

Value of repeated health screening in 259 apparently healthy mature adult and senior cats followed for 2 years

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Abstract

Background: Although regular health screening is recommended, long-term follow-up data in healthy aged cats are lacking.

Objectives: Determine the most common conditions in a large group of apparently healthy older cats and which diseases are manifested within 2 years in cats confirmed to be healthy based on extensive health screening.

Animals: Client-owned cats.

Methods: Prospective study. Thorough history, physical examination, blood tests, and urinalysis were performed in 259 apparently healthy mature adult (7–10 years) and senior (>10 years) cats. Semi-annual follow-up examinations were performed in 201 confirmed healthy cats.

Results: At baseline, 21% of apparently healthy cats were not considered healthy but were diagnosed with International Renal Interest Society (IRIS) $\geq$ stage 2 chronic kidney disease (CKD; 7.7%) or hyperthyroidism (4.6%), among other disorders. Disease occurred significantly more frequently in senior cats compared with mature adult cats. In addition, 40% cats were overweight, 35% had moderate to severe dental disease, and 22% had abnormal cardiac auscultation findings. Within 2 years, 28% of mature adult and 54% of senior cats that were confirmed healthy at inclusion developed new diseases, most commonly IRIS $\geq$ stage 2 CKD (cumulative incidence, 13.4%), hyperthyroidism (8.5%), chronic enteropathy, hepatopathy or pancreatitis (7.5%), or neoplasia (7%).

Conclusions and Clinical Importance: The high prevalence and 2-year incidence of physical examination abnormalities and systemic diseases in apparently healthy older cats argue for regular health screening in cats $\geq$ 7 years of age. Although more common in senior cats, occult disease also occurs in mature adult cats, and owners should be informed accordingly.

Abbreviations: ACVIM, American College of Veterinary Internal Medicine; BCS, body condition score; CKD, chronic kidney disease; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; IRIS, International Renal Interest Society; RI, reference interval; SBP, systolic blood pressure; SDMA, symmetric dimethylarginine; T4, total thyroxine; UPC, urinary protein : creatinine ratio; USG, urine specific gravity.

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KEYWORDS

chronic kidney disease, feline, geriatric, hyperthyroidism, incidence, prevalence

1 | INTRODUCTION

A cat's lifespan can be divided into 4 age-related stages, with the last 2 comprising mature adult (7–10 years) and senior (>10 years) cats.¹ These older cats represent an important segment of the total cat population, as a study from 2017 showed that 41.4% of cats visiting a veterinary practice in Great Britain were >7 years old.² The proportion of cats >10 years old in the United States was estimated to be 20.4% in 2011.³ Aged cats are more prone to diseases such as chronic kidney disease (CKD), hyperthyroidism, diabetes mellitus, cardiac disease, and neoplasia, and owners should be aware of early warning signs of these disorders.⁴ Owners of older cats, however, commonly fail to notice subtle clinical changes or dismiss them as an inevitable part of aging.^{4–6} Likewise, many owners do not recognize obesity in their cats, despite this condition increasing the risk of diabetes mellitus, dermatologic and lower urinary tract conditions, and potentially exacerbating cardiac and degenerative joint disease.^{6–9} Regular health checks therefore are advised in mature adult (every 1–2 years) and senior (every 6 months) cats, so that disease can be identified early and treatment instituted in a timely manner.¹ Even when initial screening results are normal, it is advised to monitor older cats longitudinally and evaluate serial clinicopathologic data of the individual cat so that changes can be identified sooner.^{4,10,11}

In contradiction to these recommendations, owners are actually more reluctant to take an older cat to their veterinarian compared to a young adult cat.¹² They potentially could be convinced otherwise if they understood the benefits of detecting certain conditions early to increase their cat's quality of life and longevity.^{4,12} To be able to educate owners, data about findings during 1-time health checks and repeated follow-up examinations in initially healthy cats are needed. However, reports about prevalence of disease in apparently healthy older cats are scarce and, to date, no studies have been published about the incidence of disease in this population during longitudinal follow-up.¹³

The 1st aim of our prospective study was to perform extensive health screening in a large group of mature adult and senior cats apparently healthy according to their owners, in order to determine the most common subclinical or unnoticed conditions. A 2nd aim was to longitudinally monitor the subgroup of confirmed healthy cats by repeated thorough health checks, to define the incidence and type of diseases they develop within the next 2 years.

2 | MATERIALS AND METHODS

Cats were prospectively enrolled from August 2019 to December 2020 (inclusion period), and data collection from confirmed healthy cats continued until December 2022 (follow-up period). Our study

was approved by the Local Ethical Committee of Ghent University (EC 2018/54), and the owners signed an informed consent form.

To be included, cats needed to be healthy according to the owner, meaning no changes in general behavior, stable body condition, and absence of clinical signs. Owners were asked to fast their cats for at least 12 hours before presentation; water could be given ad libitum. Cats were excluded if they had received preventive medications within 1 week or other medications within 2 months before presentation. Cats with previously diagnosed and ongoing metabolic or clinically relevant cardiovascular disease were excluded.

