RELIABILITY ASSESSMENT OF A NOVEL FELINE HEMATURIA HOME SCREENING TEST

Khenifar E, del Castillo JRE, Gara-Boivin C
Université de Montréal, St-Hyacinthe, Canada

Key finding: **The chromogenic screening test has the required metric characteristics for a reliable use in clinical monitoring of feline hematuria.**

Introduction

Background: Hematuria is a frequent sign in feline urinary tract diseases[1]. Detecting hematuria is a challenge for cat owners. A novel hematuria-screening test for use at home on the litter has just completed its development.

The product's sensitivity towards microhematuria and robustness to urine composition have been disclosed elsewhere[2,3]:

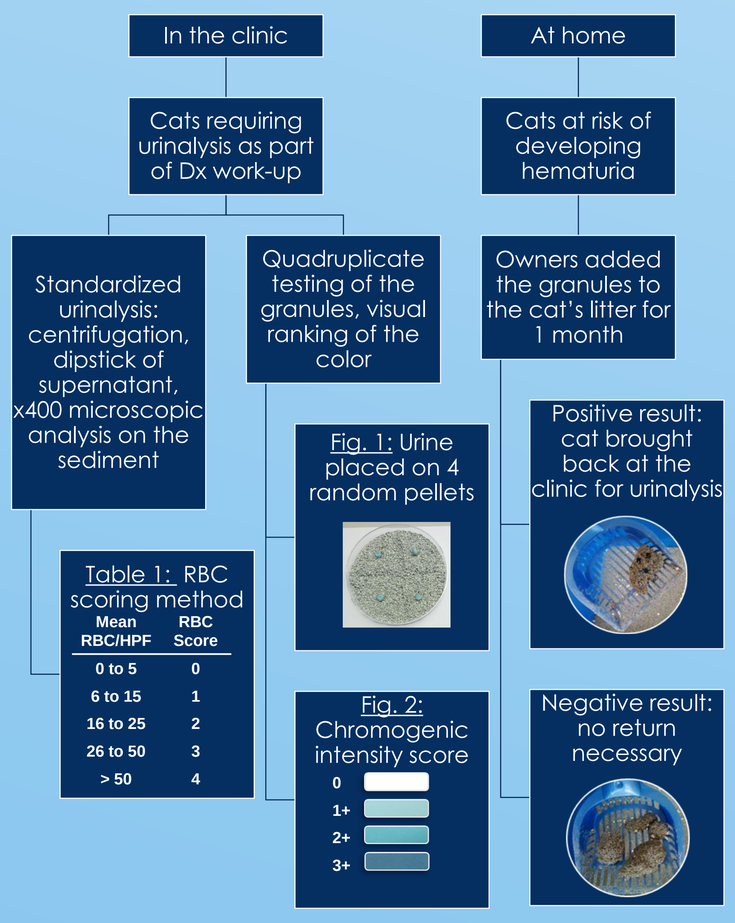
- Lower limit of detection: 100 red blood cells (RBC)/µL↔8-16 RBC/high power field (HPF)
- Color slightly decreased by urinary specific gravity, pH, and proteins but still detects microhematuria

Objectives and hypothesis

Hypothesis	**The metric characteristics of the product are adequate for the clinical monitoring of feline hematuria.**
Objectives	Assess the reliability of the screening test in the clinical setting and at home with cats afflicted by a variety of feline health problems.

Materials and methods

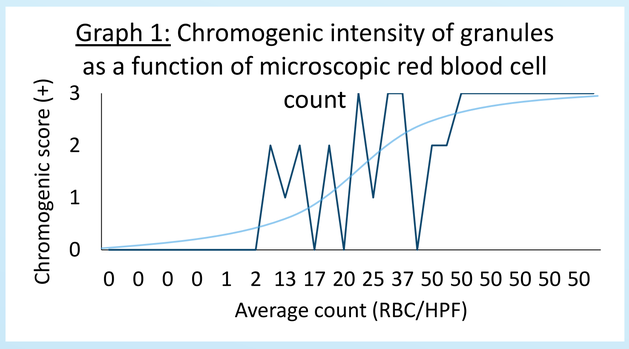
- Multicentric adaptive clinical trial, comprising a planned interim statistical analysis to assess and/or revise the experimental plan, in 6 veterinary clinics of Quebec and one shelter.
- 2 study arms:



- Cystocentesis → Initial hematuria positivity threshold of > 15 RBC/HPF.
- The test sensitivity (Se), specificity (Sp), and positive and negative predictive values (PPV, NPV) were determined at each level of the color scale.
- The test's response modifiers were assessed with a generalized linear mixed model for ordinal response variables (α = 0.05).

