<0.0001
Treatment*Time: P<0.0001



Food Intake

Treatment: P<0.0001
Time: P<0.0001
Treatment*Time: P<0.0001

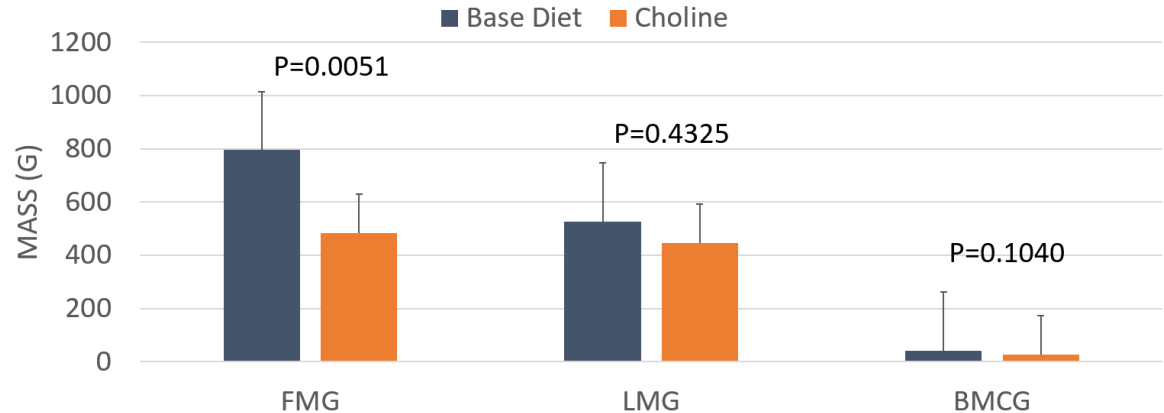
Kittens

N=16

Post-gonadectomy
3 x DER to mimic ad lib
Choline vs. control
Choline @ 3 x NRC RA
12 weeks

Body Composition

FMG = Fat Mass Gain
LMG = Lean Mass Gain
BMCG = Bone Mineral Content Gain



Circulating direct infusion MS and NMR metabolomic profiles of post-gonadectomy kittens with or without additional dietary choline supplementation

Hannah Godfrey¹, Alexandra Rankovic², Caitlin E. Grant¹, Sarah K. Abood^{1†}, Anna Kate Shoveller³, Marica Bakovic⁴ and Adronie Verbrugghe^{1*}



Kittens

N=16

Post-gonadectomy
3 x DER to mimic ad lib
Choline vs. control
Choline @ 3 x NRC RA
12 weeks

Serum Metabolomics - NMR

- * = $P_{\text{time}} < 0.05$
- ** = $P_{\text{treatment}} < 0.05$
- *** = $P_{\text{treatment} \times \text{time}} < 0.05$