The investigations done at inclusion and every 6 months thereafter for a period of 2 years were as follows: A detailed and standardized written history questionnaire was completed, and a complete physical examination performed by the 1st author of our study (Femke Mortier). Systolic blood pressure (SBP) was measured using Doppler ultrasonography following American College of Veterinary Internal Medicine (ACVIM) guidelines.¹⁴ In cats with SBP >160 mmHg, fundoscopic examination was performed and cats with signs of target organ damage were excluded and treated. If fundoscopy was normal, owners were advised to have their cat's SBP rechecked within 1 month. Body condition score (BCS) and muscle condition score were determined following World Small Animal Veterinary Association guidelines.^{15,16} A dental calculus score of 0 to 3 and gingivitis score of 0 to 3 were assigned to each cat and were combined into a dental disease score of 0 to 6: no (score 0), mild (score 1–2), moderate (score 3–4), or severe (score 5–6) dental disease.^{17,18} Thyroid gland size was determined using the classical palpation technique,¹⁹ yielding a score of 0 to 6: nonpalpable (score 0), 1 to 3 mm (score 1), 3 to 5 mm (score 2), 5 to 8 mm (score 3), 8 to 12 mm (score 4), 12 to 25 mm (score 5), or >25 mm (score 6).²⁰ In the case of bilateral enlargement, thyroid score was based on the largest palpable nodule. Blood was collected from the jugular vein or, in anxious cats, the cephalic or saphenous vein, and urine was collected by ultrasound-guided cystocentesis. Macroscopic and microscopic evaluation of urine samples, urine specific gravity (USG) determination using a handheld refractometer (MASTER-SUR/NM, Atago), and sediment analysis using an IDEXX SediVue Analyzer were performed on site. Blood and urine samples were transported overnight at ambient temperature to IDEXX Laboratories where CBC, serum biochemistry profile including electrolyte, symmetric dimethylarginine (SDMA), total thyroxine (T4) and fructosamine concentrations, and ELISA testing for feline immunodeficiency virus (FIV) antibodies and feline leukemia virus (FeLV) antigen, as well as urine dipstick analysis, urinary protein : creatinine ratio (UPC) determination, and bacterial urine culture were performed.

If a heart murmur or gallop sound was present at inclusion, owners were advised to have echocardiography performed. All cardiac exams were performed by a cardiologist, and images were assessed afterwards by a Cardiology Diplomate of the European College of Veterinary Internal Medicine (Companion Animals) and co-author

of this paper (Pascale Smets). Cats were confirmed healthy and included in the follow-up study if the examinations at baseline did not indicate metabolic or systemic disease (eg, International Renal Interest Society [IRIS] $\geq$ stage 2 CKD [serum creatinine concentration ≥ 1.6 mg/dL or $140 \mu\text{mol/L}$ and USG < 1.035 , or SDMA $\geq 18 \mu\text{g/dL}$ and USG < 1.035 , on 2 consecutive measurements]²¹; hyperthyroidism [T4 $> 4.7 \mu\text{g/dL}$ or 60 nmol/L]; diabetes mellitus [serum glucose concentration $> 140.5 \text{ mg/dL}$ or 7.8 mmol/L in combination with serum fructosamine concentration $> 51.3 \text{ mg/L}$ or $286 \mu\text{mol/L}$]; or chronic vomiting or diarrhea and concurrent weight loss indicating potential gastroenteropathy) or clinically relevant cardiovascular disease (eg, cardiomyopathy ACVIM stage B2 or higher, clinically relevant arrhythmias, or previously undetected congenital heart disease). Cats with persistent renal proteinuria (UPC > 0.4 without a prerenal or postrenal component) and serum creatinine concentration ≥ 1.6 mg/dL ($140 \mu\text{mol/L}$) also were diagnosed with IRIS $\geq$ stage 2 CKD, regardless of USG.²¹ Cats that tested positive for FIV or FeLV were excluded, as were cats with persistent macroscopic hematuria, pyuria (> 5 leukocytes/high power field), bacteriuria (≥ 1000 colony forming units/mL²² on 2 consecutive urine cultures 1-3 months apart), or renal proteinuria (UPC > 0.4 on 2 consecutive measurements 1-3 months apart).

Confirmed healthy cats were examined every 6 months for 2 years. In cats with a combination of serum creatinine concentration ≥ 1.6 mg/dL ($140 \mu\text{mol/L}$) and USG < 1.035 or with serum SDMA concentration $> 14 \mu\text{g/dL}$ at any visit during the study period, reexamination of serum creatinine and SDMA concentrations and USG was scheduled 1 to 2 months later to allow for staging of potential CKD. During the follow-up period, hyperthyroidism was diagnosed if T4 exceeded the upper limit of the laboratory reference interval (RI; $4.7 \mu\text{g/dL}$ or 60 nmol/L) or if T4 exceeded the age-appropriate RI for the same laboratory ($3 \mu\text{g/dL}$ or 38.6 nmol/L)²³ and had increased $> 34\%$ from the cat's own baseline result at inclusion (ie, the reference change value for T4)²⁴⁻²⁶ on 2 consecutive measurements 6 months apart. Cats with chronic gastrointestinal signs or unexplained weight loss during follow-up and increased liver enzyme activities, increased feline pancreas-specific lipase, decreased serum cobalamin concentration, or some combination of these were grouped under the term 'triaditis'.

