Dietary management of feline and canine chronic kidney disease

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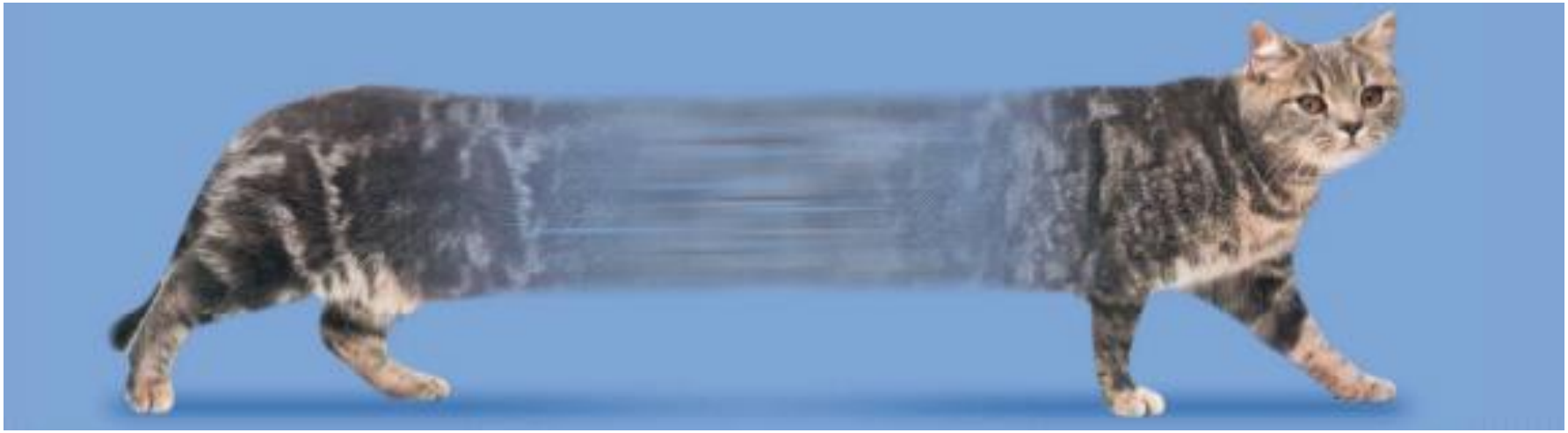
Proper dietary management increases survival time in cats with chronic renal failure



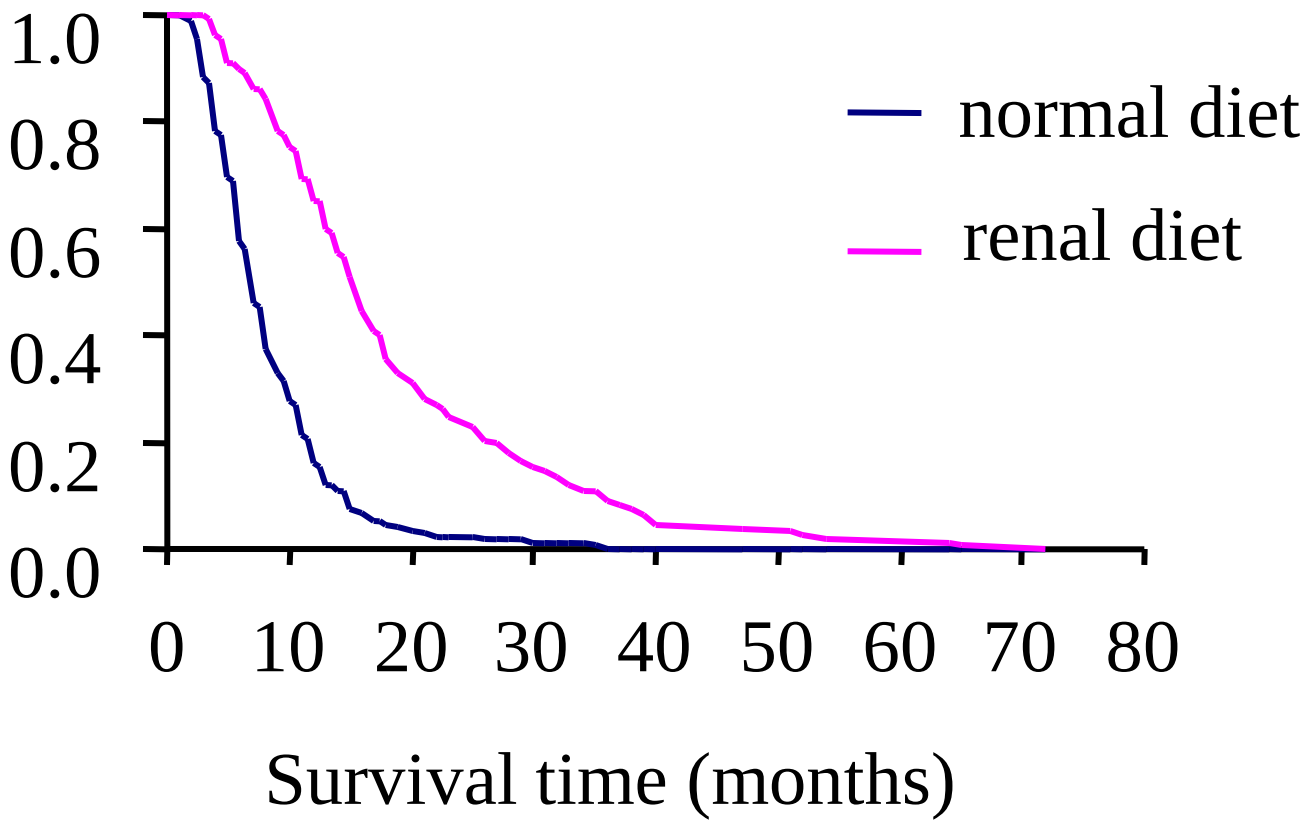
Efficacy of feline renal diets in veterinary practice (Plantinga et al., 2005)

- Retrospective study
- Computer data base of 31 veterinary clinics (88037 cats)
- Selection of cats with CKD
- Does a kidney diet versus normal diet increase survival time?
- Are there differences in efficacy between commercial kidney diets?

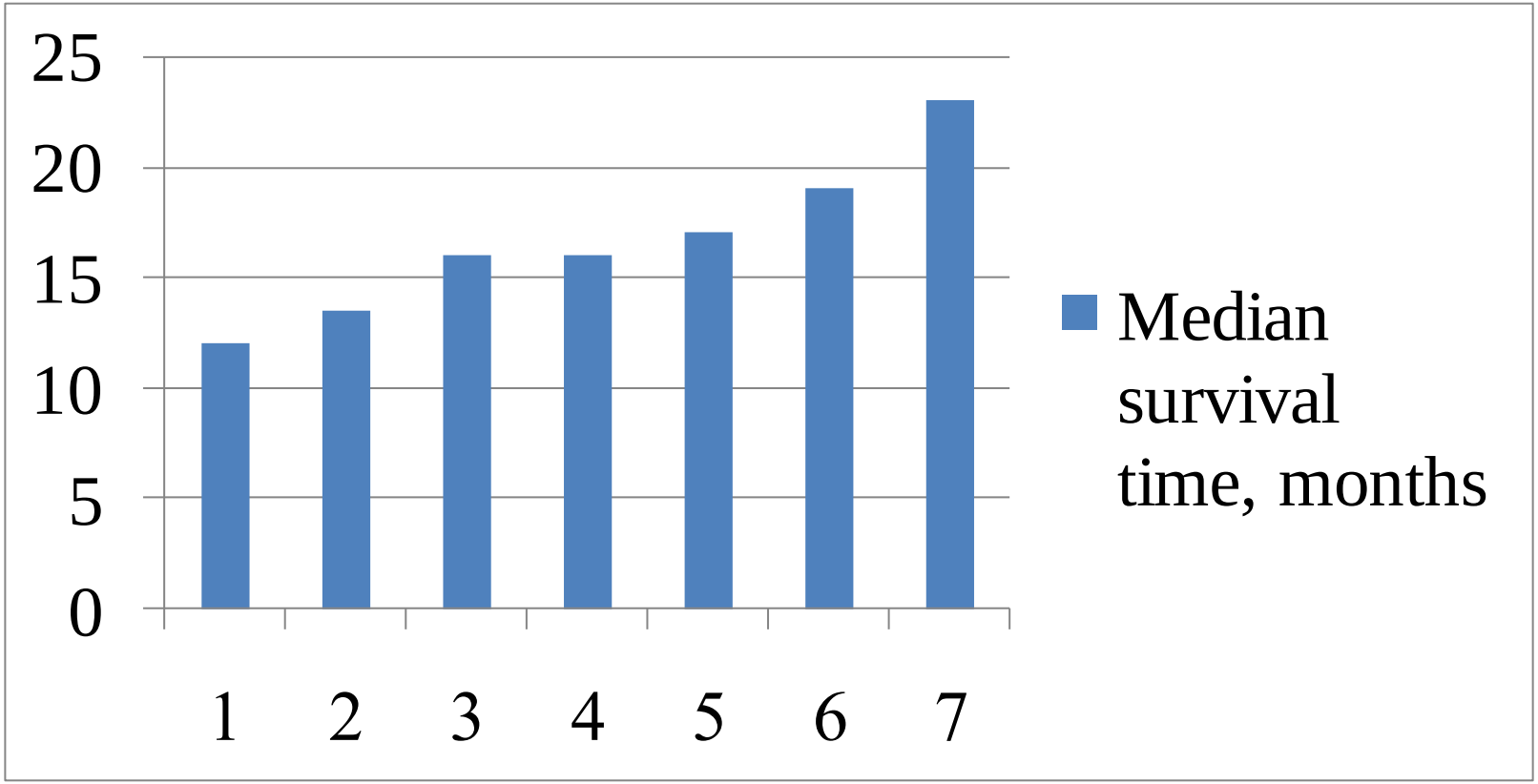
Characteristics of the selected cats with chronic kidney disease

