Community pharmacy-based *H. pylori* screening for patients with uninvestigated dyspepsia

John Papastergiou, BSc, BScPhm^{ID}; Michelle Donnelly; Terence Yuen;
Wilson Li, BScPhm, CDE; Bart van den Bemt, PharmD, PhD

JOHN PAPAISTERGIOU

Since pharmacists in the community setting frequently encounter patients on long-term acid suppression therapy or complaining of dyspepsia, we were interested in examining the feasibility of *Helicobacter pylori* testing within the pharmacy workflow and identifying the demographic characteristics and risk factors of dyspepsia patients who tested positive.

*Comme les pharmaciens dans le milieu communautaire voient souvent des patients sous traitement par suppression acide à long terme ou qui se plaignent de dyspepsie, nous souhaitons examiner la faisabilité de mener des tests de détection du *H. pylori* dans le cadre du déroulement des activités des pharmacies et déterminer les caractéristiques démographiques et les facteurs de risque liés aux patients atteints de dyspepsie dont le résultat du test est positif.*

ABSTRACT

Background: *Helicobacter pylori* is identified by the World Health Organization as a major risk factor of gastritis, peptic ulcer disease and gastric carcinomas. As point-of-care screening technology becomes more widely available, pharmacists are ideally suited to use this tool to screen patients with *H. pylori* infection.

Purpose: The objective of this study was to evaluate the feasibility of implementing point-of-care screening technology for *H. pylori* into community pharmacy practice and to assess the number of patients who are positively identified as a result of testing.

Methods: Three pharmacies in Toronto, Ontario, offered *H. pylori* screening as part of their clinical programs. Pharmacists enrolled patients with symptoms of dyspepsia and/or receiving acid

suppressant therapy for >6 weeks. Decision to screen was based on the Canadian Helicobacter Study Group Consensus (CHSG). Patients were screened using the Rapid Response *H. pylori* test.

Results: Seventy-one patients were recruited, with a mean age of 46.3 years. Patients were ethnically diverse, with a significant proportion (59.2%) identified as being born outside of North America, including Asia (26.8%), Africa (9.9%), the Middle East (7%), Europe (9.9%) and South and Central America (5.6%). Overall, the detection rate of *H. pylori* infection was 21%. North Americans had the lowest incidence of an undiagnosed *H. pylori* infection (6.9%). Europeans (28.6%), Middle Easterners (20%) and Asians (21.1%) had a moderate incidence, followed by the highest prevalence in those of African descent (71.4%).

Conclusion: These results highlight the readiness of community pharmacists to adopt *H. pylori* screening into practice and to leverage this novel technology to positively identify and treat undiagnosed *H. pylori* infection. *Can Pharm J (Ott)* 2020;153:101-107.

Introduction

Helicobacter pylori is a gram-negative bacterium that infects the gastric epithelium of up to 50% of the world's population.¹ While those infected are frequently asymptomatic,² functional dyspepsia is

the most frequently reported symptom, and nearly 25% of Canadians with uninvestigated dyspepsia have evidence of an active *H. pylori* infection.³

Although prevalence rates are high, untreated infections are typically indefinite,⁴ and the

© The Author(s) 2020

Article reuse guidelines:

sagepub.com/journals-permissions

DOI:10.1177/1715163520903065

KNOWLEDGE INTO PRACTICE

- *Helicobacter pylori* as identified by the World Health Organization is a major risk factor of gastritis, peptic ulcer disease and gastric carcinomas.
- Pharmacists are ideally suited to use point-of-care technology to screen patients with *H. pylori* infection.
- North Americans had the lowest incidence of an undiagnosed *H. pylori* infection, while those of African descent had the highest prevalence.

MISE EN PRATIQUE DES CONNAISSANCES

- Selon l'OMS, le *H. pylori* représente un important facteur de risque pour la gastrite, l'ulcère gastroduodénal et le cancer gastrique.
- Les pharmaciens sont en position idéale pour utiliser les technologies d'analyses hors laboratoire pour le dépistage des patients infectés par le *H. pylori*.
- Les Nord-Américains présentaient la plus faible incidence d'infection par le *H. pylori* non diagnostiquée, alors que les personnes d'origine africaine présentaient la prévalence la plus forte.