Statistical analysis was performed using IBM SPSS Statistics Version 29.0.1.0 (171). Fisher's exact and Chi-squared tests were used for categorical variables and $P < .05$ was considered significant.

3 | RESULTS

3.1 | Animals

Median age of the 259 apparently healthy cats was 10 years (range, 7-18 years), with 152 (58.7%) mature adult and 107 (41.3%) senior cats examined at baseline. Overall, 154 cats (59.5%) were female (146 spayed), and 105 (40.5%) were male (all neutered). Cat breeds that were represented more than once were domestic short- or longhair ($n = 188$), British short- or longhair ($n = 34$), Ragdoll ($n = 9$), Birman ($n = 4$), Maine Coon ($n = 4$), Scottish Fold ($n = 4$), Siamese

($n = 3$), Balinese ($n = 2$), exotic shorthair ($n = 2$), and Russian blue ($n = 2$). Body weight ranged from 2.15 to 9.45 kg with a median of 4.40 kg.

3.2 | Health screening results at baseline

Body condition was considered ideal (BCS 5/9) in 112/258 (43%) cats for which BCS was recorded. In total, 102 (40%) cats were overweight with BCS of 6/9 ($n = 52$), 7/9 ($n = 29$), 8/9 ($n = 16$) or 9/9 ($n = 5$). Forty-four (17%) cats had decreased BCS of 4/9 ($n = 37$), 3/9 ($n = 6$) or 2/9 ($n = 1$). Muscle condition score was normal in 169/256 (66%) cats for which it was documented. Mild, moderate, or severe muscle loss was present in 67/256 (26%), 17/256 (7%), and 3/256 (1%) cats, respectively.

Dental calculus and gingivitis score were recorded at baseline in 255 cats. No dental disease was identified in 24/255 (9.5%) cats. Mild, moderate, and severe dental disease were present in 140 (55%), 67 (26%), and 24 (9.5%) older cats, respectively.

A thyroid nodule was palpable in 63/254 (25%) cats that allowed cervical palpation. The nodule was unilateral in 58/63 (92%) cats and bilateral in 5 cats. Hyperthyroidism was diagnosed in 8 cats with a thyroid nodule (all unilateral) and in 4 cats without a palpable thyroid gland (Table 1). Cats with a palpable thyroid gland overall were significantly more likely to have hyperthyroidism than cats without a thyroid nodule ($P = .002$). However, such was not the case for cats with a thyroid nodule score of 1 ($P = 1.00$). Total thyroxine concentration was increased above the laboratory RI in 2.6% mature adult and 7.5% senior cats, with T4 ranging from 4.9 to $13.0 \mu\text{g/dL}$ ($63.1\text{--}167.3 \text{ nmol/L}$) and a median T4 of $6.7 \mu\text{g/dL}$ (86.3 nmol/L) in cats with unnoticed hyperthyroidism.

Abnormalities were heard during heart auscultation in 57/259 (22%) cats: a heart murmur in 51 cats (20%), a gallop sound in 4 cats (1.5%), and a bradyarrhythmia in 2 other cats (0.8%). The heart murmur was systolic in all 51 cats and grade 1/6 in 10/51 (20%), grade 2/6 in 28/51 (55%), and grade 3/6 in 13/51 (25%) cats. Echocardiography was performed in 24/51 (47%) cats with a heart murmur, and the murmur was most commonly caused by cardiomyopathy stage B1 ($n = 15$; 62.5%) or B2 ($n = 2$; 8.3%). In the other cases, cardiac ultrasound examination indicated no abnormalities ($n = 3$; 12.5%), trivial mitral or tricuspid valve insufficiency or both without cardiomyopathy ($n = 3$; 12.5%), or a septal bulge as the only abnormality ($n = 1$; 4.2%). Cardiac ultrasound examination in 3 of the cats with a gallop sound showed mild tricuspid insufficiency and trivial mitral insufficiency in 1 cat (with CKD), a septal bulge in another cat, and no abnormalities in the remaining cat. An ECG in 2 cats with bradyarrhythmia disclosed 3rd-degree atrioventricular block in 1 cat and 2nd-degree atrioventricular block (Mobitz type II) in the other.

It was possible to measure SBP at baseline in 231/259 (89%) cats, and SBP ranged from 90 to 210 mmHg (median, 140 mmHg). Systolic blood pressure was > 160 mmHg in 24/231 (10%) cats, 6 of which were diagnosed with hyperthyroidism ($n = 3$), stage 2 CKD ($n = 2$), or

persistent macroscopic hematuria ($n = 1$) at the same time and not followed-up in the study. Of the 18 cats that had SBP >160 mmHg at inclusion but were otherwise confirmed healthy, 1 cat was lost-to-follow-up, and SBP was rechecked after 2 weeks to 6 months in the remaining 17 cats. At reevaluation, SBP was normal in 12 cats, whereas 5/179 (3%) confirmed healthy cats that had successful SBP measurement at baseline were persistently hypertensive. None of these cats had abnormalities on fundoscopic examination. All 5 confirmed healthy cats with persistent hypertension at baseline were followed for 2 years: 3 cats remained healthy and 2 cats developed IRIS stage 2 CKD after 18 to 24 months.

