

# Framework Synthesis (FS) of Qualitative and Quantitative Evidence to Explore the Differential Diagnosis (DDx) of Diarrhea in Neuroendocrine Tumor (NET) Patients

Emma Worthington,<sup>1</sup> Molly Murton,<sup>1</sup> Mohid Khan,<sup>2</sup> Thomas Walter,<sup>3</sup> Enrique Grande,<sup>4</sup> Amy Buchanan-Hughes<sup>1</sup>

<sup>1</sup>Costello Medical, Cambridge, UK; <sup>2</sup>University Hospital of Wales, Cardiff, UK; <sup>3</sup>Centre Hospitalier Universitaire de Lyon, Lyon, France; <sup>4</sup>MD Anderson Cancer Center, Madrid, Spain

PMU90

## Objective

- To describe a novel adaptation of framework synthesis (FS), which was used to facilitate the synthesis of qualitative and quantitative evidence relating to the differential diagnosis (DDx) of diarrhea in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

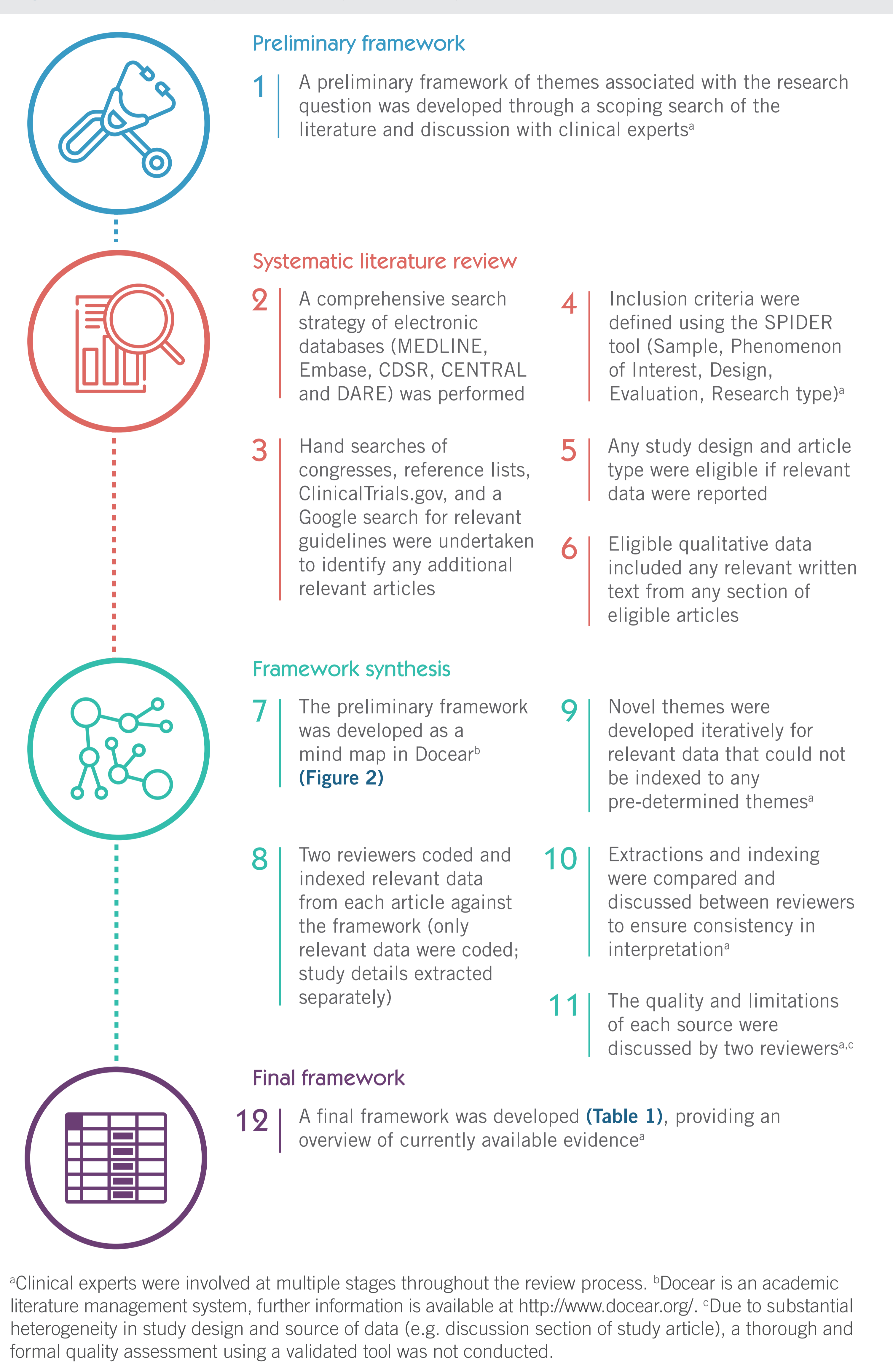
## Background

- FS is a method for synthesis of qualitative research. It can also be used to integrate quantitative and qualitative data to explore complex healthcare issues.<sup>1</sup> We used FS to explore evidence (identified via systematic literature review [SLR]) relating to DDx of diarrhea in patients with GEP-NETs, for which little quantitative data are available.