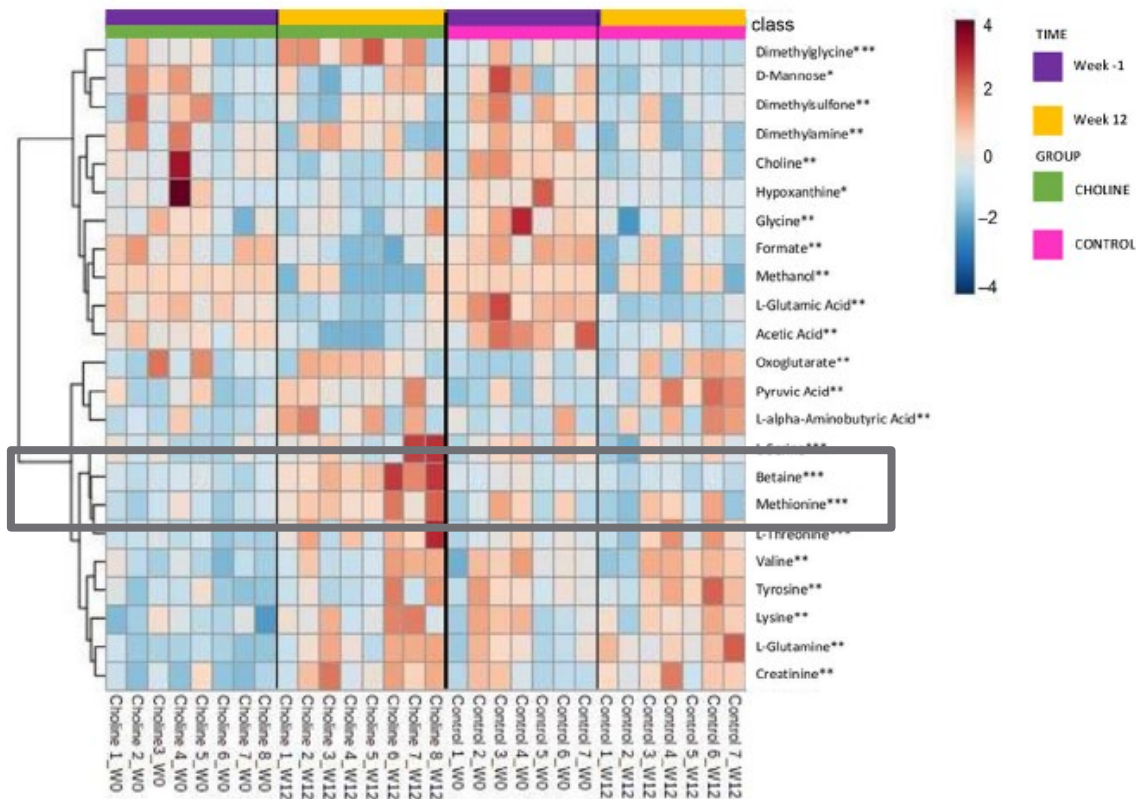
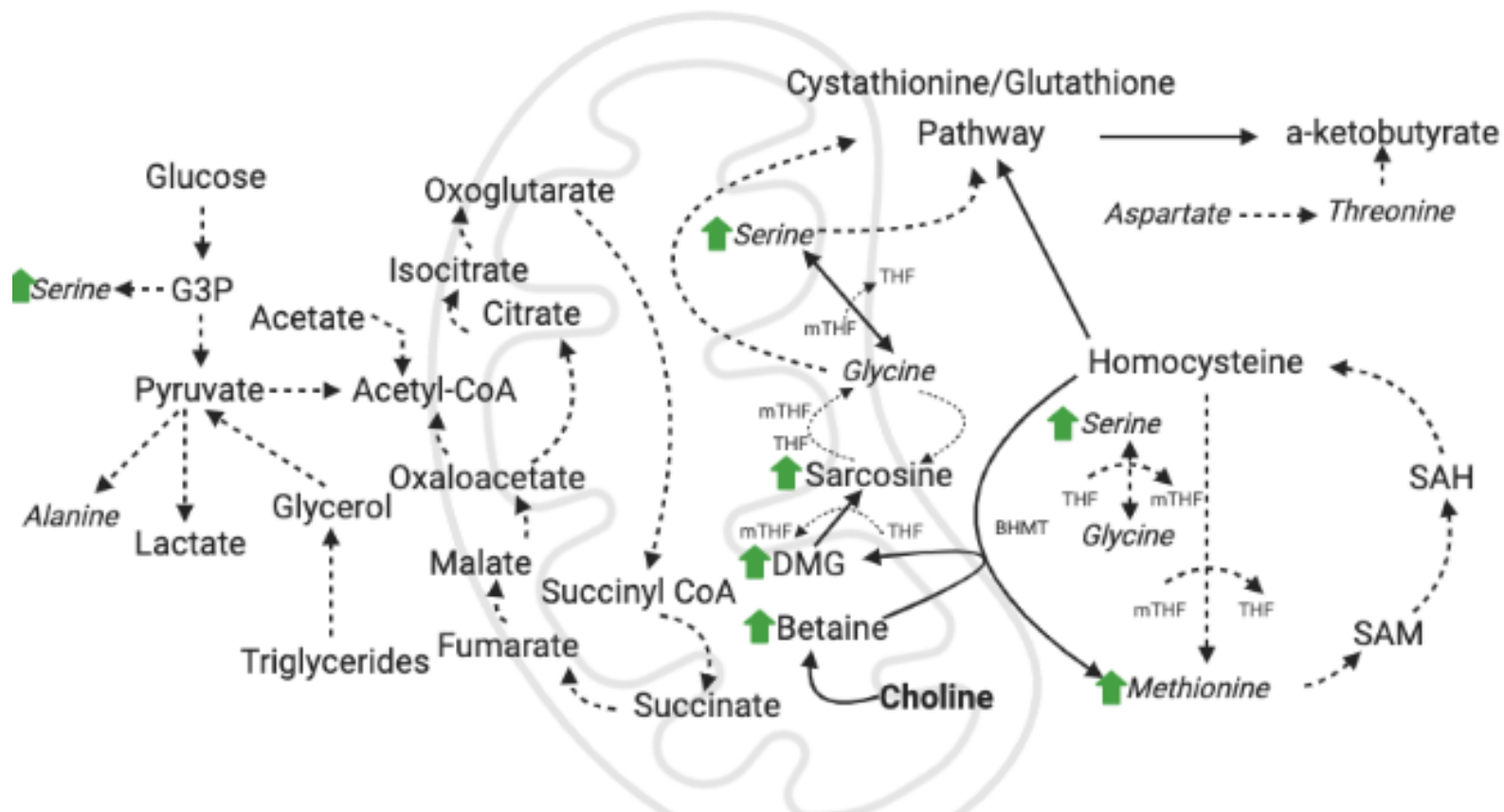


Fig. 2. Heat map with Euclidean distance and Ward clustering of mean serum metabolites analysed by quantitative NMR spectrometry in kittens pre-gonadectomy (week -1) and post-gonadectomy (week 12) following supplementation with an additional choline at 300 mg/kg BW 0-75 (CHOLINE, n 8) for 12 weeks compared to a control group (CONTROL, n 7) with a time (*), group (**) or group x time interaction (***) ($P < 0.05$) following a Tukey's *post hoc* analysis between and within groups.





Article

Serum Lipid, Amino Acid and Acylcarnitine Profiles of Obese Cats Supplemented with Dietary Choline and Fed to Maintenance Energy Requirements

Adronie Verbrugghe ^{1,*}, Alexandra Rankovic ², Shafeeq Armstrong ³, Amanda Santarossa ¹, Gordon M. Kirby ² and Marica Bakovic ³