TABLE 1 Prevalence of hyperthyroidism in 254 older cats with thyroid score recorded at baseline (T0) and development of hyperthyroidism in 198 of these cats that were confirmed healthy at T0. The percentage of cats diagnosed with hyperthyroidism at T0 or during the following 2 years is shown for all cats with a thyroid nodule, as well as for the separate thyroid scores.

Baseline = 254 apparently healthy cats	Thyroid gland size	
	Thyroid not palpable at T0 $n = 191$ (75%)	Thyroid nodule at T0 $n = 63$ (25%)
Hyperthyroid at T0		8/63 (13%) - Score 1: 1/44 (2%) - Score 2: 2/12 (17%) - Score 3: 3/5 (60%) - Score 4: 2/2 (100%)
Follow-up = 198 confirmed healthy cats	Thyroid gland size	
	Thyroid not palpable at T0 and not hyperthyroid at T0 $n = 152$ (77%)	Thyroid nodule at T0 but not hyperthyroid at T0 $n = 46$ (23%)
Hyperthyroid in ≤ 2 years	5/152 (3%)	12/46 (26%) - Score 1: 10/36 (28%) - Score 2: 1/8 (13%) - Score 3: 1/2 (50%) - Score 4: ^a

^aAll cats with a thyroid nodule score 4 at T0 were already hyperthyroid at the time.

Diagnosis of IRIS $\geq$ stage 2 CKD was made in 2.6% mature adult and 15% senior cats based on either the combination of serum creatinine and SDMA concentrations and USG (19 cats) or the presence of persistent renal proteinuria in combination with serum creatinine concentration ≥ 1.6 mg/dL (140 μ mol/L) in 1 cat. In cats with CKD, serum creatinine concentration ranged from 1.6 to 5.1 mg/dL (140–446 μ mol/L) with a median of 2.1 mg/dL (184 μ mol/L), serum SDMA from 9 to 28 μ g/dL (median, 17 μ g/dL), and USG from 1.013 to 1.039 (median, 1.022). Serum creatinine concentration was compatible with IRIS stage 2 disease in most of these cats ($n = 17$), whereas 2 cats had Stage 3 and 1 cat stage 4 CKD. Seven cats with CKD (35%) were nonproteinuric, 8/20 (40%) borderline proteinuric and 5/20 (25%) proteinuric.

Urine culture was positive in 4/258 (1.6%) cases. These cats were otherwise healthy and this subclinical bacteriuria was not treated in accordance with current guidelines.²⁷ Reevaluation within 1 to 3 months showed persistence of subclinical bacteriuria in 3/4 cats and spontaneous resolution in 1 cat.

Urine dipstick analysis was positive for ketones in 82/257 (32%) cats that had this test performed. Ketonuria was usually mild (+1 result in 80 cats and +2 in 2 cats) and 70/82 cats were completely healthy. Stress hyperglycemia (without increased serum fructosamine concentration) was present in 60/258 (23%) cats, with a median (range) glucose concentration of 169 (142–350) mg/dL (9.4 [7.9–19.4] mmol/L) in hyperglycemic cats. These cats were either healthy ($n = 48$), hyperthyroid ($n = 4$), had CKD ($n = 4$), had FIV antibodies ($n = 3$) or had hypertrophic cardiomyopathy stage B2 ($n = 1$).

After the complete health check at baseline, 55/259 (21.2%) apparently healthy older cats were diagnosed with 1 of the following diseases, excluding them from further inclusion in the longitudinal study (Table 2): IRIS $\geq$ stage 2 CKD ($n = 20$), hyperthyroidism ($n = 12$), FIV antibodies ($n = 7$), persistent proteinuria ($n = 4$) with macroscopic (2/4), or microscopic (2/4) hematuria precluding reliable UPC measurement, persistent subclinical bacteriuria precluding reliable UPC measurement ($n = 3$), cardiomyopathy stage B2 ($n = 2$), chronic vomiting with weight loss ($n = 2$), persistent renal proteinuria with serum creatinine concentration indicating IRIS stage 1, 3rd-

	All cats ($n = 259$)	Mature adult cats ($n = 152$)	Senior cats ($n = 107$)
Health screening conclusion			
Confirmed healthy	204 (79%)	134 (88%)	70 (65%)
Excluded from follow-up study	55 (21%)	18 (12%)	37 (35%)
Diseases diagnosed at T0			
CKD $\geq$ stage 2	20 (7.7%)	4 (2.6%)	16 (15%)
Hyperthyroidism	12 (4.6%)	4 (2.6%)	8 (7.5%)
FIV antibodies	7 (2.7%)	3 (2.0%)	4 (3.7%)
Subclinical bacteriuria	3 (1.2%)	1 (0.7%)	2 (1.9%)
Cardiomyopathy $\geq$ stage B2	2 (0.8%)	2 (1.3%)	0
Vomiting and weight loss	2 (0.8%)	1 (0.7%)	1 (0.9%)

Abbreviations: CKD, chronic kidney disease; FIV, feline immunodeficiency virus.

TABLE 2 Prevalence of diseases diagnosed in >1 cat at baseline (T0) for all 259 apparently healthy older cats, as well as for mature adult (7–10 years) and senior (>10 years) cats separately.

degree atrioventricular block, idiopathic chylothorax, oral mass for which owners declined further examinations, urinary bladder mass precluding cystocentesis, and diabetes mellitus in a cat also diagnosed with CKD (1 each). Senior cats were significantly more likely to have a disease than mature adult cats ($P < .001$).