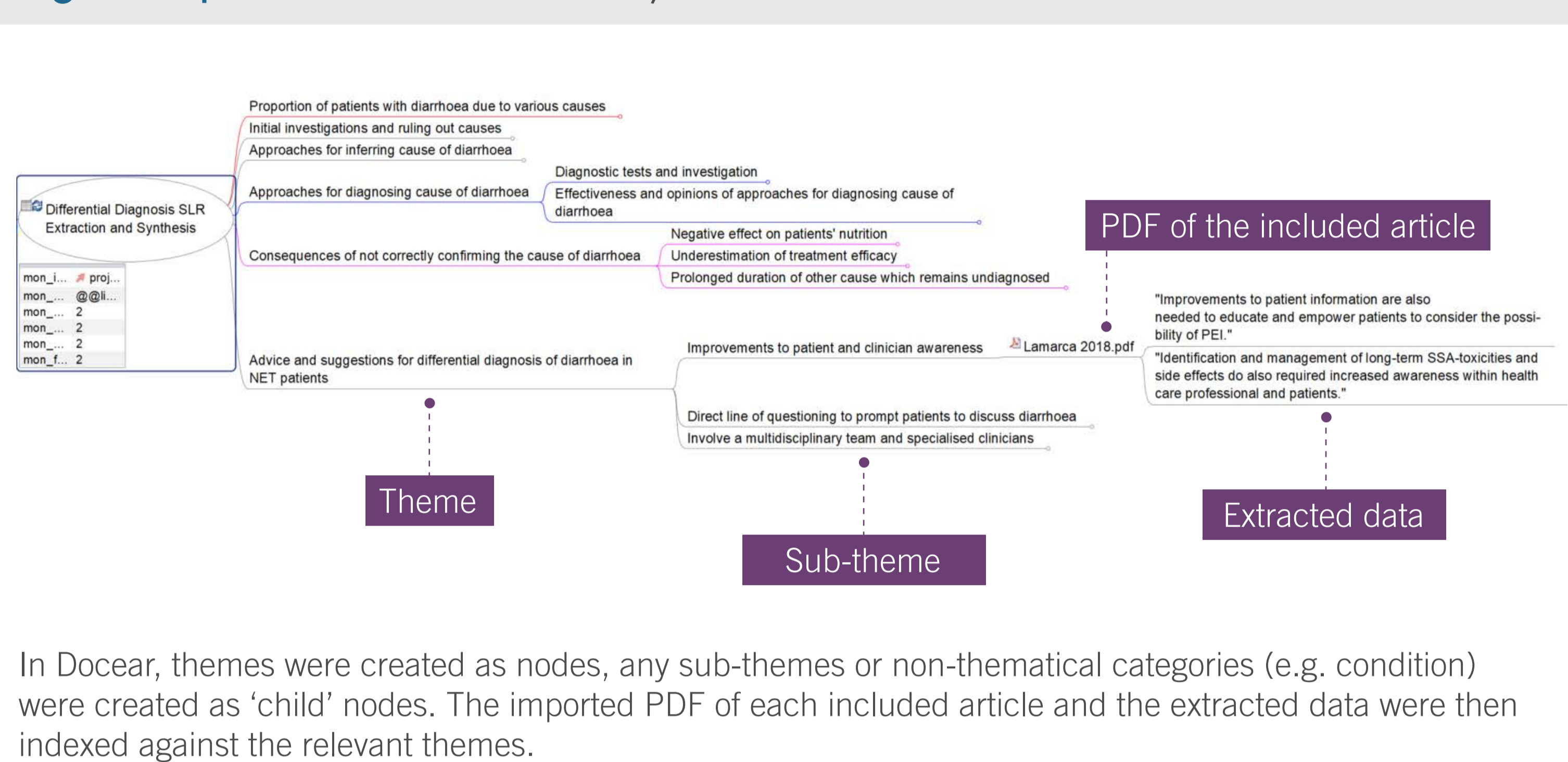
## Methods

- A summary of the review methodology is presented in **Figure 1**. A preliminary framework of themes associated with differential diagnosis of NET diarrhea was developed to inform the methodology of the SLR and facilitate data extraction and synthesis, which was performed in Docear (**Figure 2**). The final evidence framework is presented in **Table 1**.