Adult Cats

N = 12

Chronically obese

Choline vs. control

Choline @ 5 x NRC RA

5 week

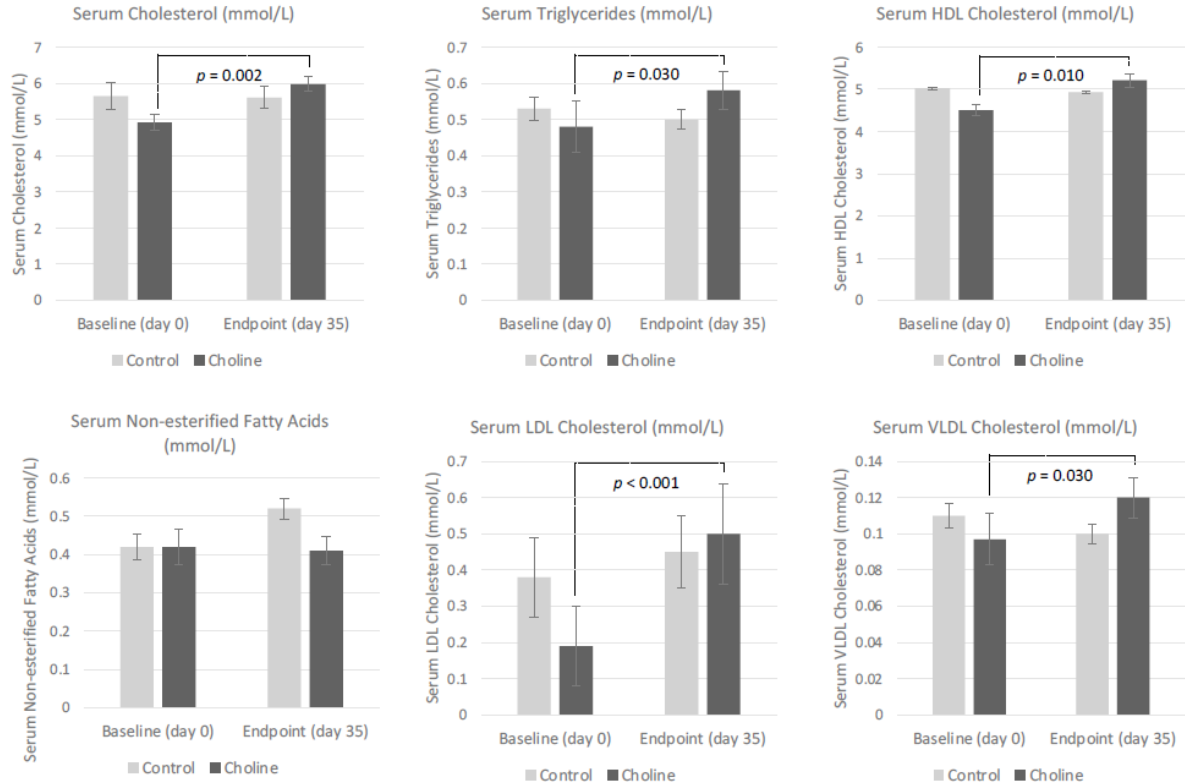
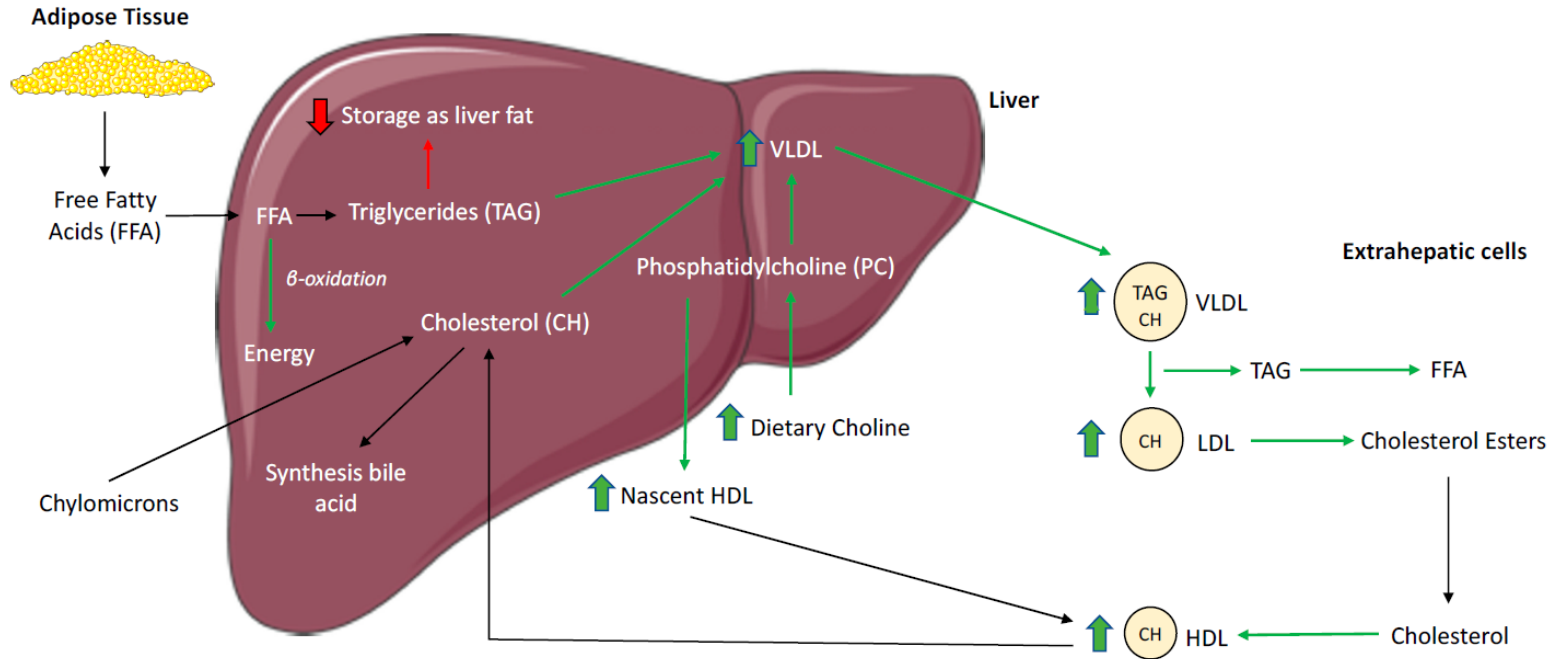


Figure 1. Serum lipoprotein concentrations (mmol/L) in 12 chronically obese cats following 5 weeks of a control extruded cat food (458.7 mg choline/100 g dry matter (DM)) ($n = 6$) or a high-choline extruded cat food (1895.7 mg choline/100 g DM) ($n = 6$). Both groups were fed at maintenance energy requirements. Values are expressed as the mean \pm SEM.

