**Supporting Information 11: Evidence Summaries and Consensus Recommendations for Feline PECOs with Minimal Evidence**

**4.1.1 In dogs/cats with confirmed thrombocytopenia (P), compared with platelet count alone (C) do platelet indices (e.g. MPV, immature platelet fraction [IPF], reticulated platelets, plateletcrit) (E) improve differentiation of ITP from non-immune thrombocytopenia (O)?**

**4.1.2 In dogs or cats with primary ITP (P), do platelet indices (E) compared to platelet count alone (C) impact predictions of disease severity including bleeding risk, blood product requirement, hospitalization duration, time to platelet recovery, response to first line therapy, survival, or relapse (O)?**

*Guidelines (cats)*

a. In cats with thrombocytopenia, use of platelet indices as routine diagnostic tests for primary ITP is not recommended.
b. There is insufficient evidence to assess the utility of MPV, reticulated platelets, or IPF for prediction of bleeding severity, duration of hospitalization, blood product requirement, or platelet count recovery in cats with primary ITP.
c. In cats with primary ITP, evaluation of platelet parameters as routine prognostic tools is not recommended.

*Level of evidence (cats)*: None. Strength of recommendation: Weak

*Evidence summary (cats)*

We found no studies that directly or indirectly assessed the utility of platelet parameters in diagnosis of ITP in cats, or to assess primary ITP severity. In cats with thrombocytopenia, there is no evidence to determine whether platelet parameters (MPV, IPF, reticulated platelets, plateletcrit) enable differentiation of ITP from non-immune causes of thrombocytopenia nor is there evidence to determine whether these parameters help predict disease severity in feline ITP.

**4.2.2 In dogs/cats with primary ITP (P), does severe thrombocytopenia (E) compared with mild to moderate thrombocytopenia (C) impact prediction of bleeding severity, response to first line therapy, relapse, survival, hospitalization duration, blood product requirement, or time to platelet count recovery (O)?**

*Guidelines (cats)*

a. There is insufficient evidence to assess the utility of admission platelet count for prediction of disease outcome in cats with ITP.
b. In cats with primary ITP, use of admission platelet count as a prognostic tool is not recommended.

*Level of evidence (cats)*: Low. Strength of recommendation: Weak

*Evidence summary (cats)*
No studies were identified that directly addressed the PECO question in cats. A retrospective study of thrombocytopenia in 41 cats identified only 1 case of primary ITP for which insufficient information was provided to apply the ITP diagnostic algorithm. This presumptive ITP cat had a platelet count < 1,000/µL and the most severe bleeding.[1] Meaningful conclusions cannot be drawn from a single cat but the study did report that bleeding was most frequent in cats with platelet counts <30,000/µL.[1] Low platelet counts alone did not predict bleeding as some cats with <10,000 platelets/µL did not bleed.[1] One case series described 5 cats with probable primary ITP and severe thrombocytopenia (< 50,000/µL), all of which had evidence of bleeding on initial evaluation.[2] Three cats received fresh whole blood transfusions, indicative of disease severity and 4 cats survived to discharge.[2] Overall, the impact of platelet count on outcome or disease severity cannot be determined from this study. In a case series of 4 cats diagnosed with primary ITP, all cats had clinical bleeding; 3 cats survived to discharge and 1 died of pulmonary hemorrhage.[3] Similarly, no conclusions can be made regarding the impact of platelet count on disease outcome.

**4.3.1 In dogs/cats with confirmed thrombocytopenia (P), compared with platelet count alone (C) does the addition of bone marrow examination (E) help differentiate ITP from non-immune thrombocytopenia (O)?**

**4.3.2 In dogs/cats with primary ITP (P) does bone marrow evaluation (E) compared with platelet count alone (C), improve prediction of bleeding severity, response to first-line therapy, survival, blood product requirement, duration of hospitalization, days to platelet recovery, or ITP relapse (O)?**

*Guidelines (cats)*

a. There is insufficient evidence to determine whether bone marrow examination improves the diagnosis of primary ITP in cats or is useful as a prognostic indicator.
b. Bone marrow examination is not recommended as a routine diagnostic test or prognostic indicator for primary ITP in cats.
c. We suggest that bone marrow examination should be considered to characterize ill-defined cytopenias, recognizing that there is no bone marrow abnormality diagnostic for primary ITP.

*Level of evidence (cats)*: None. Strength of recommendation: Weak

*Evidence summary (cats)*
No studies were identified that directly addressed the PECO question, and none provided guidance on diagnostic utility of bone marrow examination in cats.

**4.4.1 In dogs/cats with confirmed thrombocytopenia (P), compared with platelet count alone(C) do PSAIG/megakaryocyte-associated antibody assays (E) help differentiate ITP from non-immune thrombocytopenia (O)?**

*Guidelines (cats)*

a. In thrombocytopenic cats, there is insufficient evidence to determine whether measurement of PSAIG/megakaryocyte-associated antibodies is useful for differentiation of ITP from non-immune causes of thrombocytopenia.
b. We suggest that in thrombocytopenic cats, positive PSAIG/megakaryocyte-associated antibody tests indicate an immune component is contributing to thrombocytopenia but are not diagnostic for ITP.
c. In cats with thrombocytopenia, routine measurement of PSAIG/megakaryocyte-associated antibodies is not recommended.