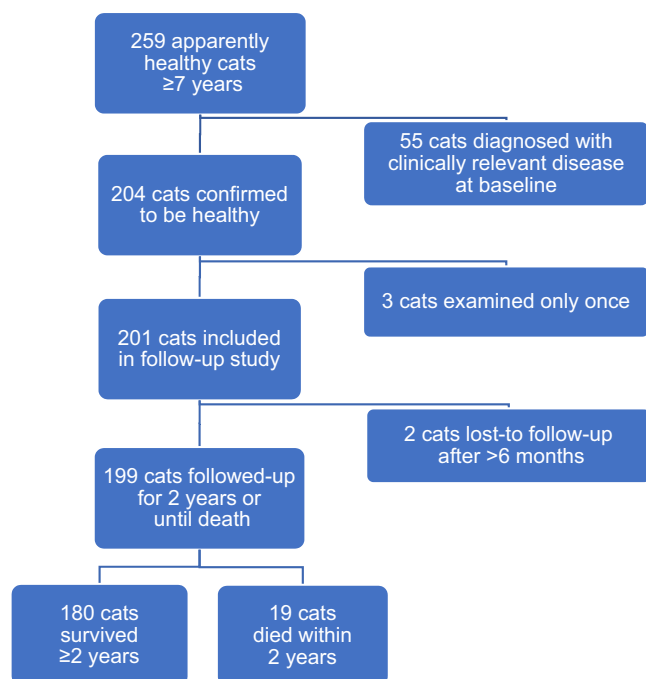


FIGURE 1 Schematic overview of cats included in the follow-up study.

3.3 | Follow-up examinations

Confirmed healthy cats were definitively included in the longitudinal study if at least 1 follow-up examination was performed, which was the case in 201 healthy cats (Figure 1). Two of these 201 cats (1%) were lost-to follow-up after their 1st reevaluation, at which they were still healthy. The remaining 199 cats (132 mature adult and 67 senior cats) were monitored until they completed the 2-year follow-up period or until they died, if death occurred before the end of the study. An overview of the number of cats with available results of the different examinations at each time point is shown in Table 3. Clinically relevant disease developed in 28% mature adult and 54% senior cats (Table 4). Eighteen cats developed >1 of these diseases within 2 years, with the most frequent combination being CKD and triaditis ($n = 5$). In addition, 1 cat (0.5%) previously diagnosed with CKD developed diabetes mellitus. In total, 6/132 (4.5%) mature adult and 13/67 (19.4%) senior cats that were followed-up for 2 years developed comorbidities.

Of cats that were confirmed healthy at baseline but had a thyroid nodule, 26% developed hyperthyroidism within the next 2 years, compared with 3% of confirmed healthy cats without a palpable thyroid gland at inclusion (Table 1). This difference was significant ($P < .001$), and also when comparing cats with a thyroid nodule score 1 to cats without a thyroid nodule at inclusion ($P < .001$). Five of 17 cats with hyperthyroidism were only diagnosed at their last examination of the 2-year follow-up period, 6/17 cats were treated with radioactive iodine and 6/17 with medication (PO methimazole). Three cats had concurrent CKD and hyperthyroidism. Two of these cats were diagnosed with CKD ≥ 6 months before their hyperthyroidism diagnosis.

TABLE 3 Examinations performed at baseline (T0) and each reevaluation with the number of cats for which results of each examination were available.

	T0	6 months	12 months	18 months	24 months
Died after previous visit	0	1	5	5	9
Lost to follow-up after previous visit	0	2	2	0	0
Cats left in the study	259	201	194	189	180
Skipped current visit	0	2	1	3	0
Presented for current visit	259	199	193	186	180
Examinations performed					
SBP measurement	231	181	178	174	169
CBC	258 ^a	199	192	186	179
Serum biochemistry (including T4)	258 ^a	199	193	186	180
FIV/FelV testing	258 ^a	198	193	186	179
Urine dipstick and sediment analysis	257 ^a	198	189	181	175
USG	258 ^a	199	190	185	179
UPC	258 ^a	199	190	185	179
Urine culture	258 ^a	198	188	184	176

Abbreviations: FelV, feline leukemia virus; FIV, feline immunodeficiency virus; SBP, systolic blood pressure; T4, total thyroxine; UPC, urinary protein : creatinine ratio; USG, urine specific gravity.

^aUrinalysis and blood examination were not performed at presentation in 1 cat with a urinary bladder mass seen at the moment ultrasound-guided cystocentesis was going to be undertaken. This cat was immediately excluded and laboratory analysis not performed.