Adult Cats



Assists in eliminating hepatic fat
→ Lipolysis & mobilization ↑

Adult Cats

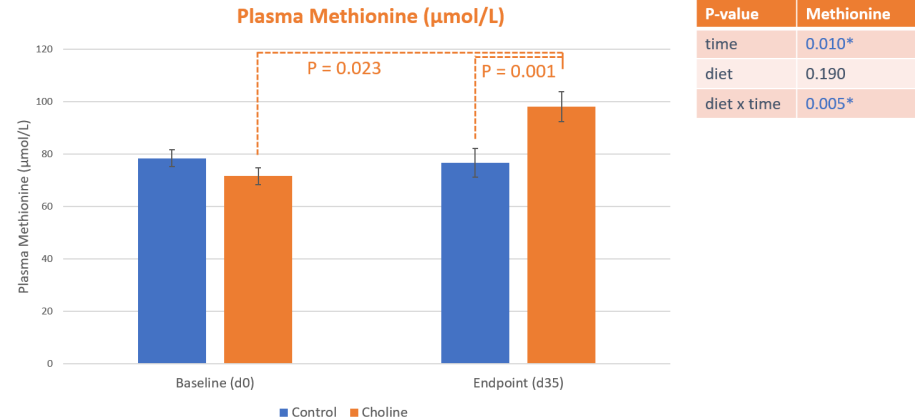
N = 12

Chronically obese

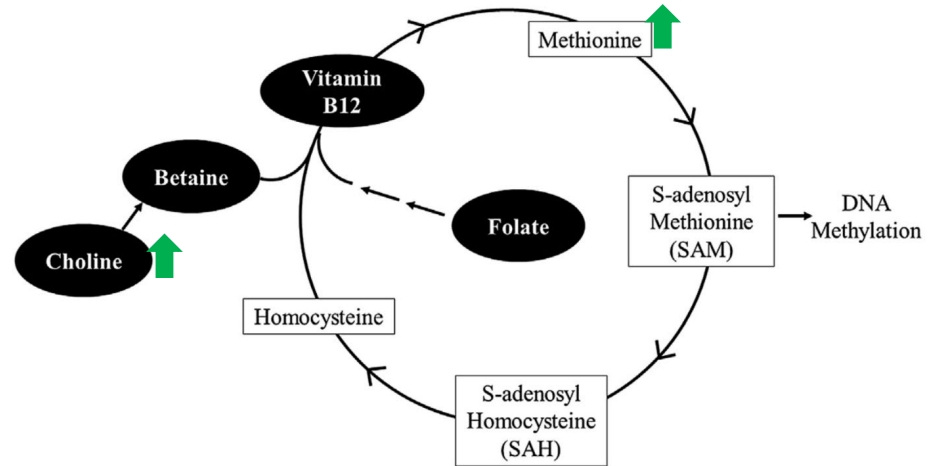
Choline vs. control

Choline @ 5 x NRC RA

5 week



Methionine recycling \uparrow





Dose-response relationship between dietary choline and serum lipid profile, energy expenditure, and respiratory quotient in overweight adult cats fed at maintenance energy requirements

Alexandra Rankovic,[†]  Hannah Godfrey,[‡] Caitlin E Grant,[‡] Anna K Shoveller,^{||} 
Marica Bakovic,[§]  Gordon Kirby,[†] and Adronie Verbrugghe^{‡,1} 



Adult Cats

N = 14
Overweight
Choline dose response
2 week

mmol/L	Control	2 x NRC RA	4 X NRC RA	6 X NRC RA	8 X NRC RA	P _{Dose}
TAG	0.371 ± 0.044 ^b	0.387 ± 0.044 ^{ab}	0.422 ± 0.044 ^{ab}	0.458 ± 0.044 ^a	0.377 ± 0.044 ^{ab}	0.027*
CHOL	6.65 ± 0.35 ^a	6.58 ± 0.35 ^a	6.83 ± 0.35 ^{ab}	7.15 ± 0.35 ^b	6.90 ± 0.35 ^{ab}	0.012*
HDL-C	5.20 ± 0.20 ^b	5.28 ± 0.20 ^{ab}	5.40 ± 0.20 ^{ab}	5.54 ± 0.20 ^a	5.42 ± 0.20 ^{ab}	0.026*
LDL-C	1.29 ± 0.18	1.13 ± 0.18	1.24 ± 0.18	1.40 ± 0.18	1.31 ± 0.18	0.066
VLDL	0.074 ± 0.009 ^b	0.077 ± 0.009 ^{ab}	0.084 ± 0.009 ^{ab}	0.092 ± 0.009 ^a	0.075 ± 0.009 ^{ab}	0.027*
NEFA	0.22 ± 0.021	0.23 ± 0.021	0.21 ± 0.021	0.20 ± 0.021	0.17 ± 0.021	0.071

RESEARCH ARTICLE

Serum metabolomic analysis of the dose-response effect of dietary choline in overweight male cats fed at maintenance energy requirements

Alexandra Rankovic¹ , Hannah Godfrey², Caitlin E. Grant², Anna K. Shoveller³, Marica Bakovic⁴, Gordon Kirby¹, Adronie Verbrugghe^{2*} 