**Figure 1** | Development of a preliminary framework



**Figure 2** | Data extraction and synthesis in Docear

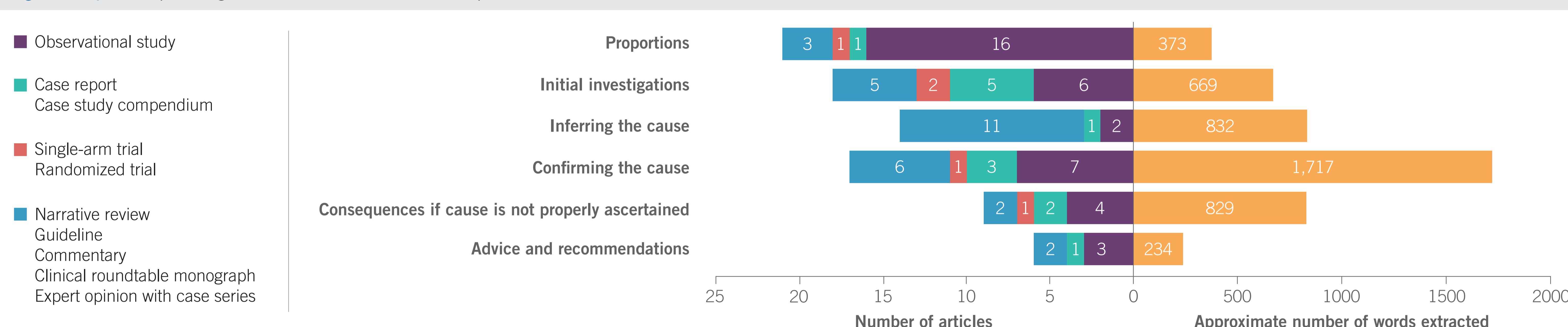


**Table 1** | The final framework of themes associated with differential diagnosis of NET diarrhea

Theme	Subthemes
Proportion of NET patients with diarrhea due to various causes	Proportion inferred from underlying conditions Proportion fulfilling diagnostic criteria for alternative cause (but not diagnosed with the condition) Proportion directly confirmed through clinical tests
Initial investigations	Assessing disease progression Dose escalation Regular screening for malnutrition Assessing patient history of diarrhea
Approaches for inferring the cause of diarrhea	Characteristics of CSD Characteristics of non-NET diarrhea
Approaches for confirming/excluding other causes of diarrhea	Diagnostic tests Treatment trials Treatment discontinuation Quantitative data on effectiveness or suitability of approaches/ Opinions on effectiveness or suitability of approaches
Consequences if the cause of diarrhea is not properly ascertained	Targeted treatments perceived to be ineffective in patients with non-CSD Missed opportunity to diagnose and treat other underlying conditions – remains undiagnosed and prolongs duration of diarrhea Negative impact on patient nutrition
Advice and suggestions for differential diagnosis of diarrhea in NETs	Improvements to patient and clinician awareness Involvement of a multidisciplinary team and specialized clinicians Screening for malnutrition Direct line of questioning to prompt patients to discuss their diarrhea

Purple shaded text indicates the novel themes that arose iteratively during data synthesis. CSD: carcinoid syndrome diarrhea; NET: neuroendocrine tumor.

**Figure 3** | Study designs and words extracted by theme



It is important to note that with the exception of the 'Proportions' theme, data extracted from publications reporting on observational studies and single-arm or randomized trials largely comprised qualitative data from the discussion section of each article. The volume of relevant data reported within each article varied; therefore, the number of articles in each theme is not an accurate reflection of the evidence base. For example, more data were extracted and indexed to the 'inferring the cause' theme than for 'initial investigations', from fewer articles.

## Results

- Data from 47 articles (44 unique studies) were included in the final framework. Information supporting all predefined themes was identified from observational studies, case reports, guidelines and narrative reviews. Three novel themes emerged (**Table 1**), and data were often indexed to more than one theme.
- Quantitative data were primarily obtained from observational studies, while the majority of qualitative data relevant to the 'inferring' and 'confirming the cause of diarrhea' themes were extracted from reviews, guidelines, case reports, and the discussion section of articles reporting on observational studies (**Figure 3**).
- A total of 4,654 words were extracted from the 47 included articles, although in some articles only one sentence of text was relevant, demonstrating the sparsity of the evidence base (**Figure 3**).

- As most data were qualitative and sourced from discussion sections, findings may be subject to author opinion and lack supporting evidence.
- However, these findings provided valuable insight on the importance of DDx of NET diarrhea and allowed for the development of a theoretical chronological framework including approaches for DDx of NET diarrhea, highlighting diagnostic methods to further investigate for use in clinical practice.

## References

1. Booth A *et al.* *BMJ Qual Saf* 2015;24:700–708; 2. Lamarca A *et al.* *Expert Rev Gastroent* 2018;12(7):723–731.

## Acknowledgements

The authors thank Lisa Yang, Costello Medical, London for graphic design assistance with the development of this poster.

## Conclusions

- We demonstrate a novel use of FS, which allowed for comprehensive synthesis of heterogeneous data identified from a systematic review.
- However, there are limitations associated with evidence quality and assessment due to substantial heterogeneity; since data were obtained from any section of a variety of articles, it was not feasible to use a validated quality assessment tool.
- This adaptation of FS may therefore be most appropriate for unexplored or complex research topics, where little high-quality evidence is available.