- Age > 8 years
- Survival time after diagnosis > 2 months
- Plasma urea > 14 mmol/L
- Plasma creatinine > 175 µmol/L
- Normal cat food (n=175) or kidney diet (n=146) for at least 75% of survival time
- No other diseases than CKD
- Death related to CKD

Survival time of cats with chronic kidney disease fed a normal or kidney diet



Commercial, feline renal diets have different efficacy



Ideal characteristics of a kidney diet

- Low phosphorus
- Protein restriction (+ nitrogen trap)
- High eicosapentaenoic acid (EPA)
- Low sodium
- High (?) potassium
- Positive base excess
- High vitamin E

What is the evidence for the ideal characteristics?

- In patients with naturally occurring CKD single dietary variables have not been tested
- Low phoshorus, low protein and high EPA: evidence from studies with dog or cat models with subtotal nephrectomy
- Other items: theoretical basis only

Ideal composition of a feline renal diet (Plantinga and Beynen, 2004)

Protein*, g/MJ	12-15
Phoshorus^, g/MJ	0.1-0.2
Sodium, g/MJ	0.04-0.06
EPA, g/MJ	0.2-1.0
CAD, mmol/kg DM	150-350
*Carbohydrates > 2.5 g/MJ	
^Dry diets: 0.13-0.27 g/MJ	

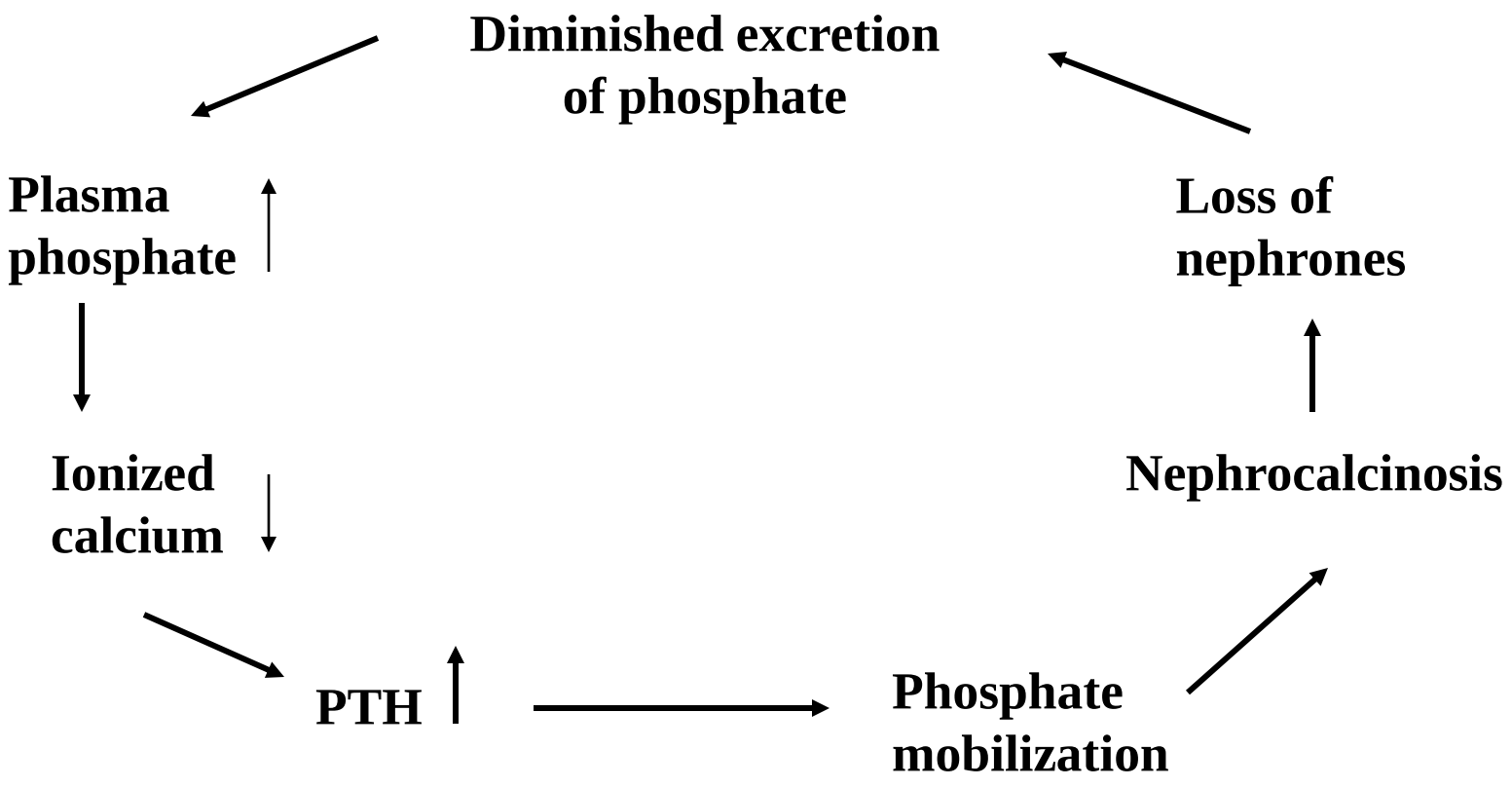
Phosphorus restriction reduces progression of kidney disease in cats with reduced renal mass (Ross et al., 1982)

	High P	**Low P**
Phosphorus, g/MJ	0.80	0.22
Protein, g/MJ	14.4	14.4
Mineralization, score^	3.13	0.75
Fibrosis, score^	2.63	0.50
^ 0-5 scale		

Phosphorus restriction reduces progression of kidney disease in dogs with 15/16 nephrectomy (Finco et al., 1992)

	High P	**Low P**
Phosphorus, g/MJ	1.06	0.29
Protein, g/MJ	12.0	11.1
Mineralization, score^	1.07	0.99
Fibrosis, score^	1.71	1.48
^ 0-3 scale		

Phosphorus restriction reduces progression of chronic kidney disease



Phosphorus restriction lowers kidney calcium in healthy cats (Pastoor et al., 1995)

	High P	**Low P**
Dietary phosphorus, g/MJ	0.28	0.14
Kidney calcium, mg/g DM	0.80	0.24

Protein restriction reduces progression of kidney disease in uninephrectomized dogs (Finco et al., 1994)

	High Protein	**Low Protein**
Protein, g/MJ	19.4	10.4
Phosphorus, g/MJ	0.52	0.51
Fibrosis, score^	0.71	0.41
Cell infiltration, score^	0.92	0.49
Pelvic lesions, score^	0.45	0.28
^ 0-3 scale		

High EPA intake reduces progression of kidney disease in dogs with 15/16 nephrectomy (Brown et al., 1998)