Adult Cats

N = 14

Overweight

Choline dose response

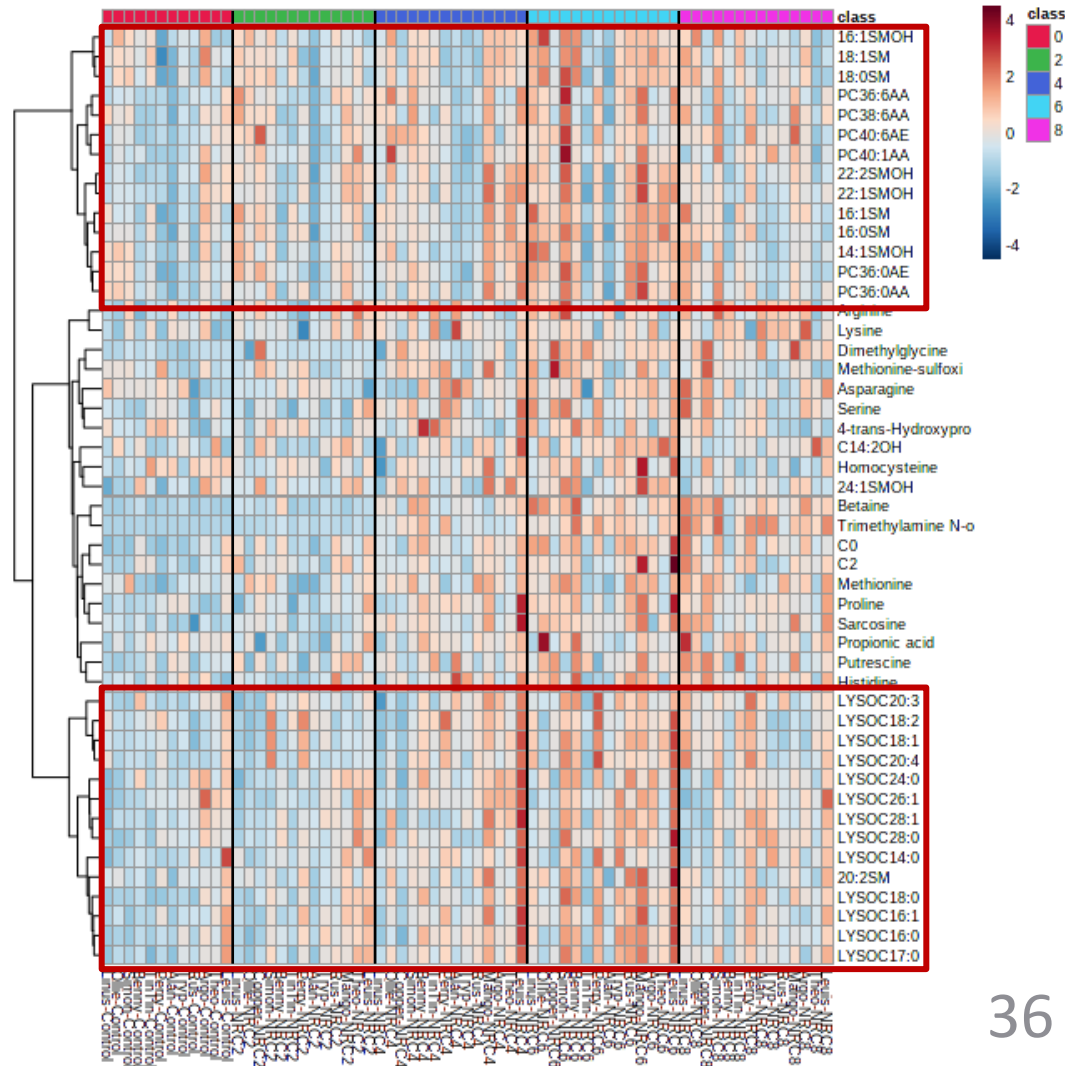
2 week

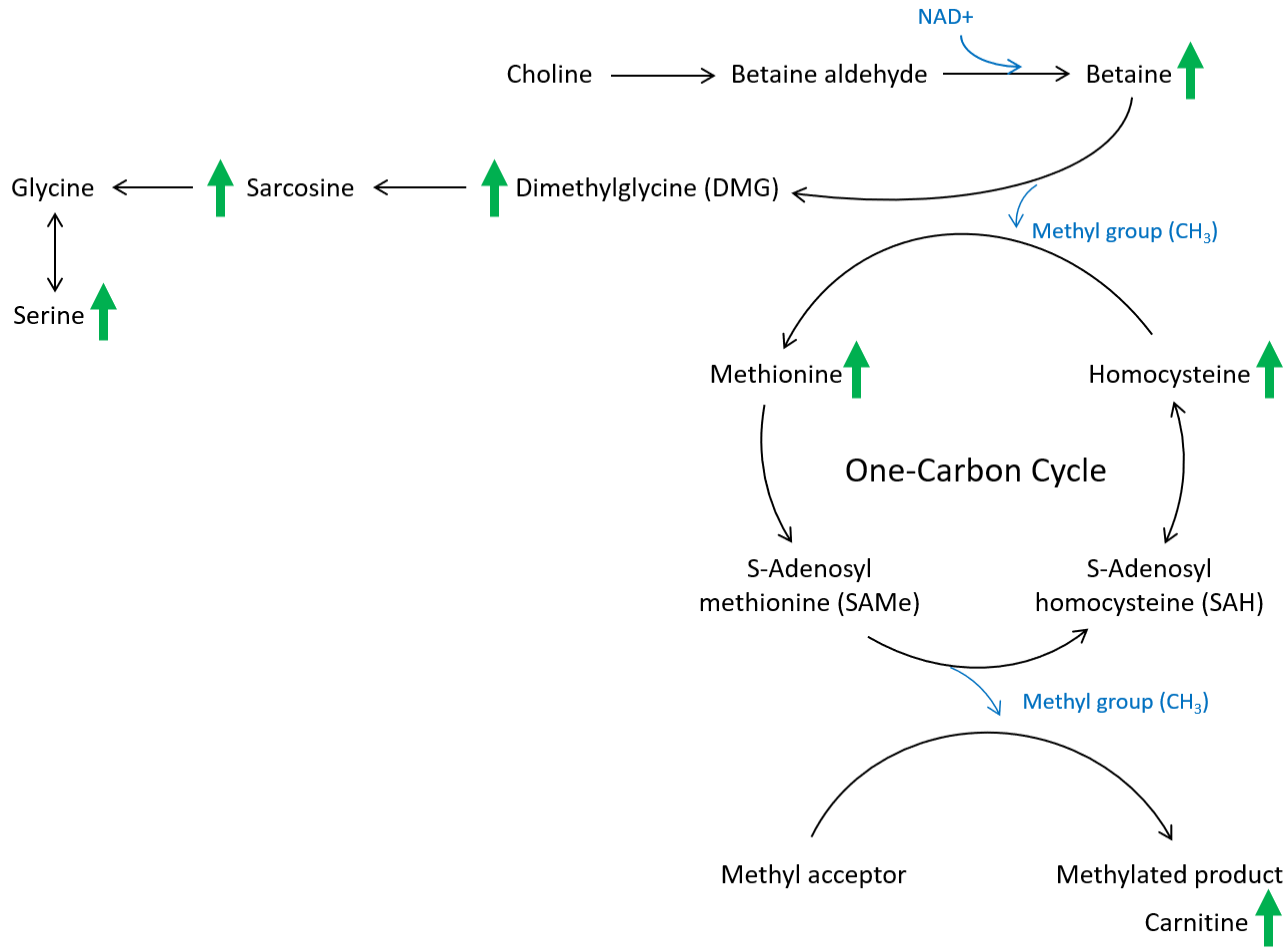