*Level of evidence (cats)*: None. Strength of recommendation: Weak

*Evidence summary (cats)*

No studies directly addressed the PECO question. Two studies were identified that described PSAIG in cats; 1 prospective, cross-sectional study and 1 retrospective case series (total n=99 cats; 24 ITP cats; 6 primary ITP cats).[2,4] However, both studies used PSAIG positivity as a criterion for ITP diagnosis, precluding evaluation of the diagnostic performance metrics of the assays. The prospective study identified 17 cats with underlying secondary diseases thought to be triggers of secondary ITP, but it could not be determined whether comorbidities such as hyperthyroidism or pyelonephritis resulted in non-immune thrombocytopenia with false positive PSAIG results.[4] This study suggests that primary and secondary ITP in cats cannot be differentiated using PSAIG testing.[4] Neither study presented data about megakaryocyte-associated antibody assays for the diagnosis of feline ITP.

There are insufficient data within the reviewed literature to formulate a recommendation about the diagnostic performance of platelet/megakaryocyte antibody assays, relative to platelet count, for differentiating ITP from non-immune thrombocytopenia in cats.

**Lack of consensus:** While 13/14 panelists and diagnosis evidence evaluators agreed with the above recommendations, 1/14 stated that when available in ITP suspects, PSAIGs should be tested for if possible.

### 4.4.2 In dogs/cats with primary ITP (P), do PSAIG or megakaryocyte-associated antibody determinations (E) compared to platelet count alone (C) impact prediction of bleeding severity, response to first line therapy, relapse, survival, hospitalization duration, blood product requirement, or time to platelet count recovery (O)?

*Guidelines (cats)*

a. In cats with primary ITP, there is insufficient evidence to determine whether measurement of platelet/megakaryocyte-associated antibodies is useful for outcome prediction.

b. In cats with primary ITP, evaluation of platelet/megakaryocyte-associated antibodies for outcome prediction is not recommended.

*Level of evidence (cats):* None. Strength of recommendation: Weak

*Evidence summary (cats)*
Three studies were evaluated that described PSAIG measurement in cats (1 observational, cross-sectional study, 1 retrospective case series, and 1 case report), but none addressed the PECO question.[2,4,5] Therefore, in cats there is inadequate published evidence to assess the capacity of platelet/megakaryocyte-associated antibody assays to predict bleeding severity, response to front line therapy, relapse, hospitalization duration, blood product requirement, time to platelet count recovery, and survival in cats with primary ITP.

**4.5.2 In dogs/cats with primary ITP (P), compared to determination of platelet count alone (C) does determination of bleeding severity score (E) improve prediction of bleeding severity, response to first-line therapy, survival, blood product requirement, duration of hospitalization, days to platelet recovery, or ITP relapse (O)?**

*Guidelines (cats)*
a. There is insufficient evidence to make recommendations regarding the use of bleeding severity scoring in cats with primary ITP.

*Level of evidence (cats):* None. Strength of recommendation: None

*Evidence summary (cats)*

No studies relevant to this question were identified.

**4.6.1 In dogs/cats with primary ITP (P), compared to platelet count alone (C) do CBC or chemistry panel abnormalities (E) improve prediction of bleeding severity, response to first-line therapy, survival, blood product requirement, duration of hospitalization, days to platelet recovery, or ITP relapse (O)?**

*Guidelines (cats)*

a. In cats with primary ITP, we suggest that CBC and chemistry panels should be considered to aid assessment of disease severity.

*Level of evidence (cats)*: None. Strength of recommendation: Weak

*Evidence summary (cats)*
Two studies relevant to the PECO question were identified,[2,6] but the relationship between disease severity metrics and clinicopathologic parameters were not explored in either study.

**References:**

1. Jordan HL, Grindem CB, Breitschwerdt EB. Thrombocytopenia in cats: a retrospective study of 41 cases. J Vet Intern Med 1993;7:261-265.
2. Wondratschek C, Weingart C, Kohn B. Primary immune-mediated thrombocytopenia in cats. J Am Anim Hosp Assoc 2010;46:12-19.
3. Bianco D, Armstrong PJ, Washabau RJ. Presumed primary immune-mediated thrombocytopenia in four cats. J Feline Med Surg 2008;10:495-500.
4. Kohn B, Linden T, Leibold W. Platelet-bound antibodies detected by a flow cytometric assay in cats with thrombocytopenia. J Feline Med Surg 2006;8:254-260.
5. Tasker S, Mackin AJ, Day MJ. Primary immune-mediated thrombocytopenia in a cat. J Small Anim Pract 1999;40:127-131.
6. Ellis J, Bell R, Barnes DC, et al. Prevalence and disease associations in feline thrombocytopenia: a retrospective study of 194 cases. J Small Anim Pract 2018;59:531-538.