	Dietary fat		
	Beef tallow	Safflower oil	Fish oil
Phosphorus, g/MJ	0.2	0.2	0.2
Protein, g/MJ	10	10	10
Linoleic acid, g/MJ	0.6	6.5	0.3
EPA, g/MJ	0	0	1.1

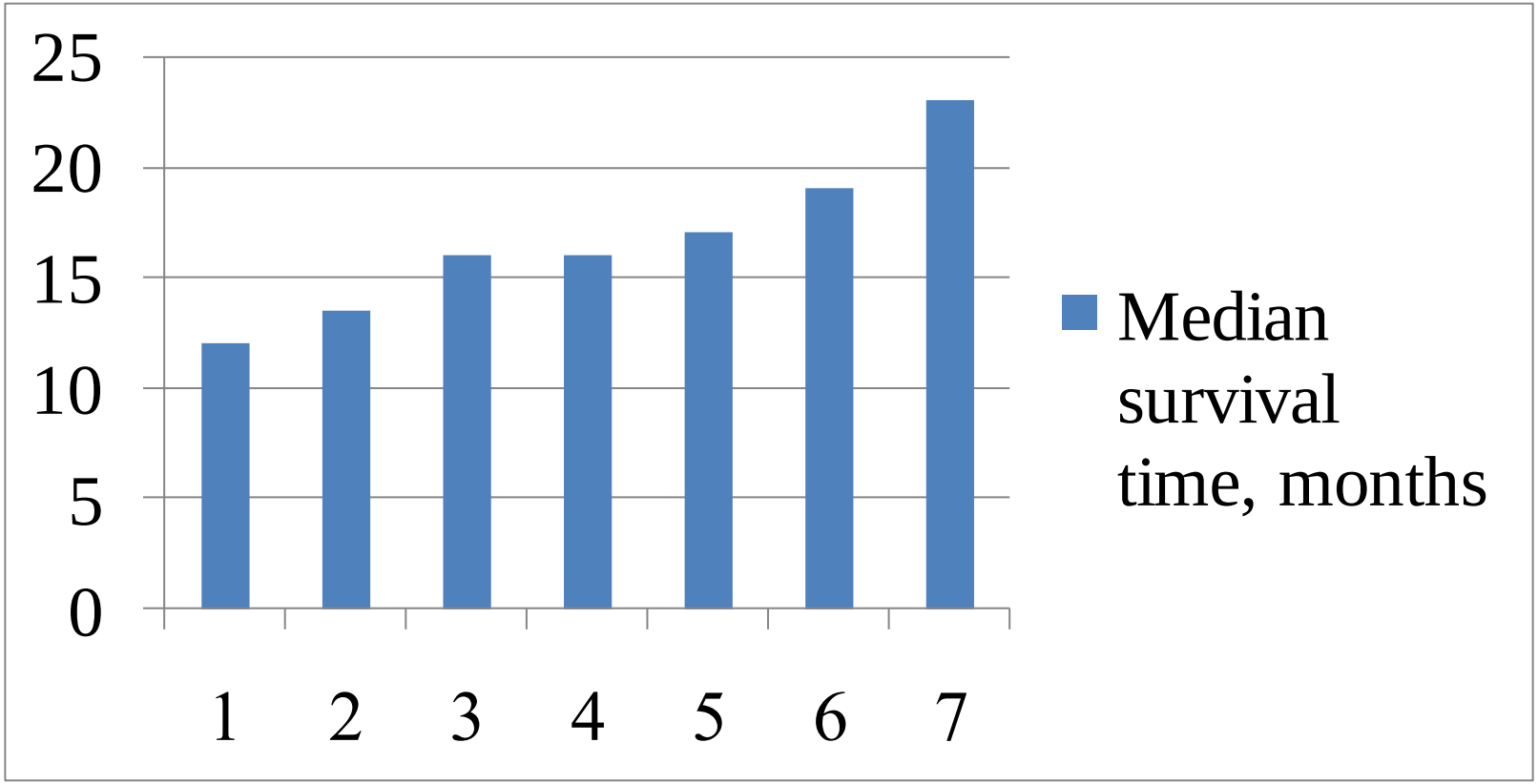
High EPA intake reduces progression of kidney disease in dogs with 15/16 nephrectomy

	Dietary fat		
	Beef tallow	Safflower oil	Fish oil
Creatinine, µmol/L	265	309	203
GFR, ml/min.kg	1.21	0.89	1.43
Glomerulosclerosis, %	63	67	28
Survival at 20 months	6/7	3/7	7/7

Ideal characteristics of a renal diet

- Low phosphorus
- Low protein restriction (+ nitrogen trap)
- High eicosapentaenoic acid (EPA)
- Low sodium
- High (?) potassium
- Positive base excess
- High vitamin E

Different commercial, feline renal diets have different efficacy



Prospective, dietary study in cats with chronic kidney disease (Harte et al., 1994)

- Client-owned cats
- Diagnosis CKD: serum creatinine > 167 μmol/L
- Control diet: n =10. Kidney diet: n= 25
- Duration of trial: 24 weeks
- Efficacy variables: serum creatinine, rate of clinical deterioration

Composition of the diets used in the trial with cats (Harte et al., 1994)

	Control diet	**Kidney diet**
Protein, g/MJ	23.6	15.1
Phosphorus, g/MJ	0.48	0.23

Outcomes of prospective dietary trial in cats with chronic kidney disease

- On the control diet, serum urea and creatinine concentrations increased over time, but the kidney diet induced lowering versus baseline
- Deterioration in halitosis, gingivitis, appetite and body condition was less apparent in the cats fed the kidney diet

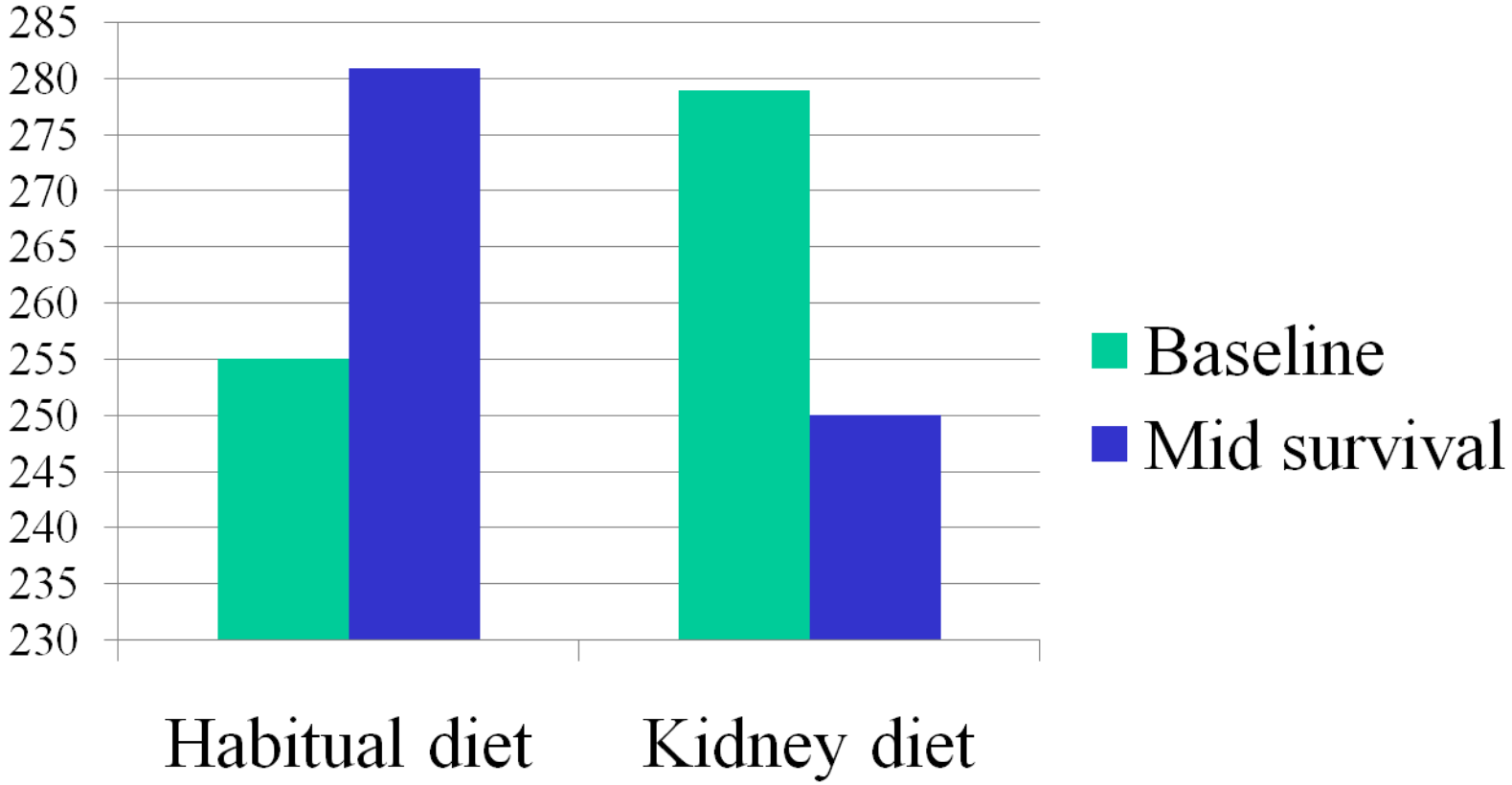
Prospective, dietary study in cats with chronic kidney disease (Elliot et al., 2000)