Serum metabolomics

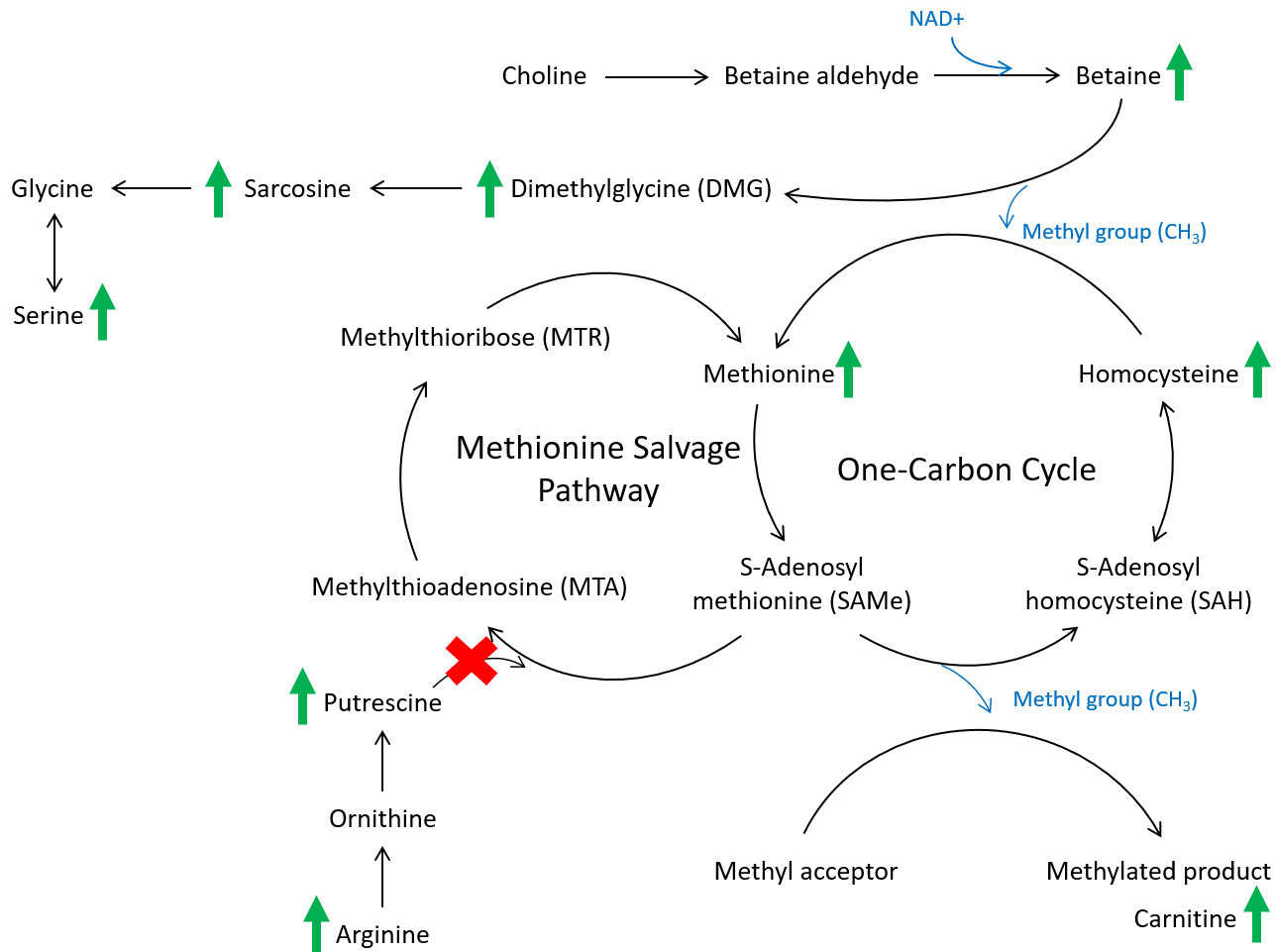
NMR & DiMS

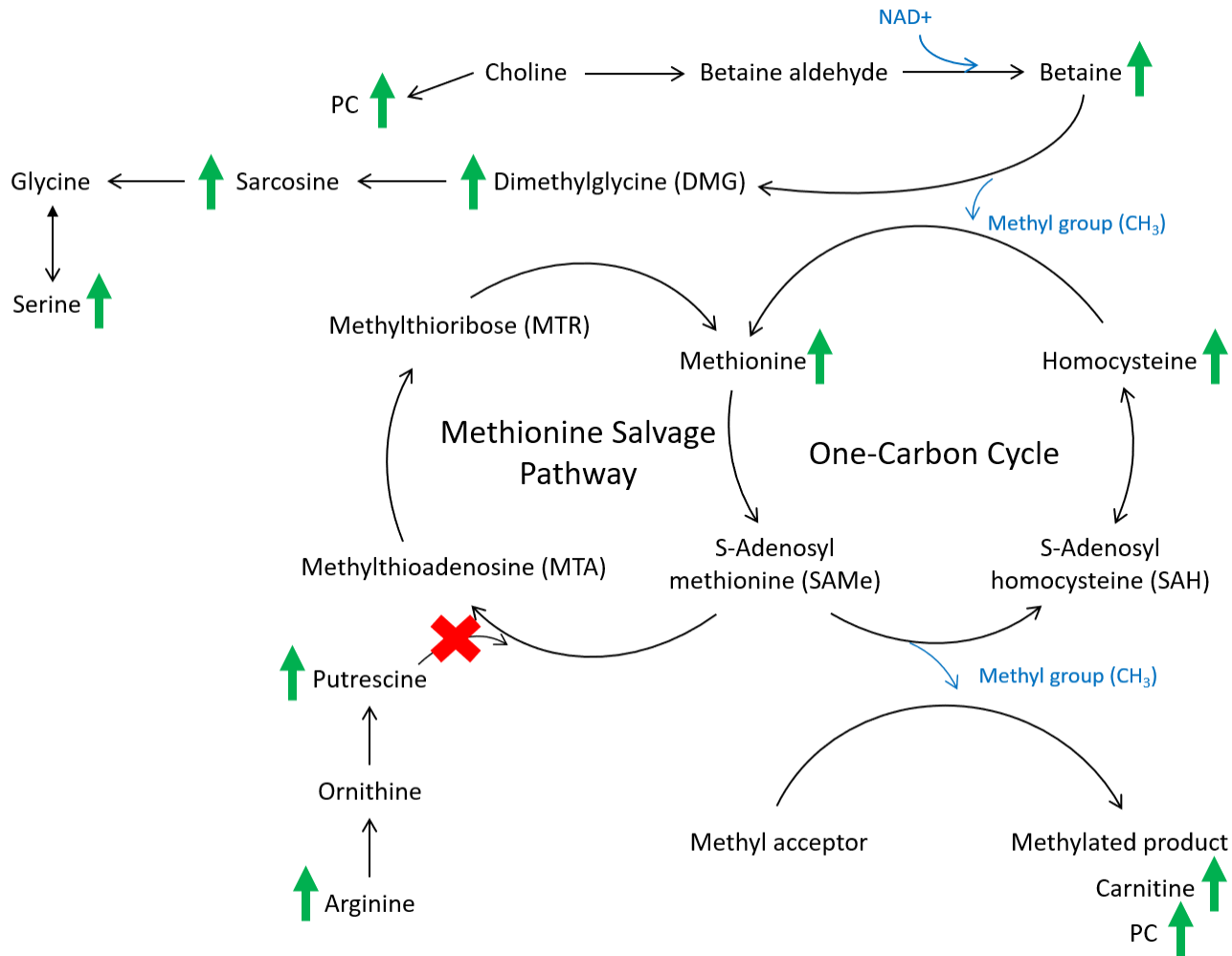