	All cats (n = 201)	Mature adult cats (n = 133)	Senior cats (n = 68)
Available follow-up data			
Completed the study period	180 (90%)	125 (94%)	55 (81%)
Died within 2 years	19 (9%)	7 (5.3%)	12 (17.6%)
Lost to follow-up	2 (1%)	1 (0.8%)	1 (1.5%)
Health status after 2 years			
Remained healthy	126 (63%)	95 (72%)	31 (46%)
Developed disease(s) below	73 (37%)	37 (28%)	36 (54%)
Newly diagnosed diseases between baseline and 1 year			
CKD ≥ stage 2	11 (5.5%)	2 (1.5%)	9 (13.2%)
Hyperthyroidism	7 (3.5%)	5 (3.8%)	2 (2.9%)
Triaditis ^a	5 (2.5%)	3 (2.3%)	2 (2.9%)
Neoplasia	5 (2.5%)	2 (1.5%)	3 (4.4%)
FIV antibodies	3 (1.5%)	3 (2.3%)	0
Subclinical bacteriuria	3 (1.5%)	2 (1.5%)	1 (1.5%)
Renal proteinuria	2 (1%)	2 (1.5%)	0
FeLV antigen	2 (1%)	1 (0.8%)	1 (1.5%)
Newly diagnosed diseases between baseline and 2 years			
CKD ≥ stage 2	27 (13.4%)	11 (8.3%)	16 (23.5%)
Hyperthyroidism	17 (8.5%)	9 (6.8%)	8 (11.8%)
Triaditis ^a	15 (7.5%)	5 (3.8%)	10 (14.7%)
Neoplasia	14 (7%)	5 (3.8%)	9 (13.2%)
FIV antibodies	8 (4%)	7 (5.3%)	1 (1.5%)
Subclinical bacteriuria	5 (2.5%)	3 (2.3%)	2 (2.9%)
Renal proteinuria	5 (2.5%)	3 (2.3%)	2 (2.9%)
FeLV antigen	2 (1%)	1 (0.8%)	1 (1.5%)

Note: Eighteen cats developed >1 of these diseases during 2-year follow-up and are represented twice (n = 16) or 3 times (n = 2).

Abbreviations: CKD, chronic kidney disease; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus.

^aTriaditis = chronic gastroenteropathy, chronic hepatopathy, chronic pancreatitis or some combination of these.

The 3rd cat was diagnosed with hyperthyroidism 1st, treated medically, and subsequently had newly developed or unmasked CKD.

The 15/201 (7.5%) cats diagnosed with “triaditis” had clinical signs of chronic vomiting, diarrhea, weight loss or some combination of these with increased serum feline pancreas-specific lipase activity in 6 cats, decreased serum cobalamin concentration in 5 cats, and persistent moderate increase in serum alanine aminotransferase activity in 4 cats.

Systemic or metastatic neoplasia developed in 10/201 (5%) cats, more specifically large cell lymphoma (n = 7; gastrointestinal location in 4, abdominal lymph nodes in 2, and renal in 1), metastatic nasal adenocarcinoma, metastatic mammary carcinoma (in a male castrated cat), and hepatic cystadenocarcinoma with progressive increases in liver enzyme activities and associated clinical signs (n = 1). In addition, local tumors were diagnosed in an early stage in 4/201 (2%) cats: cutaneous mast cell tumor in 2 cats, mammary carcinoma in 1 (female spayed) cat, and SC myxosarcoma in 1 cat. These were completely

excised, and all 4 cats survived until the end of the follow-up period without signs of local recurrence or metastasis.

Antibodies against FIV were detected in 8/201 (4%) cats during follow-up. The same test was negative after 6 months in 5/8 (63%) cats, persistently positive after 1 to 6 months in 2/8 (25%) cats, and not repeated in 1 cat. Antigen testing for FeLV was positive in 2/201 (1%) cats, 6 months after inclusion. A test from a different manufacturer 1 week to 2 months later was negative in both cases, and the original test was also negative in both cats at 12, 18 and 24 months after inclusion.

Urine culture was positive on ≥1 occasion during the follow-up period in 8 cats. Bacteriuria was subclinical in 5/201 (2.5%) cats (3 healthy cats and 2 with IRIS stage 2 CKD), and symptomatic in 3/201 (1.5%) cats (1 healthy cat and 2 with IRIS stage 2 or 3 CKD) requiring antibiotic treatment for lower (n = 2) or upper (n = 1) urinary tract signs. Persistent proteinuria without a prerenal or postrenal cause was present in 5/201 cats (2.5%) that were otherwise still

TABLE 4 Cumulative incidence of diseases diagnosed in >1 cat during the 2-year follow-up period for 201 older cats that were confirmed to be healthy at baseline, as well as for mature adult (7–10 years) and senior (>10 years) cats separately.

healthy. One of the 48 healthy cats with hyperglycemia at baseline developed diabetes mellitus within 2 years.

The most common cause of death was systemic or metastatic neoplasia in 8/19 (42%) cats that died; the 2 other cats with systemic neoplasia died after the follow-up period. An accidental death occurred in 2 cats (dog bite, tumble dryer) and sudden death at home without previous clinical signs in 2 cats that were still healthy at their most recent examination. Two cats were euthanized because of uncontrolled chronic enteropathy or hepatopathy, 1 cat because of congestive heart failure in combination with CKD, and 1 cat because of uncontrollable diabetes mellitus. Three cats were euthanized by their own veterinarians without a definitive diagnosis.

4 | DISCUSSION

Repeated health screenings in apparently healthy older cats are useful in all cats ≥ 7 years of age. First, physical examination already frequently identifies abnormalities requiring intervention (increased body condition, moderate to severe dental disease) or further investigation (abnormal cardiac auscultation finding). Second, and even more important, 21% of all cats had unnoticed but clinically relevant disease at the 1st health screening and 37% of initially healthy cats developed such disease within the next 2 years. The benefit of health screening is even more pronounced in senior cats compared with mature adult cats.