- Client-owned cats
- Diagnosis of CKD: plasma creatinine > 180 μmol/L
- All owners were offered the kidney diet in dry or canned form; when owners or cats refused, the cats were kept on their habitual diet
- Habitual diet: n = 21. Kidney diet: n = 29
- Efficacy variables: plasma creatinine, survival time

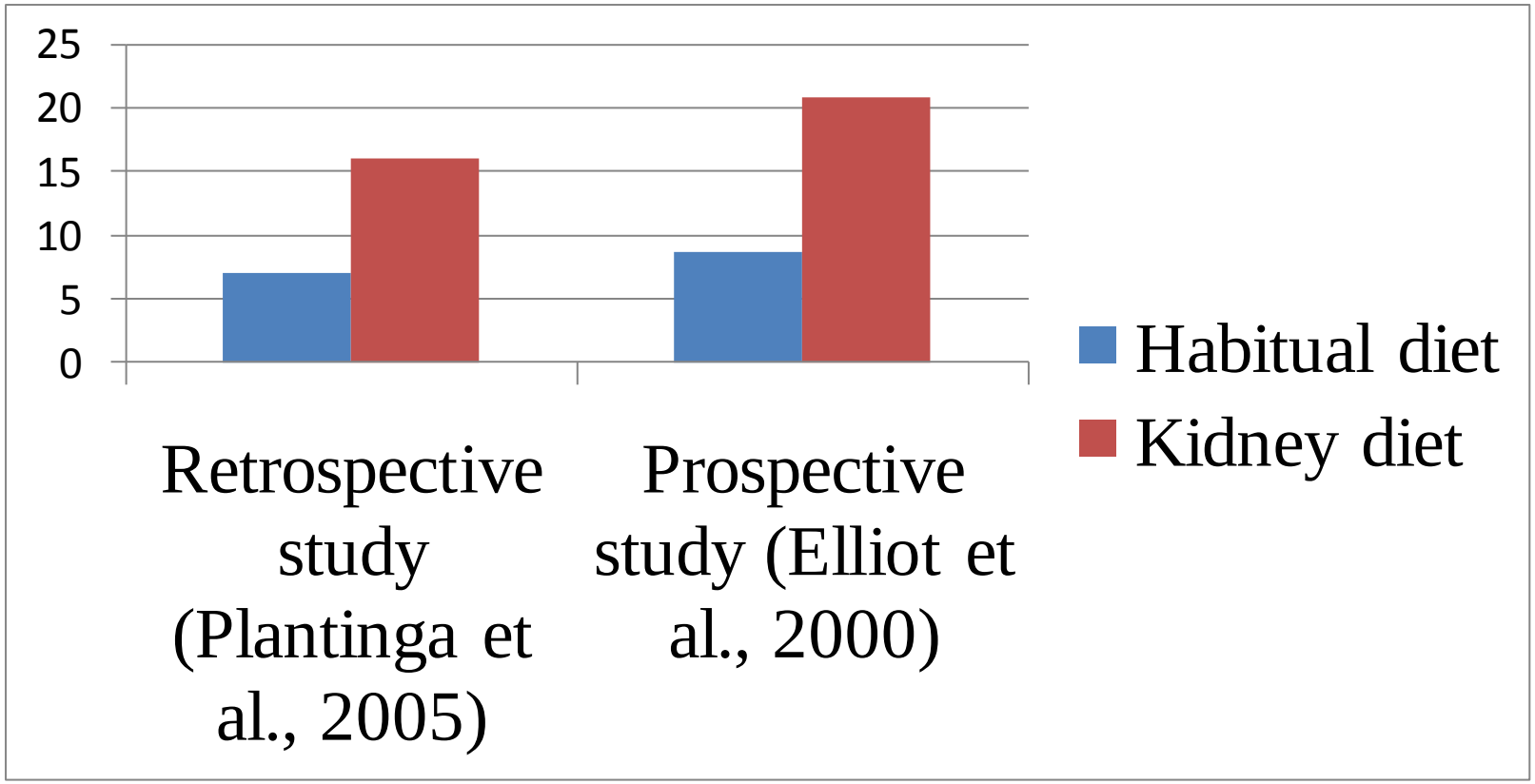
Composition of the kidney diet used in the trial with cats (Elliot et al., 2000)

	Habitual diet	**Kidney diet**
Protein, g/MJ	?	14.0
Phosphorus, g/MJ	?	0.19

Serum creatinine concentrations (μmol/L) in the cats with chronic kidney disease



Median survival time (months) of cats with chronic kidney disease fed a kidney diet



Dietary management of chronic kidney disease in dogs

- Barsanti and Finco (1984)
- Grandjean et al. (1990)
- Hansen et al. (1992)
- Jacob et al. (2002)

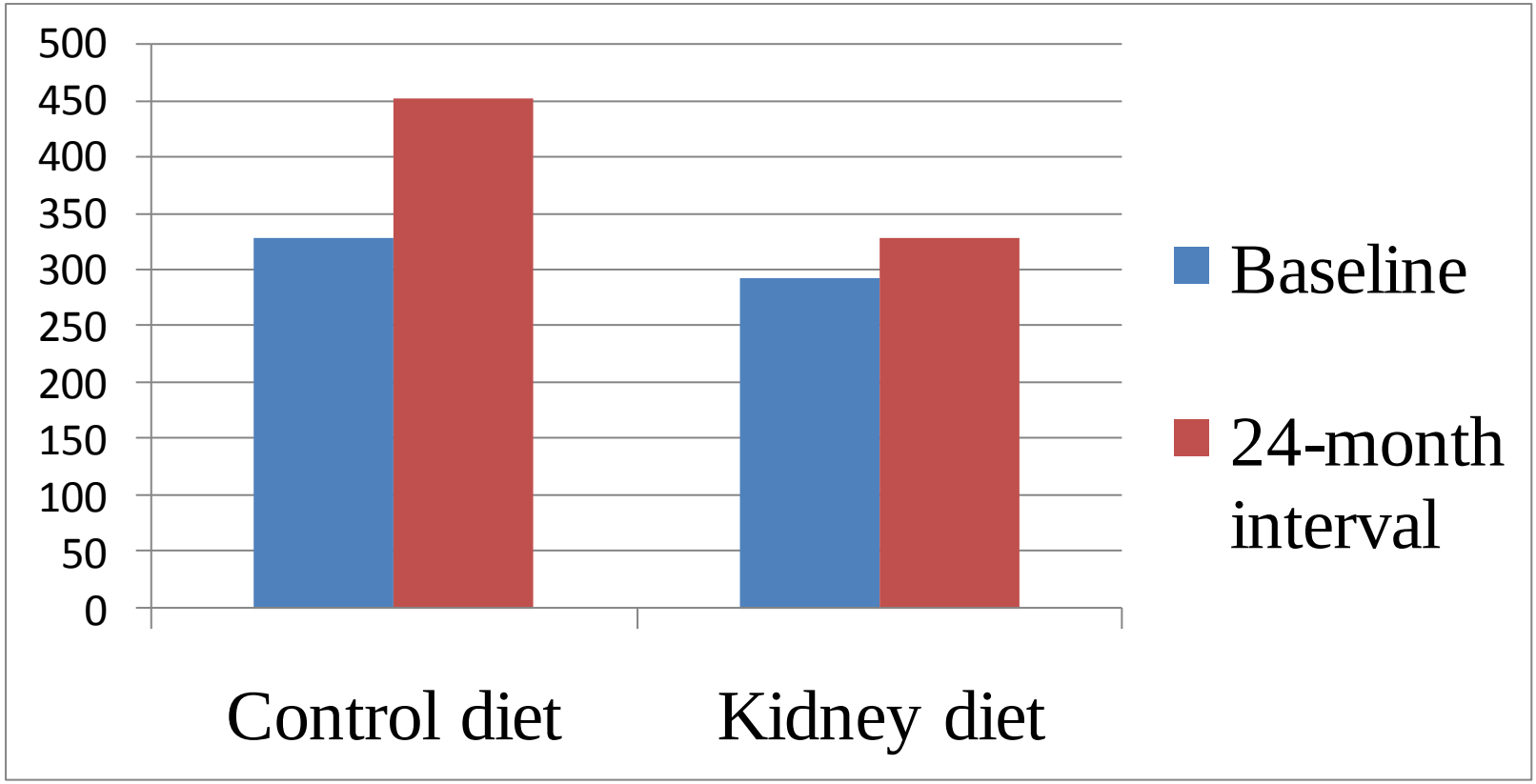
Prospective, dietary study in cats with chronic kidney disease (Jacob et al., 2002)