H. pylori host-bacterium relationship is not entirely symbiotic. In 2008, the World Health Organization (WHO) identified *H. pylori* as a major risk factor for gastritis, peptic ulcer disease, gastric adenocarcinoma and lymphomas.^{5,6} These complications are costly, and the financial burden of *H. pylori* in the United States was estimated to be \$5.65 billion annually from treatment of complications, acid suppression therapy, decreased productivity and days of lost work. In the United Kingdom, around 1.1 billion pounds was spent annually on dyspepsia treatment alone.⁷

Several trials, including the 10-year CADET-Hp placebo-controlled trial, have shown that *H. pylori* testing and subsequent eradication therapy are cost-effective when compared to symptom and complication management.^{8,9} Determining who to screen is essential to using these data as a cost-savings measure in Canada. Although route of transmission has not been fully elucidated, *H. pylori* is transmitted through intrapersonal contact, leading rates to be highest among rural residents, those living in crowded spaces or those whose source of drinking water has been contaminated. As such, incidence seems to be increased in less economically developed countries where these risk factors are more prevalent.¹⁰ Nonetheless, it is still predicted that 7.1% of Canadians 5 to 18 years of age and 23.1% of

those 50 to 80 are infected at any one time.⁴ Screening for these patients is usually done via endoscopy, urea breath test or serology testing,¹¹ but more recently, novel point-of-care technology has been used to screen and treat patients in the community.

Pharmacists in the community setting frequently encounter patients on long-term acid suppression therapy or those complaining of dyspepsia. Given the accessibility of the community pharmacist, the expanded scope of pharmacy practice and the unique needs of this patient population, pharmacists are ideally suited to use point-of-care technology to screen patients for *H. pylori* infection. Although there are data supporting the benefit of screening and treatment, there have been no studies that specifically examine point-of-care testing for *H. pylori* in the community pharmacy setting within Canada. The objective of this study was to examine the feasibility of *H. pylori* testing within the pharmacy workflow and to identify the demographic characteristics and risk factors of dyspepsia patients who tested positive.

Methods

The study was designed as an open-label, nonrandomized and observational evaluation of an *H. pylori* screening program offered in 3 community pharmacies in Toronto, Ontario. Data collection occurred between September 2016 and March 2017 and included patients 18 years of age or older who had symptoms of dyspepsia and/or were receiving acid suppressant therapy for longer than the standard recommended 6-week treatment for heartburn. Dyspepsia was defined as stomach pain or discomfort, heartburn, sour taste in the mouth, excessive burping/belching, increased abdominal bloating, nausea or early satiety. Demographic information and symptoms were collected using a standardized form (Appendix 1, available at www.cpjjournal.ca). Verbal consent was obtained from all patients.

Exclusion criteria included patients who had previously been infected with *H. pylori* and patients with “alarm” symptoms. Seroantibody tests performed on those previously infected can result in a false positive due to the presence of residual antibodies from the prior infection. Alarm symptoms such as unexplained weight loss, anemia, dysphagia, hematochezia, severe nausea/vomiting or hematemesis warrant further assessment by a physician.

Staff pharmacists offered eligible patients *H. pylori* antibody screening using the Rapid Response *H. pylori* test. This is a noninvasive serological test with 93% sensitivity and 89.2% specificity¹² to detect anti-*H. pylori* IgG antibodies in the blood. Two drops of whole blood were collected from a finger prick and gathered into a dropper.¹³ The collected blood and supplied buffer were added sequentially to the sample well and results were interpreted after 10 minutes.

Ethics approval was not obtained as the screening was already a routine clinical service within these locations and the results were collected to determine the success of the program as part of a continuous improvement initiative.

Patient screening and recommendations

Participants were identified by pharmacists based on the presence of risk factors, dyspepsia or the use of proton pump inhibitors (PPIs) or H_2 -receptor antagonists (H_2 RAs). If the patient was eligible, written consent was obtained and the *H. pylori* screening test was performed by the pharmacist.

For all patients who tested positive, the pharmacist faxed the primary care physician the screening form detailing the assessment performed along with a recommendation. The physician was given the option of initiating eradication therapy with an HP-PAC (lansoprazole 30 mg, clarithromycin 500 mg, amoxicillin 500 mg) twice daily for 7 days or was provided the opportunity to suggest an alternative *H. pylori* eradication regimen. Although current guidelines recommend quadruple therapy due to increasing clarithromycin resistance, triple therapy was still the gold standard at the time of conducting the study.^{14,15}

Notifying physicians of the status of seronegative patients was left to the discretion of the pharmacist. Generally, these patients were managed with recommendations for lifestyle modifications in addition to either an over-the-counter acid-lowering agent or continuation of PPI therapy.

Results

Patient demographic characteristics and description of symptoms are summarized in Table 1. A total of 71 patients were included in the study, with a mean age of 46.3 (19-78) years. Recruitment started January 2017 and continued over a 6-month period. Fifteen patients (21.1%) tested positive for anti-*H. pylori* IgG antibodies.