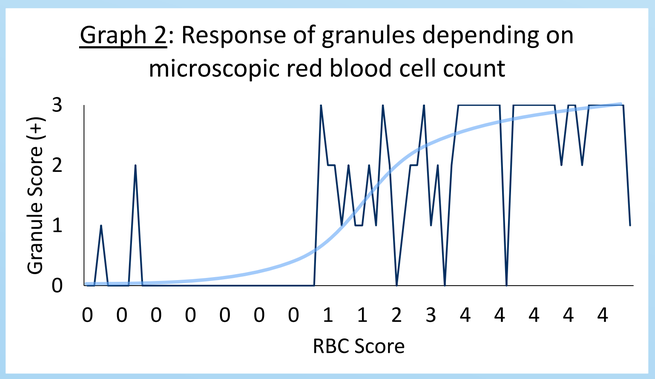
Results

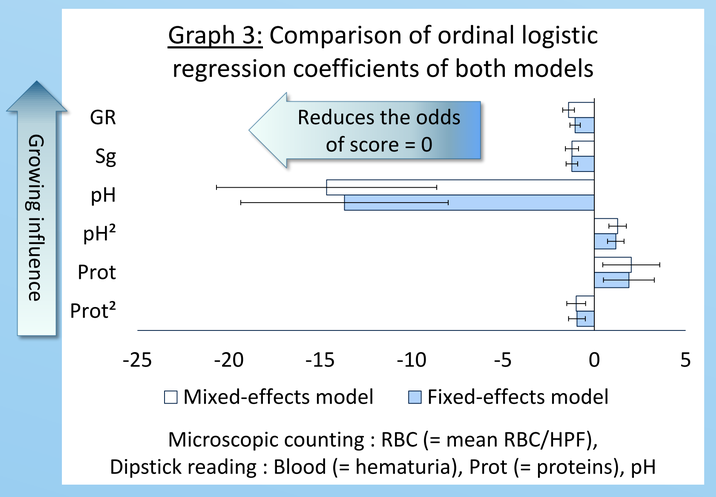
- **Interim statistical analysis:**
  - Performed on the first 34 cats (4 clinics)



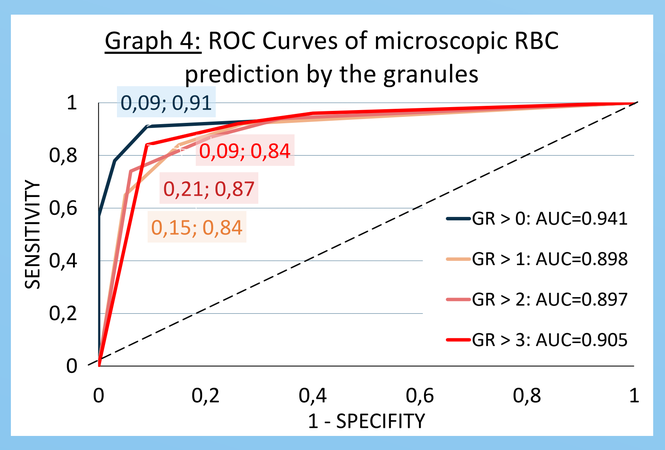
  - Sigmoid positive correlation between granules score and RBC count (Graph 1).
  - Hematuria threshold was too conservative and could be decreased back to 5 RBC/HPF.
  - The 2nd study arm is underrepresented → Recruitment of a cat shelter.
  - To detect at least one false negative and false positive and perform the final statistical analysis, 80 cases are required.

- **Final statistical analysis:**
  - Performed on the data of 80 cats: 69 in the 1st arm, plus 11 in the 2nd arm.





  - Number of RBC/HPF, blood, proteinuria and pH significantly increased cumulative odds of positive screening result ($p<0.05$). (Graph 2,3)
  - The quadratic effects of pH (Graph 3) and proteinuria (not shown) slightly decreased the color intensity of a positive result ($p<0.05$).



  - For a positive result of ≥1+, Se=91.5%, Sp=90.9%, PPV=93.5% and NPV=88.2%.

Discussion

- **Response modifiers of the test:**
  - Blood on dipstick: hemolysis that cannot be detected with microscopy
  - pH: quadratic effect
    - Optimal reaction pH ≈ 7
    - Hindrance at alkaline pH
  - Proteins: quadratic effect
    - Higher urinary protein values likely related to albuminuria

- **Relevance of this detection limit:**
  - > 5 RBC/high power field (x400) is considered as pathologic[4].
  - The pellets detect as low as 12 RBC/HPF (x400)↔100 RBC/µL, over the pathological limit and under the lower limit of macrohematuria (2500 RBC/µL)[5].

- **Variation Factors**

	Suspected hemolysis	pH ≥ 8	UD > 1,060	Unexplained
Total False Positives = **3**/46	2			1
Total False Negatives = **4**/34		3	1	0

Total unexplained= 1

- **Limits of this study**
  - Hemolysis and "false positive"
  - Proteinuria measured with strips and not protein-to-creatinine ratio

Conclusion

- The chromogenic screening product has the required metric characteristics for a reliable use in clinical monitoring of feline hematuria. Further studies are under progress to confirm the test reliability on a wider sample of patients and document the prevalence of hematuria among the North American feline population.

Literature cited

1. Dorsch, R., et al. (2014). "Feline lower urinary tract disease in a German cat population. A retrospective analysis of demographic data, causes and clinical signs." Tierarztl Prax Ausg K Kleintiere Heimtiere 42(4): 231-239.

2. Khenifar E. et al., 2016, ACVP Annual meeting, New Orleans, LA, U.S.A.

3. Gara-Boivin C. et al., 2018, WVAC Annual meeting, Barcelona, Spain

4. Fundamentals of Veterinary Clinical Pathology Second Edition, 2008

5. American Urological Association

For further information

elodie.khenifar@umontreal.ca