

## INTRODUCTION

Irritable bowel syndrome (IBS) is a relapsing gastrointestinal (GI) disorder characterized by abdominal pain and discomfort, bloating, and changes in bowel habit.<sup>1</sup> IBS is one of the most common functional GI disorders, with a prevalence in the general population that ranges from 5% to 15%.<sup>2</sup> In a large survey of 8,386 patients from community-based practices, the prevalence of IBS was 10.5%.<sup>3</sup> Symptoms of IBS adversely affect quality of life, including social and psychological aspects, and are associated with considerable costs to the health care system.<sup>2-6</sup> The syndrome is subclassified according to predominant bowel habit: diarrhea predominant (IBS-D), constipation predominant (IBS-C), mixed subtype (IBS-M), or unclassified (IBS-U).<sup>2</sup> Among patients surveyed in community-based practices, symptom profiles were evenly split between those patients with predominant diarrhea (25.4%) and constipation (24.1%), with and overall more females than males are affected by IBS.<sup>3</sup> Diagnosis is based on clinical findings ~~in~~ because of the absence of abnormal radiologic or endoscopic findings ~~or~~ and lack of a reliable (biomarker) test.<sup>2</sup> Although the etiology of IBS is unknown, changes in composition of gut microbiota have been proposed to underlie the symptoms of IBS in some cases.<sup>7-9</sup>

Support for a gut-microbiota etiology includes the relative clinical success of dietary approaches and pharmacologic agents that modulate gut flora, including use of some probiotics<sup>2</sup> and nonsystemic antibiotics, such as rifaximin.<sup>2, 10-16</sup> Rifaximin exhibits a number of properties ~~and attributes~~ that may be beneficial for the management of patients with IBS-D. Indeed, rifaximin is a derivative of rifamycin that contains an extra benzpyrido-imidazole ring that prevents systemic absorption, with  $\leq 0.4\%$  of the dose absorbed systemically.<sup>17</sup> Rifaximin has a high level of solubility in the small intestine (ie, it targets the small intestine).<sup>18</sup> Data from experimental and clinical pharmacology studies indicate that rifaximin has broad

Comment [LN9]: NOTE: Writer has cited reference abstracts in many annotations throughout. Many changes to annotations (up to p. 8) were done to avoid abstracts.

Comment [A10]: Harkness 2013/p92A

Comment [MBM11]: Edit: RefMan won't even let me open a database. Therefore, I couldn't run citations at this point. Please run if you can. If not, I'll do it when it comes back from you. Thank you.

Comment [LN12]: Ford cites IBS and chronic idiopathic constipation as the 2 most common.

Comment [A13]: Ford 2014/pS2A

Comment [L14]: Wilson 2004/p495A/p497A/p498A

Comment [A15]: Ford 2014/pS2D  
Halder 2004/p239A  
Casiday 2009/p42A-C  
Maxion-Bergemann 2006/p33A  
Wilson 2004/p498B

Comment [A16]: Ford 2014/pS2B

Comment [L17]: Wilson 2004/p496A/p499A

Comment [LN18]: More females than males overall, not just with these subtypes.

Comment [A19]: Ford 2014/pS2C

Comment [A20]: Ringel 2009/p146A  
Posserud 2007/p802A  
Kassinen 2007/p32A

Comment [A21]:  
Ford 2014/pS6A

Comment [LN22]: Not until below in Scarpignato ref 19 did I see it called a nonsystemic antibiotic.

Comment [A23]: Ford 2014/pS6A  
Pimentel 2006/p560A-B/p561A-C  
Sharara 2006/p327A-B/p328A/p329A-C  
Cuoco 2006/p91A/p92A-B  
Pimentel 2011/p24A/p26A-C/p27A/p30A-B  
Meyrat 2012/p1086A/p1087A-C/p1089A  
Scarpignati 2013/p1315A/p1316A-D  
Menees 2012/p30A-C/p32C-D

Comment [A24]: Huang 2005/p98A/p99A  
Can't find  $\leq 0.4\%$  in Huang. However, I accidentally found this ( $< 0.4\%$ ) in Scarpignato