The most common symptoms of dyspepsia included heartburn (68%), stomach pain (59%) and abdominal bloating (56%), while nausea (37%) and early satiety (28%) were least common. Patients reported these features having a negative impact on their quality of life due to changes in sleep habits (42%), difficulty eating/drinking (45%) and/or inability to perform normal daily activities (37%). Seventy-two percent of patients reported using a PPI to manage their symptoms, while 38% identified using over-the-counter (OTC) therapy.

Patients were ethnically diverse, with a significant proportion (59.1%) identified as being born outside of North America, including Asia (26.8%), Africa (9.9%), the Middle East (7.0%), Europe (9.9%) and South and Central America (5.6%). North Americans had the lowest incidence of an undiagnosed *H. pylori* infection (6.9%). Europeans (28.6%), South/Central Americans (25.0%), Middle Easterners (20.0%) and Asians (21.1%) had a moderate incidence, and the highest prevalence was seen in those of African (71.4%) descent. Relative risk varied depending on the geographic origin of patients and was least significant in those from North America and most significant in those from Africa at 4.57 ($p < 0.0001$).

Pharmacists recommended and successfully initiated *H. pylori* eradication therapy for all positive patients. In the *H. pylori*-negative subgroup, in addition to suggestions for

lifestyle modification, 27 (48.2%) patients were advised to continue PPI therapy, 28 (50%) patients were recommended an OTC product and 1 (1.8%) patient was referred to a physician for follow-up.

Discussion

The study identified a total of 15 patients (21.1%) who tested positive for *H. pylori* antibody. Pharmacists recommended and successfully initiated *H. pylori* eradication therapy for all positive patients. North Americans had the lowest incidence of an undiagnosed *H. pylori* infection (6.9%). Patients originally from Europe (28.6%), South/Central America (25%), the Middle East (20%) and Asia (21.1%) had a moderate incidence, followed by the highest prevalence for those from Africa (71.4%).

As the most available health care practitioners, pharmacists in community practice are ideally positioned to improve access to *H. pylori* screening and education.¹⁶ A number of studies have demonstrated the positive impact that pharmacists can have when implementing similar point-of-care testing programs in other therapeutic areas.¹⁷⁻¹⁹ Pharmacy-based POCT for both chronic and acute disease state management, including A1C and group A strep testing, has been evaluated and yielded positive results.¹⁷⁻¹⁹ Wider-scale adoption of pharmacy-based *H. pylori* screening may improve access to eradication therapy and ultimately reduce the complications of untreated active infection. Moreover, convenience and accessibility are key drivers for patient adherence and engagement. Pharmacy-based screening programs eliminate the need for patients to make multiple appointments, visit the lab for bloodwork and return for interpretation of their results.

Symptoms of *H. pylori* are very nonspecific, and our data support that infection cannot be diagnosed solely based on clinical presentation. Almost half of the patients included in our study presented with at least 1 symptom of heartburn, stomach pain, abdominal bloating or excessive burping. Although these can be associated with dyspepsia, the differential diagnosis can also include gastroesophageal reflux, peptic ulcer disease or a hiatal hernia.²⁰ The frequency of all the reported symptoms, with the exception of sour taste, was similar between both the *H. pylori*-negative and *H. pylori*-positive patients. Testing is essential for a confirmatory diagnosis, and arming the pharmacist with the ability to offer the test will facilitate more accurate recommendations for therapy. Interestingly, sour taste appeared to be a particularly strong predictor for active infection. This could simply be an anomaly given the small sample size or may serve as a cue to pharmacists when deciding whom to screen. Moreover, 42% of patients reported that their symptoms affected their sleep, 45% had their eating or drinking impacted and 37% were unable to perform some aspects of their daily activities. Almost all (93.3%) of positive patients and over half (62.5%) of negative patients reported that their quality of life was adversely affected by dyspeptic symptoms. This dramatic impact on quality of life reiterates