- Client-owned dogs
- Double-blinded, controlled trial
- Dogs evaluated for up to 24 months
- Serum creatinine between 177 and 707 μmol/L
- Control diet: n = 17. Kidney diet: n = 21

Composition of the diets used in the trial with dogs (Jacob et al., 2002)

	Control diet	**Kidney diet**
Protein, g/MJ	13.5	7.1
Phosphorus, g/MJ	0.64	0.16
Ratio of n-6/n-3 fatty acids	15:1	2:1

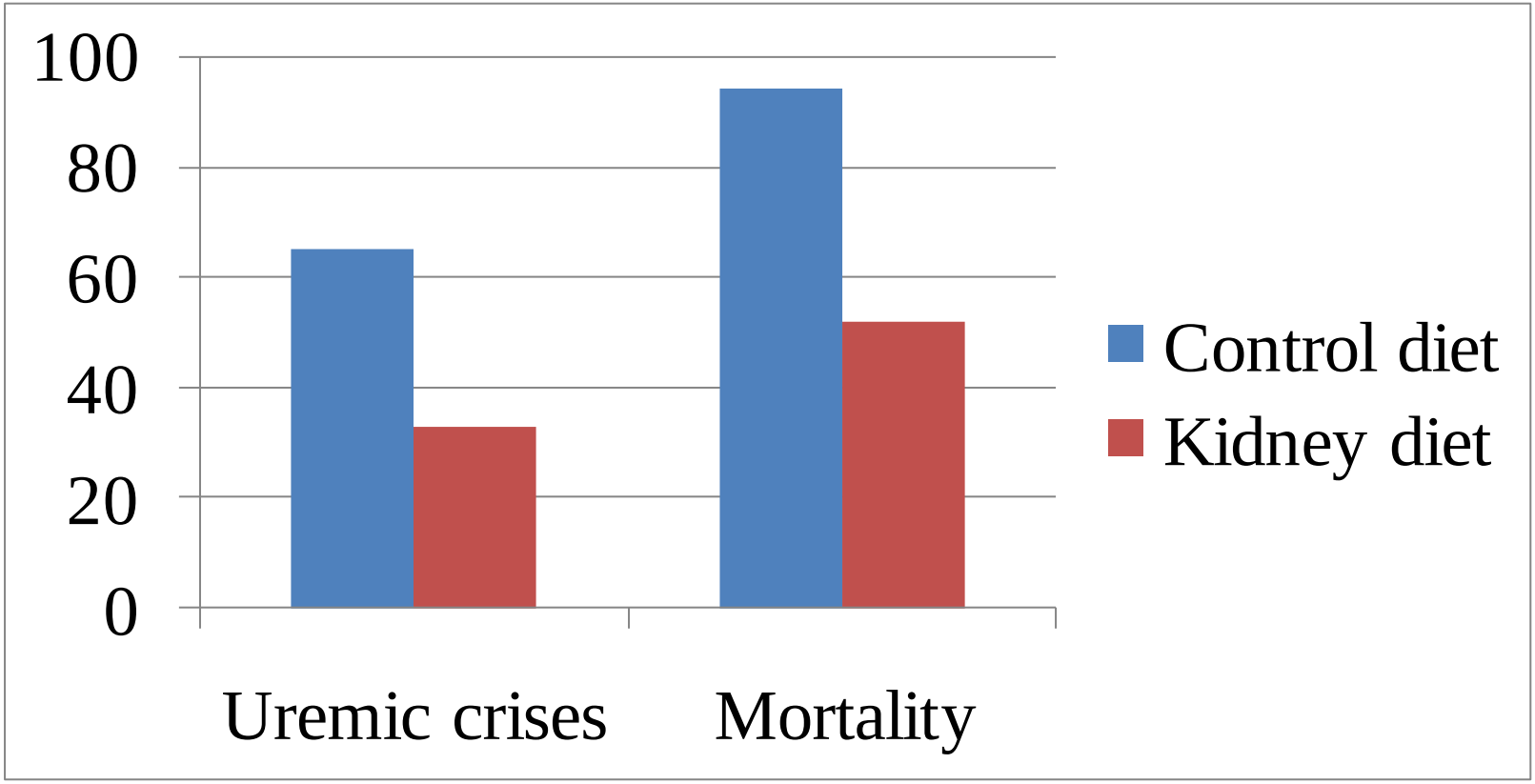
Serum creatinine concentrations (μmol/L) in the dogs with chronic kidney disease



Uremic crises and mortality in the dogs with chronic kidney disease during 24 months

	Control diet	**Kidney diet**
Uremic crises	11/17	7/21
All cause mortality	16/17	11/21
Renal mortality	11/17	7/21

Renal diet lowers uremic crises and mortality in dogs with chronic kidney disease



Conclusions

- Kidney diets should be low in phosphorus and protein and high in EPA
- Kidney diets are effective in the management of canine and feline chronic renal failure
- Median survival time after diagnosis may be about 20 months in cats, which equals survival-time extension by about 1 year

Sanimed Anti-Osteoarthritis in the management of canine osteoarthritis

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SIGNS OF OSTEOARTHRITIS

- Lameness
- Stiffness
- Reduced movement in joint
- Reluctance or difficulty with exercise
- Crepitus
- Painful, warm, swollen joints
- Muscle atrophy

Dietary prevention of osteoarthritis development

- Food restriction
- Functional ingredients

Effect of restricted feeding on skeletal disease and life span in dogs (Kealy et al., 1992 etc)

- 48 Labrador Retrievers, 8 weeks old
- Paired feeding (male and female littermates)
- Dry, extruded diet: ad libitum versus 75 %
- As from 3 years: 261 kJ/kg BW versus 75 %
- Hip dysplasia (1992), osteoarthritis (1997)
- Life span; euthanasia according to protocol (2002)

Restricted feeding and osteoarthritis in dogs at 5 years of age (Kealy et al., 1997)

Feeding regimen	Body condition score (1-9 scale)	Osteoarthritis incidence
Ad lib./controlled	6.5	12/23
Restricted	4.0	3/23*
*P < 0.05		

PURINA®

BODY CONDITION SYSTEM

1 **EMACIATED** Ribs, lumbar vertebrae, pelvic bones and all bony prominences evident from a distance. No discernible body fat. Obvious loss of muscle mass.

2 **VERY THIN** Ribs, lumbar vertebrae and pelvic bones easily visible. No palpable fat. Some evidence of other bony prominence. Minimal loss of muscle mass.

3 **THIN** Ribs easily palpated and may be visible with no palpable fat. Tops of lumbar vertebrae visible. Pelvic bones becoming prominent. Obvious waist and abdominal tuck.

4 **UNDERWEIGHT** Ribs easily palpable, with minimal fat covering. Waist easily noted, viewed from above. Abdominal tuck evident.

5 **IDEAL** Ribs palpable without excess fat covering. Waist observed behind ribs when viewed from above. Abdomen tucked up when viewed from side.

6 **OVERWEIGHT** Ribs palpable with slight excess fat covering. Waist is discernable viewed from above but is not prominent. Abdominal tuck apparent.