Body condition scores at baseline in our study are consistent with the percentage of overweight or obese cats ≥ 6 years of age in previous studies examining cats from the same region (40%) and from the southern part of Belgium (42%).^{13,28} Despite the clear negative effects of being overweight or obese and awareness campaigns directed at pet owners, the percentage of overweight and obese cats in this region has not decreased over the past 10 years. Moderate to severe dental disease was present in 35.5% of study cats. The actual percentage of cats that would benefit from dental treatment might be even higher, because periodontal pockets or bone loss cannot be reliably detected in awake cats.²⁹ When including mild disease, 89.5% of cats had dental calculus, gingivitis, or both, which is identical to the 90% of cats ≥ 4 years of age in the same region having calculus and gingivitis in 2004.²⁹ Because none of the owners in our study brushed their cats' teeth at inclusion, it is necessary to stress the importance of preventative measures.

The prevalence of a heart murmur in our study corresponded with the 11% to 34% reported in other studies.^{13,30-33} A more recent study detected heart murmurs in 60% of cats >8 years of age, which was a cumulative percentage over multiple auscultation periods.³⁴ In our study, echocardiographic evidence of cardiomyopathy was present in 18/24 (75%) cats with a heart murmur that had cardiac ultrasound examination performed. This percentage is somewhat higher than the 54% in a previous study that included a younger population (with a median age of 5 years) and confirms that further investigation is necessary when a heart murmur is found on routine physical examination in cats.³⁵ When auscultation is normal, cardiac disease however

cannot be excluded because the negative predictive value of a heart murmur for hypertrophic cardiomyopathy in cats >8 years of age is only 90%.³⁴ The thyroid gland was palpable in 55/242 (23%) euthyroid cats at baseline, comparable to the 20% reported in earlier studies of healthy aged cats,^{13,36} but less than the 59% reported in a study using a different palpation technique.³⁷ In accordance with a study about cats showing clinical signs consistent with hyperthyroidism, the likelihood of being hyperthyroid also increased with increasing gland size for asymptomatic cats in our study.²⁰ In 8/12 (67%) hyperthyroid cats in our study, a nodule could be palpated, which is slightly lower than the 79% in another study,³⁶ and markedly lower than the 96% in a study using another palpation technique.³⁷ Cats from the latter study, however, had a median T4 of 11.5 $\mu\text{g/dL}$ (147.8 nmol/L) compared with a median T4 of 6.7 $\mu\text{g/dL}$ (86.3 nmol/L) for hyperthyroid cats in our study, and higher T4 concentrations are associated with larger thyroid size.^{20,37} The fact that one third of hyperthyroid cats in our study did not have a thyroid nodule emphasizes the usefulness of measuring T4 during health screening of older cats, even in the absence of clinical signs or a palpable thyroid gland.

The prevalence of systemic hypertension in our study was between the 8% (cats ≥ 6 years of age) and 13% (cats ≥ 9 years of age) in previous studies examining apparently healthy cats.^{13,33} When rechecking SBP in confirmed healthy cats from our study, 3% were persistently hypertensive. These cats still were considered healthy because no fundoscopic abnormalities were found and stress was thought to be the cause of the hypertension (ie, 'white coat' or situational hypertension). To date, unfortunately, no reliable diagnostic test distinguishes white coat from true hypertension in cats.³⁸

Markedly more cats had a positive urine dipstick result for ketones in our study compared with a previous health screening study reporting traces of ketones in only 3% of cats.¹³ Mild positive results for ketones in urine are not necessarily concerning in cats with well-concentrated urine and can represent a false-positive result.³⁹ In our study, USG measured in the external laboratory was >1.050 in 78/82 cats with a positive result for ketones in urine and 1.040 to 1.050 in the remaining 4 cats. Most (70/82) cats with ketonuria were confirmed healthy, 6 cats had hyperthyroidism, and 6 cats had various diagnoses, but none had diabetes mellitus. Stress hyperglycemia occurred in 23% of all cats at baseline. Similarly, hyperglycemia was present in 25/100 (25%) apparently healthy older cats and 70/297 (23%) cats undergoing preanesthetic blood examination, but serum fructosamine concentration was not measured in these studies, and diabetes mellitus therefore could not be fully excluded.^{13,40} Special care was taken to use cat-friendly practices in our study, but the prevalence of stress hyperglycemia remained high nonetheless. Diabetes mellitus was present at baseline in only 1 cat and the 2-year cumulative incidence in confirmed healthy cats also was low (0.5%). The reported overall prevalence of 0.2% to 1% for diabetes mellitus in the general cat population also remains lower than that of CKD and hyperthyroidism, but the prevalence of diabetes mellitus in cats is increasing, and the odds are significantly higher in cats >6 years of age—the target population of regular health screening.⁴¹⁻⁴³