TABLE 1 Patient demographics and symptoms

	All patients (%)		<i>H. pylori</i> -positive patients			
Total number of patients, <i>n</i> (%)	71		15 (21)			
Age (mean), <i>y</i>	46.3		50.3			
Previous OTC use, <i>n</i> (%)	27 (38)		7 (47)			
PPI use, <i>n</i> (%)	51 (72)		9 (60)			
No PPI use	20		6			
New prescription	22		2			
1 week to 3 months	6		2			
5 months to 2 years	10		3			
3 years to 11 years	13		2			
	<i>H. pylori</i> -positive patients, <i>n</i> (%)	<i>H. pylori</i> -negative patients, <i>n</i> (%)	All patients, <i>n</i> (%)	Relative risk	95% Confidence Interval	<i>p</i> value
Dyspepsia symptoms						
Heartburn	10 (67)	38 (68)	48 (68)	0.96	0.37-2.48	0.93
Stomach pain	8 (53)	34 (61)	42 (59)	0.79	0.32-1.94	0.60
Abdominal bloating	8 (53)	32 (57)	40 (56)	0.89	0.36-2.18	0.79
Excessive burping	8 (53)	26 (46)	34 (48)	1.24	0.50-3.06	0.63
Sour taste	10 (67)	17 (30)	27 (38)	3.26	1.25-8.52	2.41
Nausea	4 (27)	22 (39)	26 (37)	0.63	0.22-1.78	0.38
Satiety	4 (27)	16 (29)	20 (28)	0.93	0.33-2.58	0.88
Quality of life						
Sleep	30 (42)	8 (53)				
Eating and/or drinking	32 (45)	5 (33)				
Daily activities	26 (37)	7 (47)				
Area of origin						
North America	2 (6.9)*	27 (48)	29 (40.8)	0.22	0.05-0.91	0.04
Africa	5 (71.4)	2 (4)	7 (9.9)	4.57	2.19-9.56	<0.0001
Asia	4 (21.1)	15 (27)	19 (26.8)	0.99	0.36-2.75	0.99
Europe	2 (28.6)	5 (9)	7 (9.9)	0.88	0.25-3.04	0.83
Middle East	1 (20.0)	4 (7)	5 (7.0)	0.94	0.15-5.78	0.95
South/Central America	1 (25.0)	3 (5)	4 (5.6)	1.20	0.21-6.96	0.84
Prescribed eradication therapy	15 (100)					
Continue PPI	27 (48.2)					
Recommend OTC product	28 (50.0)					
Refer to physician	1 (1.8)					

OTC, over the counter; PPI, proton pump inhibitor.

*Number of positive patients/number of patients screened within the same area of origin.

the importance of rapid identification and treatment in both patient subgroups.

Many Canadians currently manage symptoms of dyspepsia with chronic acid suppression therapy rather than seeking to identify and address the underlying cause. It is not uncommon to see patients on acid suppression therapy for months to years, frequently with no known indication,^{21,22} although most indications for PPI use warrant a maximum of 4 weeks of therapy. In the *H. pylori*-positive group, 60% of patients were using a PPI therapy, with the longest duration of therapy being 11 years. In fact, 4 patients (26.7%) had been using a PPI for over 1 year. Recently, long-term PPI use has become a more significant clinical concern as it can contribute to increased risk of drug interactions, *Clostridium difficile* infections, noninfectious diarrhea, hip fracture, pneumonia and vitamin deficiencies (particularly of vitamin B12 and magnesium).²²⁻²⁴ New guidelines from the College of Family Physicians of Canada suggest tapering down, stopping or using an “on-demand” dosing regimen of PPIs for patients who have completed a 4-week regimen for mild heartburn or mild to moderate gastroesophageal reflux disease.²⁰

The prevalence of *H. pylori* infection is known to be higher in countries outside North America or Asia.^{3,10} Previous studies have examined the effect of patients’ area of residence in relation to *H. pylori* infection rates. Our study differs in that although all patients resided in the same country, we were able to compare infection rates based on their original place of origin. Since untreated *H. pylori* infections usually persist indefinitely,⁴ it may be possible to predict infection risk based on ethnicity. Our data revealed the highest prevalence in patients originating from Africa (71.4%), a nearly 5-fold increase over the average study participant. Africa was followed by Asia, Europe and the Middle East. North Americans had the lowest prevalence (6.9%), nearly 5 times lower than the average study participant.¹⁰ Although our prevalence rates differed slightly from previous studies (most likely due to our smaller sample size), the overall general trends were similar.¹⁰

Childhood appears to be the major period for *H. pylori* infection and transmission. The bacterium itself is commonly found in saliva, the stomach and even water reserves.²³ Close contact with others carries a much higher risk for person-to-person transmission.²³ Although all our study participants currently reside in a country of very low risk, their infection rates appear to vary depending on childhood living conditions. Our results suggest that pharmacists managing patients with symptoms of dyspepsia should be encouraged to ask about childhood ethnic origin and recommend *H. pylori* screening and eradication, if appropriate. This may be of particular importance for those patients originating from Africa, the Middle East, Europe or Central or South America.