7 **HEAVY** Ribs palpable with difficulty, heavy fat cover. Noticeable fat deposits over lumbar area and base of tail. Waist absent or barely visible. Abdominal tuck may be absent.

8 **OBESE** Ribs not palpable under very heavy fat cover, or palpable only with significant pressure. Heavy fat deposits over lumbar area and base of tail. Waist absent. No abdominal tuck. Obvious abdominal distention may be present.

9 **GROSSLY OBESE** Massive fat deposits over thorax, spine and base of tail. Waist and abdominal tuck absent. Fat deposits on neck and limbs. Obvious abdominal distention.

This Body Condition System was developed and tested at the Purina Pet Care Center, and has been documented in the following publications:

Laflamme DP. **Body Condition Scoring and Weight Maintenance.** Proc N Am Vet Conf, Jan 16-21, 1993. Orlando, FL. pp 290-291.
Laflamme DP, Kealy RD, Schmidt DA. **Estimation of Body Fat by Body Condition Score.** J Vet Int Med 1994; 8:154.
Laflamme DP, Kuhlman G, Lawler DF, Kealy RD, Schmidt DA. **Obesity Management in Dogs.** J Vet Clin Nutr 1994; 1:59-65.

Functional ingredients for regular and therapeutic joint foods and treats

- Fish oil
- Gelatin hydrolysate
- Beta-1,3/1,6-glucans
- Glucosamine
- Chondroitin sulfate
- Green-lipped mussel
- Boswellia resin
- Mulberry extract
- Undenaturated type-II collagen
- Curcumin
- Milk protein concentrate
- Methyl sulfonyl methane
- Devil’s claw
- Green tea
- Grape skin
- Vitamin E

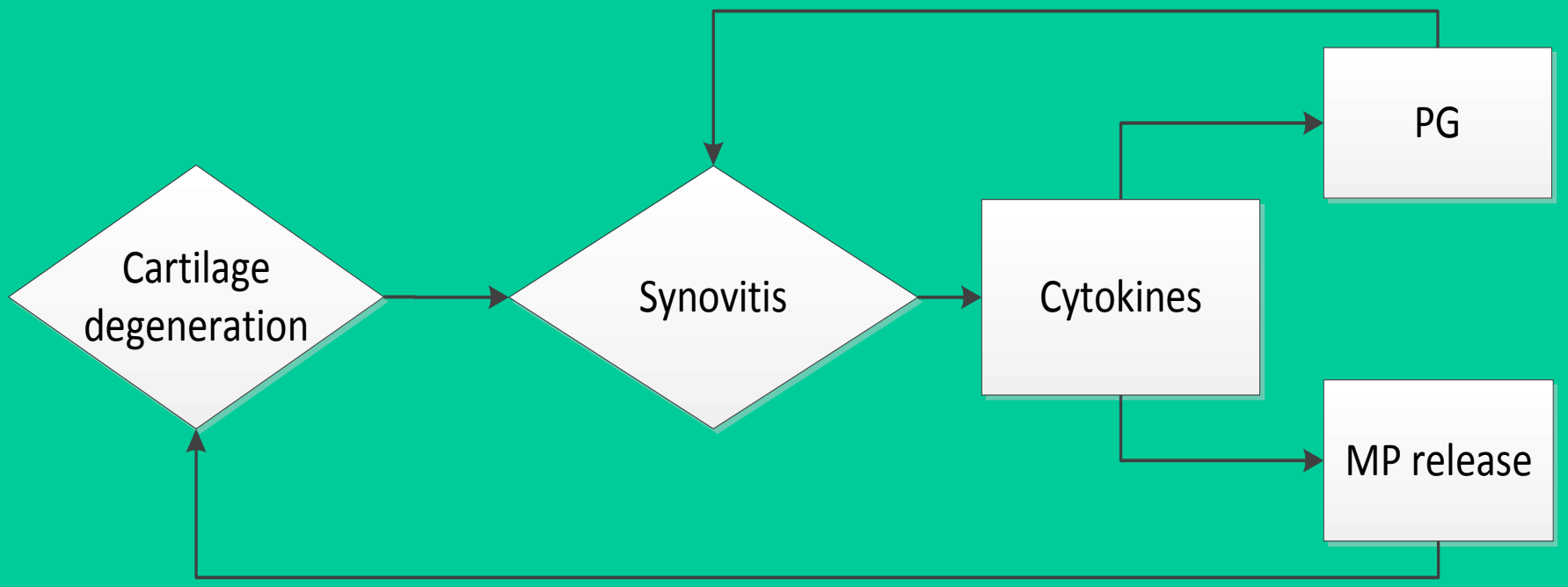
Functional ingredients in regular joint foods and treats

- Efficacy, if proven, only so in affected dogs. Health claims are based on trials with patients
- Prevention of joint disease has not (yet) been investigated
- Dose should be sufficiently high
- Functionality should survive food processing

Effective ingredients in treatment of canine osteoarthritis

- Fish oil
- Undenaturated type-II collagen
- Gelatin hydrolysate
- Beta-1,3/1,6-glucans

PERPETUATING CYCLE OF OSTEOARTHRITIS



Basis for dietary treatment of osteoarthritis

- Reduction of overweight-induced mechanical stress
- Inhibition of inflammation
- Stimulation of cartilage-matrix synthesis
- Inhibition of cartilage-matrix catabolism
- Scavenging of free radicals

Weight loss reduces clinical signs in overweight dogs with osteoarthritis

- 3 studies: Impellizeri et al. (2000), Mlacnik et al. (2006), Marshall et al. (2010).
- Average weight loss was 11%, and mean decrease in lameness severity score was 29 on a scale of 0 (no signs of lameness) to 100 (maximum lameness)

Effective functional ingredients

- Provoke a better effect in trials than placebo treatments
- Have a likely mechanism of action

Proof for efficacy of functional ingredients

- Trials with target species
- Proper experimental design
- Placebo controlled, double blinded
- Statistically significant effect
- Meaningful effect
- Reproducible effect

Placebo effects in trials on canine osteoarthritis

- Shown in many studies
- Biased evaluation of clinical signs and/or time effects
- Non-controlled, open studies are inconclusive

Undenaturated type-II collagen in canine osteoarthritis

- Efficacy shown in one open and three double-blinded placebo-controlled studies carried out by the same research group

(Literature available on request: beynen@freeler.nl)

Glucosamine and chondroitin sulfate in canine osteoarthritis

- Glucosamine preparations effective in two open, non-controlled studies
- Chondroitin sulfate ineffective in double-blind, placebo-controlled trial
- Combination ineffective or non-systematic effects in three double-blinded, controlled studies
- Combination effective in double-blind study with positive control, but no placebo treatment

Green-lipped mussel in canine osteoarthritis

- Effective in two studies with recognizable test treatment
- Effective in one open, non-controlled study and one double-blinded study without simultaneous control
- Effective in three out of four double-blinded, controlled studies, but in one study control and test dogs were poorly comparable

Various functional ingredients in canine osteoarthritis (1)

- Preparations of curcumin and “special milk protein concentrate” each effective in one double-blinded, placebo-controlled trial
- Bosewellia resin effective in one open study
- Efficacy of devil’s claw based on anecdotal observations

Various functional ingredients in canine osteoarthritis (2)

- Efficacy of mulberry extract, grape skin and green tea only described for rodents with induced arthritis
- No reported canine studies on methyl sulfonyl methane or vitamin E

EU legislation on therapeutic foods for osteoarthritis (Regulation 1070/2010)

- Particular nutritional purpose: supporting joint metabolism in case of osteoarthritis
- Dog foods: minimum contents of 3.3% omega-3 fatty acids and 0.38% EPA in dietary dry matter
- Cat foods: minimum contents of 1.2% omega-3 fatty acids and 0.28% DHA in dietary dry matter
- No requirements as to proven efficacy

Long-chain omega-3 fatty acids

- EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid)
- Sources: fish oil, krill oil
- Health claims: supporting immunity, learning behavior and joints
- Applications in therapeutic foods: atopy, osteoarthritis, chronic kidney disease, heart failure, cancer