The 2.6% of mature adult and 15% of senior cats with CKD at baseline confirm that, although CKD can occur at all ages, it is more common in older cats.^{1,44-46} Other studies examining clinically healthy cats ≥ 6 and ≥ 8 years of age found a similar proportion of cats (8% and 11%, respectively) with azotemic CKD.^{13,47} This percentage range is lower than the 28% to 81% reported for cats >12 years of age,^{6,44,48-50} possibly because CKD prevalence increases with age, because CKD prevalence is determined for the general cat population which includes cats with clinical signs, and because cats with IRIS stage 1 CKD sometimes also are included in the calculations. During follow-up, another 8.3% of cats 7 to 10 years of age and 23.5% of cats ≥ 11 years of age developed CKD within 2 years. These percentages are less than the 18% to 30.5% of cats ≥ 9 years of age that developed azotemic CKD within 1 year in 2 previous studies, but these studies included older cats (median age, 12-13 years) and excluded cats that died, developed hyperthyroidism during follow-up, or were lost to follow-up from the final number of study cats, thus overestimating the percentage of study cats that developed CKD.^{17,33} Furthermore, we emphasize that it is hard to compare prevalence and incidence of age-related diseases among studies that use different age limits. This situation also is true for CKD for the other diseases described below. It is therefore recommended always to apply feline life stage guidelines¹ to define age limits for study patients.

Hyperthyroidism prevalence in our study is somewhat less than the 12.3% of cats ≥ 8 years of age in Germany and 8.7% to 21.1% of cats ≥ 10 years of age presented to primary care veterinary practices in the United Kingdom and Ireland.⁵¹⁻⁵³ However, most cats in these studies were not clinically healthy, whereas our prevalence data include cats having asymptomatic or unnoticed hyperthyroidism, which appears to be an important group. A recent study examined only apparently healthy cats ≥ 8 years of age and found 16.2% of them to have hyperthyroidism.⁴⁷ This higher percentage of unnoticed hyperthyroidism compared to our study is likely because of the lower cutoff for T4 (≥ 3.1 vs >4.7 $\mu\text{g/dL}$ [60 nmol/L]) which approximates the upper limit of the recently established age-appropriate RI (3.0 $\mu\text{g/dL}$ [38.6 nmol/L]).²³ Regarding the mature adult subgroup, feline life stage guidelines state that T4 testing should be strongly considered in apparently healthy cats 7 to 10 years of age, but mention that incidence data are limited for this age group.¹ Because 6.8% of confirmed healthy mature adult cats in our study however developed hyperthyroidism within 2 years, ongoing regular T4 testing also appears useful in this group.

In a previous study with cats ≥ 6 years of age from the same region, a larger proportion (14%) of cats had FIV antibodies.¹³ This finding could be a consequence of more cats having outdoor access in the older study (81%, of which 20% were strictly outdoor cats, vs 69%, none of which lived outdoors only), a possible decrease in FIV prevalence in the general cat population over the past 10 years as a result of trap-neuter-return programs in the area, or both.⁵⁴

Subclinical bacteriuria prevalence at baseline was comparable to a previous study,¹³ but lower than the 4.6% to 13% of cats with subclinical bacteriuria in other studies examining similar cat populations.^{47,55-57} Not only does a positive urine culture appear uncommon in apparently healthy older cats, it also is not recommended to treat subclinical

bacteriuria when present,^{27,57} and thus urine culture should not be included in routine health examinations. Therefore, urine collected by voiding and cystocentesis are both appropriate for urinalysis in the context of health screening, as long as the same collection method is used when monitoring the UPC and USG of the same cat over time.⁵⁸

Our study had some limitations. First, the study group may not entirely represent the general client-owned cat population, because owners had to be motivated to bring their cat to the clinic at least 5 times in 2 years. This stipulation may have caused inclusion bias toward owners who are more involved and notice changes earlier. On the other hand, some owners may have intentionally failed to mention clinical signs they noticed in their cat to obtain free health screening, leading to an overestimation of disease prevalence at baseline. Second, it cannot be excluded that some confirmed healthy cats already had early renal disease at inclusion, because glomerular filtration rate was not measured. However, very strict criteria were applied for the laboratory tests used in clinical practice to diagnose CKD. Third, the cumulative incidence over 2 years is given for disease manifestation during follow-up, but 10% of cats died or were lost to follow-up before the end of the 2-year period and could therefore no longer develop disease. Incidence rates would overcome this limitation by taking into account the exact timeframe during which each cat was monitored, but are less intuitive to interpret.

In conclusion, we demonstrated the value of repeated health screenings in apparently healthy older cats in order to detect subclinical or unnoticed disease and allow early therapeutic intervention. Common abnormalities on physical examination that require further management are increased body condition, moderate to severe dental disease, and abnormal cardiac auscultation findings. With subsequent investigations, 12% of mature adult and 35% of senior cats do not appear to be actually healthy, with unnoticed CKD and hyperthyroidism occurring most frequently. Furthermore, clinically relevant disease manifests itself within 2 years in 28% of mature adult and 54% of senior cats that were confirmed healthy at baseline. Although illness occurs more frequently in senior cats than in mature adult cats, all cats ≥ 7 years of age would benefit from ongoing health checks, and owners should be informed accordingly.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflicts of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Approval granted by the Ethical Committee of the Faculty of Veterinary Medicine and the Faculty of Bioscience Engineering of Ghent University (Institutional Animal Care and Use Committee) and

the Deontological Committee of the Belgian Federal Agency for the Safety of the Food Chain (EC 2018/54).

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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