6 x NRC RA

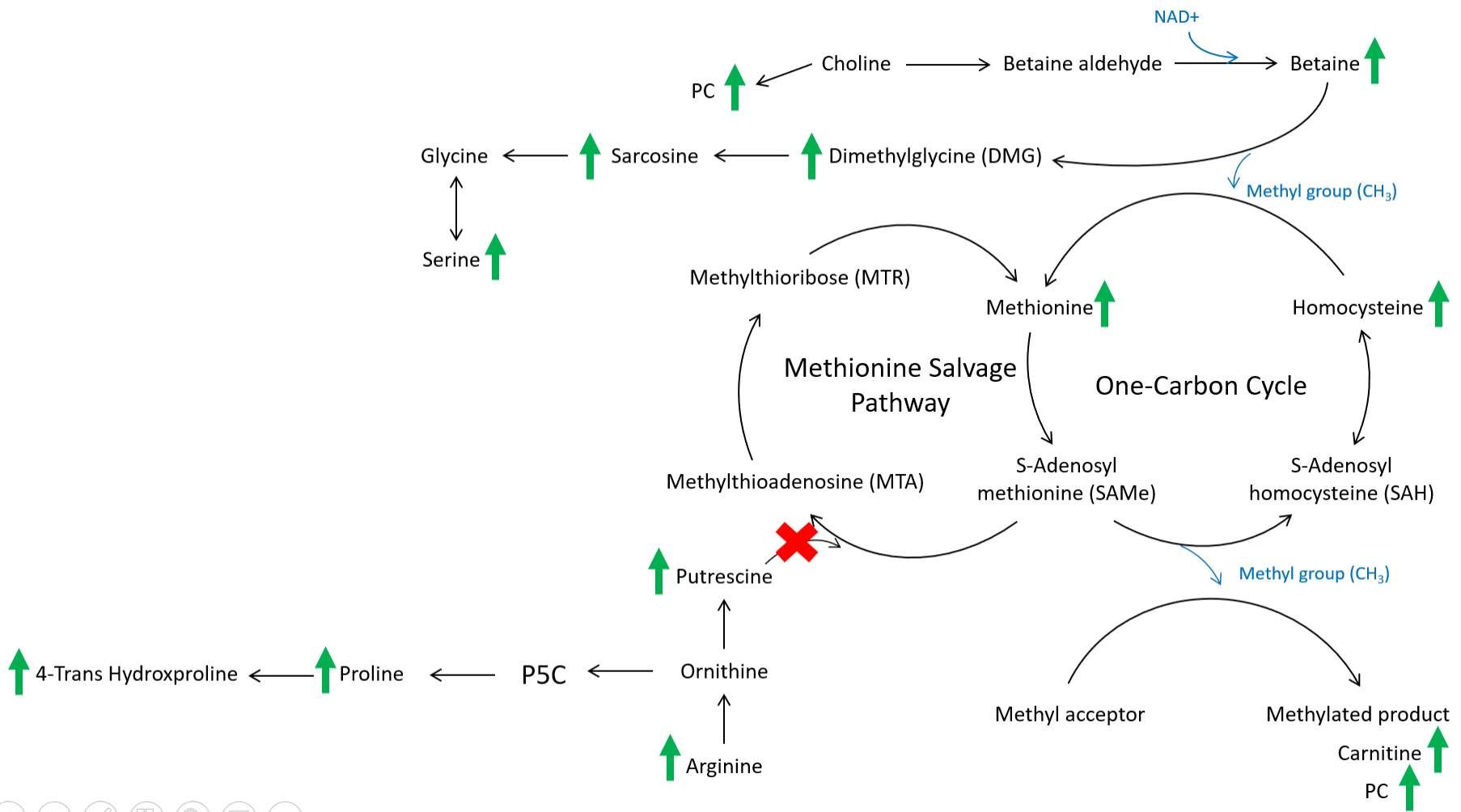
- ↑ serum phospholipids and sphingolipids
- ↑ one-carbon cycle metabolites