Nomenclature of fatty acids

CH_3-C-C-C-C-C…….-COOH

Omega- or methyl end

- Number of C atoms
- Number of double bonds
- Position of first double bond from the methyl end (omega end)

omega-6 family		omega-3 family
C18:2n-6 (LA)		**C18:3n-3 (ALA)**
⬇	← D-6 desaturase →	⬇
C18:3n-6 (<u>GLA</u>)		C18:4n-3
⬇	← Elongase →	⬇
C20:3n-6 (DGLA)		C20:4n-3
⬇	← D-5 desaturase →	⬇
C20:4n-6 (<u>AA</u>)		**C20:5n-3 (<u>EPA</u>)**
⬇	← Elongase →	⬇
C22:4n-6		C22:5n-3
⬇	← D-4 desaturase →	⬇
		C22:6n-3 (DHA)

Fish oils

- Active principle: EPA
- Inhibits inflammation
- Inhibition of cartilage proteoglycan catabolism
- Efficacy shown in one open trial and four randomized, double-blind, controlled trials

Dietary omega-6:3 ratio and LPS-induced LTB concentrations in dog skin (Vaughn et al., 1994)

	10:1	5:1
Change in LTB, pg/mg protein		
LTB4	-15	- 21
LTB5	+ 14	+ 23
Omega-6:3 ratio baseline diet = 28:1		
LPS = lipopolysaccharide LTB = leukotriene B		

Dietary fish oil diminishes cartilage breakdown

- Fish oil supplementation lowered plasma levels of TNFα and IL-1 in dogs (Freeman et al., 1998)
- Fish oil feeding decreased proMMP-2 and proMMP-9 expression in knee synovia of dogs with osteoarthritis (Hansen et al., 2008)
- EPA and DHA addition to cultures of bovine chondrocytes reduced aggrecanase activity (Curtis et al., 2000)

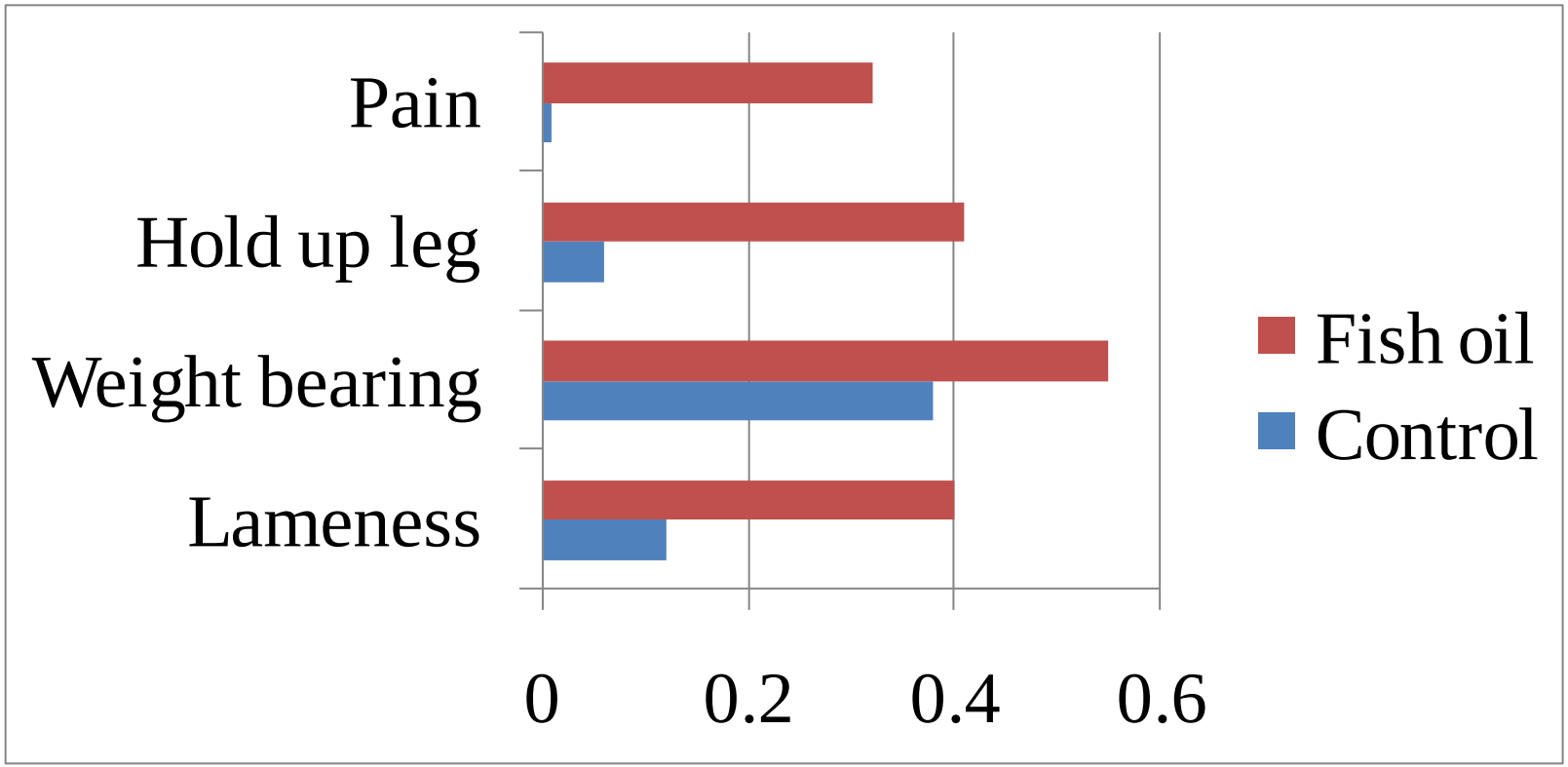
Dietary fish oil reduces clinical osteoarthritis in dogs and cats

- 5 studies in dogs: Roush et al. (2010a,b), Fritsch et al. (2010a,b), Hielm-Björkman et al. (2012)
- 2 studies in cats: Lascelles et al. (2010), Corbee et al. (2012)

Design of clinical trial with fish oil (Roush et al., 2010)

- Double-blinded, placebo-controlled trial
- Client-owned dogs; 16 or 22 per treatment
- Dry and canned foods without or with 0.4% EPA on a dry matter basis for 90 days
- Assessment by veterinarians of lameness, weight bearing, reluctance to hold up contralateral limb and pain on a 1-5 scale

Improvement of clinical osteoarthritis after feeding fish oil



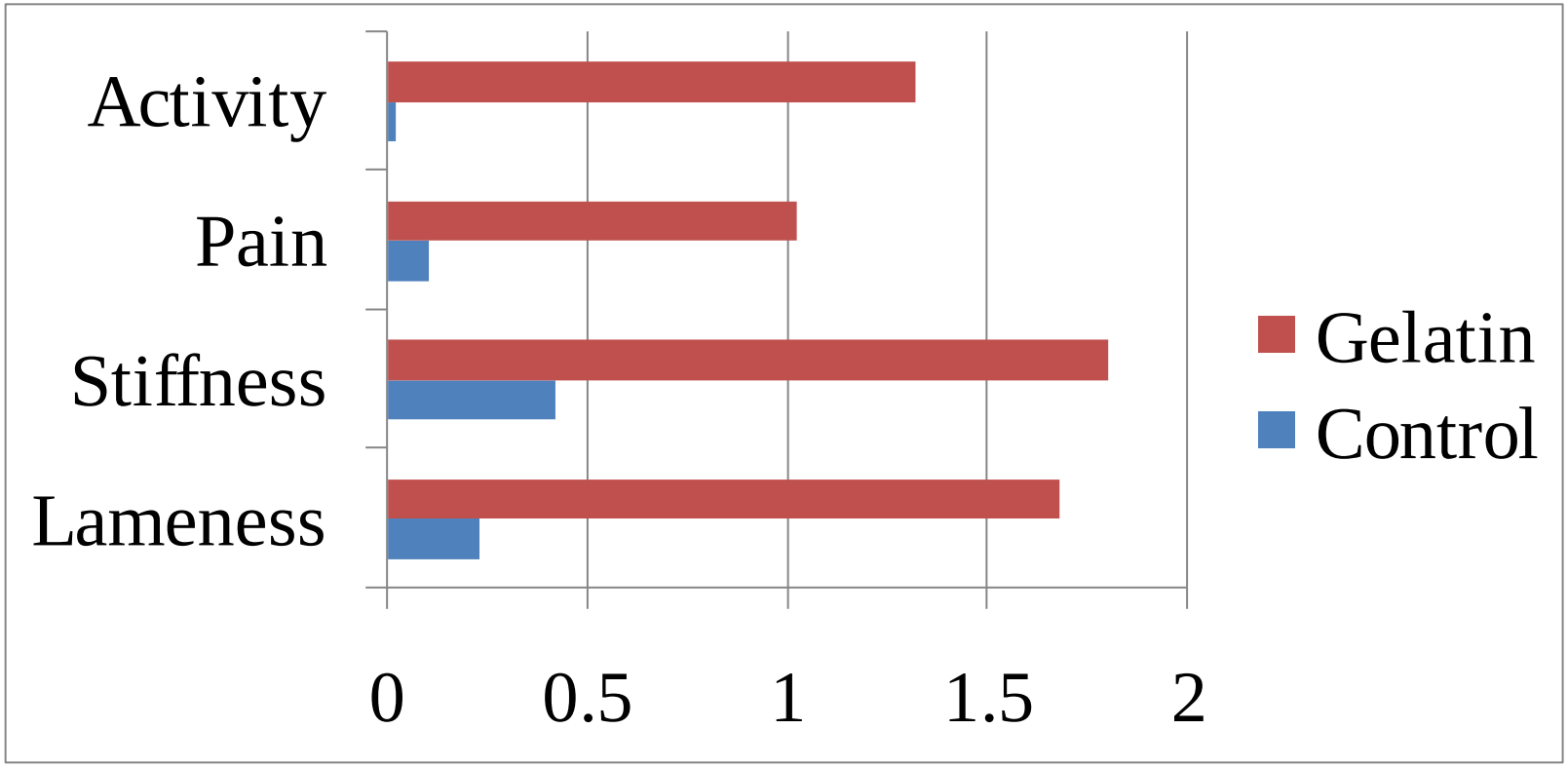
Dietary gelatin hydrolysate reduces clinical osteoarthritis in dogs