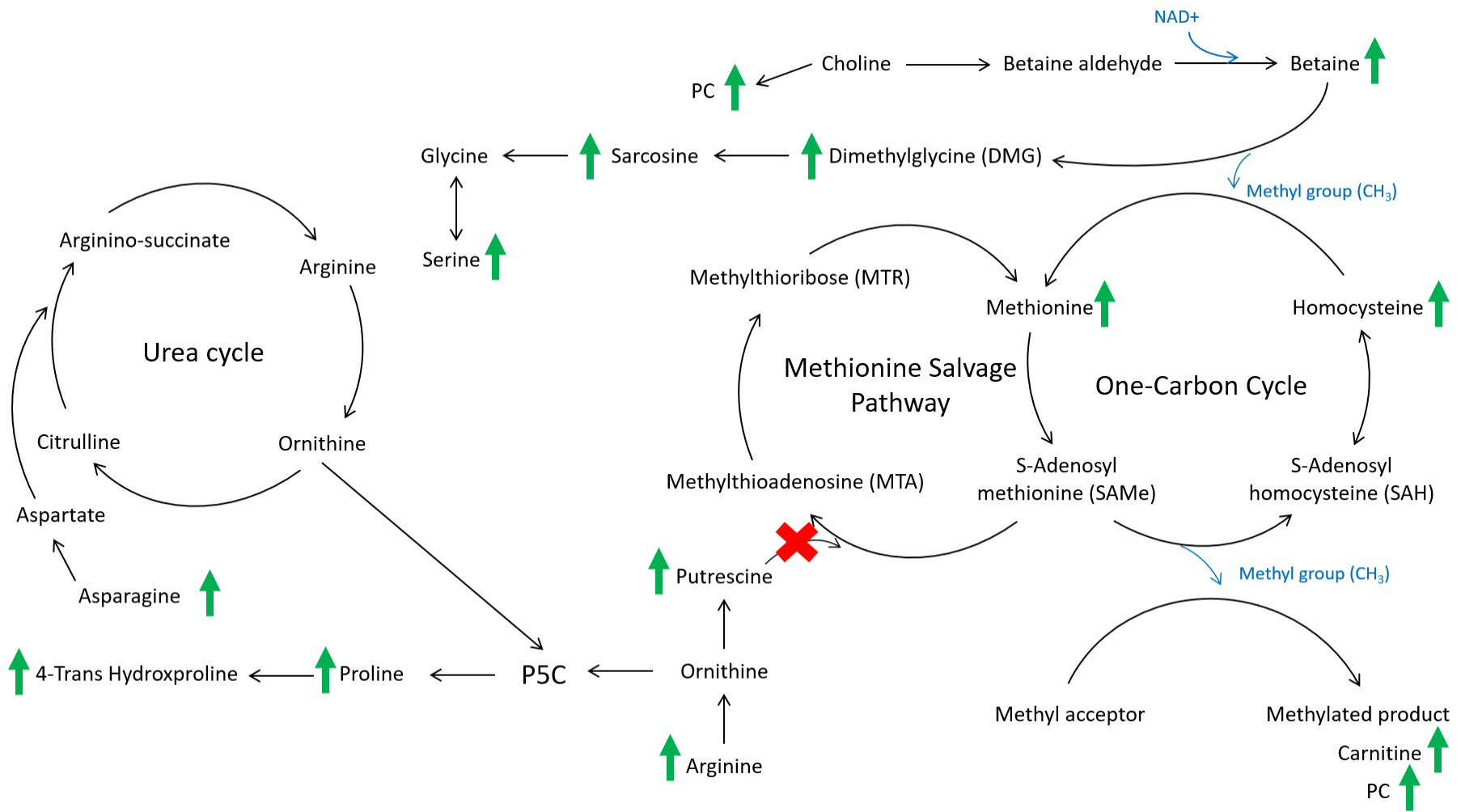












Study Limitations

- Most studies only male cats
- Not chronically obese, young cats
- Did not investigate weight loss or energy restriction
- Only one choline source tested



Case Report

Presumed Choline Chloride Toxicosis in Cats With Positive Ethylene Glycol Tests After Consuming a Recalled Cat Food





Sarah K. Peloquin, DVM^{a,*}, David S. Rotstein, DVM, MPVM^b, Jennifer L. Jones, DVM^a, Jake Guag, MPH^a, Lauren Carey, DVM^b, Lee Anne Palmer, VMD, MPH^b, Krisztina Wolf, MS, DVM^b, William Burkholder, DVM, PhD^b, April Hodges, PhD, LN^b, Lloyd Payne^b, Renate Reimschuessel, VMD, PhD^a



Article







Effects of an Herbal Source of Choline on Diet Digestibility and Palatability, Blood Lipid Profile, Liver Morphology, and Cardiac Function in Dogs

Rosandra Colpani do Nascimento, Camilla Mariane Menezes Souza , Taís Silvino Bastos, Gislaine Cristina Bill Kaelle *, Simone Gisele de Oliveira and Ananda Portella Félix



Article

Influence of a Polyherbal Choline Source in Dogs: Body Weight Changes, Blood Metabolites, and Gene Expression

Germán David Mendoza-Martínez ¹, Pedro Abel Hernández-García ², Fernando Xicoténcatl Plata-Pérez ¹, José Antonio Martínez-García ¹, Augusto Cesar Lizarazo-Chaparro ³, Ismael Martínez-Cortés ¹, Marcia Campillo-Navarro ⁴, Héctor Aarón Lee-Rangel ⁵, María Eugenia De la Torre-Hernández ^{1,6} and Adrian Gloria-Trujillo ^{1,*}

Conclusion

Choline supplementation

→ Potential strategy for prevention and treatment of obesity

Gonadectomy → higher food intake, body weight and fat mass

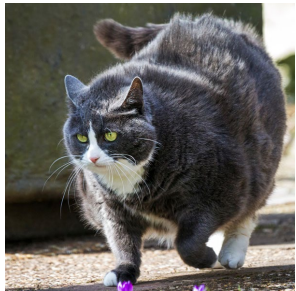
Choline above NRC recommended allowance (3 x)

Minimize effects of gonadectomy → Reduce risk of obesity

Choline above NRC recommended allowance (6 x)

Hepatic lipid mobilization & liver health → Reduce risk FHL

No effect on body composition → Context weight loss



Acknowledgements





Dr. Adronie Verbrugge

Email: averbrug@uoguelph.ca

<https://ovcpetnutrition.uoguelph.ca/>