- Efficacy shown in open, non-controlled trial (Weide, 2004) and double-blind, controlled trial (Beynen et al., 2010)
- Stimulation of collagen synthesis through supply of substrates: glycine, proline, hydroxyproline
- Inhibition of cartilage-matrix breakdown through reduction of matrix metalloproteinase-3

Design of clinical trial with gelatin hydrolysate (Beynen et al., 2010)

- Double-blinded, placebo-controlled trial
- Privately owned dogs; 15 per treatment
- Identical, dry diet
- 10 g per day of either gelatin hydrolysate (Rousselot ASF) or soya protein isolate for 8 weeks
- Questionnaire (activity, stiffness, lameness, pain on a 1-10 scale)

Improvement of clinical osteoarthritis after feeding gelatin hydrolysate



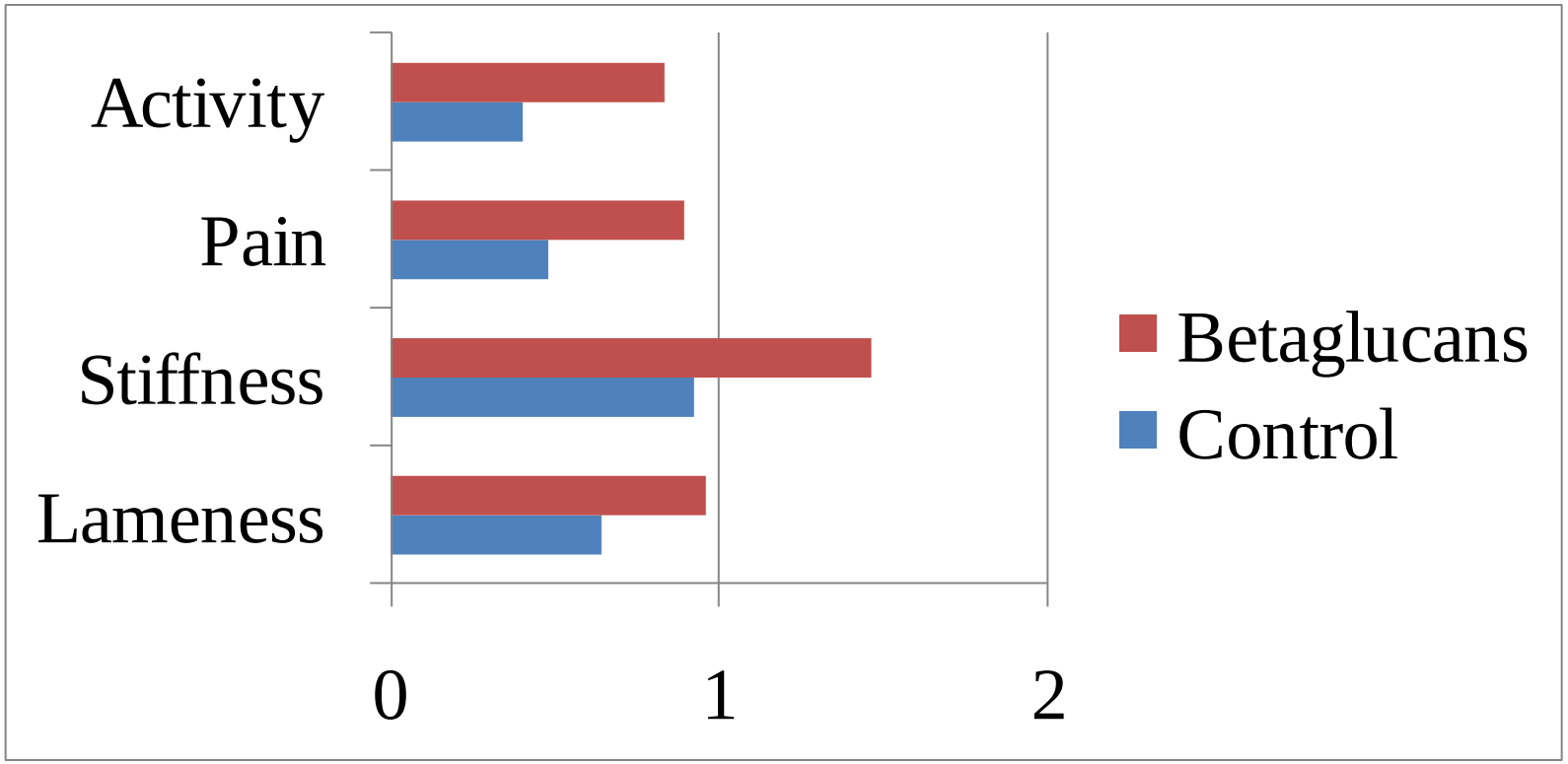
Beta-1,3/1,6-glucans and joint disorders

- Efficacy shown in open, non-controlled trial (unpublished) and double-blind, controlled trial (Beynen and Legerstee, 2010)
- Inhibition of inflammation
- Inhibition of cartilage-matrix breakdown

Design of clinical trial on beta-1,3/1,6-glucans in canine osteoarthritis (Beynen and Legerstee, 2010)

- Double-blind, placebo-controlled trial
- Privately owned dogs; 23 per treatment
- Dry diet without or with 800 ppm MacroGard® for 8 weeks
- Questionnaire (activity, stiffness, lameness, pain)

Improvement of clinical osteoarthritis after feeding beta-1,3/1,6-glucans



Summary of the three clinical trials on canine osteoarthritis

- In the studies presented, fish oil, gelatin hydrolysate and beta-1,3/1,6-glucans were equally effective
- It may be anticipated that the combination of the three functional ingredients is more effective than an individual ingredient

SANIMED ANTI-OSTEOARTHRITIS

Characteristics of therapeutic joint diets

	EPA*	Additional agents
Sanimed AntiOsteo	0.21	Gelatin, betaglucans
Specific CΩD	0.36	G + C
RC Mobility	0.34^	GLM, G + C
RC Mobility LD	0.52^	GLM, G + C
Hill's j/d dry	0.27	G + C
Hill's j/d dry SB	0.27	G + C
Hill's j/d canned	0.45	G + C
* g/MJ ^EPA + DHA GLM = green-lipped mussel		
G + C = glucosamine + chondroitin		

Sanimed Anti-Osteoarthritis for dogs

- 0.38% EPA in the dietary dry matter as legally dictated
- 2.5% gelatin hydrolysate; dose and preparation as used in supporting study
- 0.08% beta-1,3/1,6-glucans; dose and preparation as used in supporting study
- The three functional ingredients have different modes of action and may act cumulatively or even synergistically