Although overall infection rates are considerably lower in Canada, *H. pylori* continues to present a significant public health burden. Additionally, since reinfection rates after

eradication therapy are extremely low,²⁵ guidelines suggest that all positive patients be treated. Pharmacists in our study were able to successfully obtain physician authorization for eradication in 100% of *H. pylori*-positive patients. This suggests that not only were pharmacists appropriately acting on the point-of-care screening results but that physicians were unanimously accepting the recommendations. It is also important to note that most patients were seronegative (75%). In this group, pharmacists were able to rule out *H. pylori* infection as the possible underlying symptom etiology. Management varied depending on the pharmacist but typically included suggestions for lifestyle modification. Twenty-seven (48.2%) patients were advised to continue PPI therapy, 28 (50%) patients were recommended an OTC product and 1 (1.8%) patient was referred to a physician for follow-up.

Recently, there has been some controversy surrounding POCT in community pharmacies in certain jurisdictions across Canada. Concerned stakeholders argue that pharmacies are not well equipped to collect blood samples or ensure sterile conditions and that bloodletting should be reserved for accredited laboratories.²⁶ The accuracy of POC devices has also been questioned, with rising concerns over false negatives and positives. Finally, the perceived conflict of interest over offering testing and selling therapies has been argued. Pharmacists reported that they could easily incorporate POC *H. pylori* screening into practice and successfully collaborate with local physicians to shape prescribing decisions. Moreover, anecdotal patient feedback seems to propose that patients value the convenience and accessibility of receiving this type of service in community pharmacies. Endoscopy or urea breath test, although still the gold standard, may remain a barrier to access to screening for many patients. Wait times to see a specialist in Canada can be extensive, with 1 in 2 Canadians reporting waiting over 4 weeks to see a specialist.²⁷ The Rapid Response *H. pylori* test is highly accurate, with a 93% sensitivity and 89.2% specificity¹² to detect anti-*H. pylori* IgG antibodies in the blood. Although the possibility of false negatives exists, given our recruitment strategy, these patients would have been unlikely to have been screened if the service was not available in the community pharmacy. Given the quality-of-life struggles reported by many of them, access to screening appears to dramatically outweigh any risk of false negatives.

Our study was limited by the relatively small sample size ($N = 71$) and a lack of follow-up with patients after eradication therapy. A larger sample size would empower us to make stronger conclusions with respect to both the detection rate of *H. pylori* and the ethnic variability in prevalence rates. A lack of follow-up limits our ability to quantify the success of each intervention and whether or not eradication was successful in patients prescribed an HP-PAC. Moreover, physicians were given the option to manage active *H. pylori* infection with an HP-PAC (lansoprazole 30 mg, clarithromycin 500 mg, amoxicillin 500 mg) twice daily for 7 days or given the opportunity

to suggest an alternative regimen. Triple therapy for 7 days was still the gold standard at the time of the study, but guidelines have since been updated.^{14,15} The current recommendations from the Canadian Association of Gastroenterology and the American College of Gastroenterology advise 14 days of quadruple therapy and suggest triple therapy is only acceptable if the local clarithromycin resistance is less than 15%.²⁸⁻³⁰ Finally, gender was not documented as part of the basic demographic data. This omission may be significant, as a recent longitudinal study has suggested female gender may be a possible risk factor

for *H. pylori*-related complications and, as such, may affect the generalizability of our conclusions.³¹

In the end, these results highlight the readiness of community pharmacists to adopt *H. pylori* screening into practice and their ability to leverage this novel technology to positively identify and treat undiagnosed *H. pylori* infection. Particular focus should be directed to patients presenting with risk factors and those born in geographical regions with the highest prevalence of disease. Interprofessional collaboration is key in order to optimize rapid treatment and prevent complications. ■

From the Leslie Dan Faculty of Pharmacy (Papastergiou, Donnelly, Yeung), University of Toronto; Shoppers Drug Mart (Papastergiou, Li), Toronto, Ontario; and Radboud University Medical Center (van den Bemt), Nijmegen, The Netherlands. Contact asdm500@shoppersdrugmart.ca.

Author Contributions: J. Papastergiou conceptualized the project, designed the methods for data collection, interpreted the results and authored the manuscript. W. Li reviewed the protocol, provided data collection and contributed to the revision of the manuscript. M. Donnelly conducted the data analysis and assisted with writing of the manuscript. T. Yeung provided data collection and maintained the patient database. B. van den Bemt provided guidance and feedback on the analysis and revision of the manuscript.

Declaration of Conflicting Interests: The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

ORCID iD: John Papastergiou <https://orcid.org/0000-0002-5475-0929>

References

- Goodwin CS, Worsley BW. Microbiology of *Helicobacter pylori*. *Gastroenterol Clin North Am* 1993;22:5.
- McColl K. *Helicobacter pylori* infection. *N Engl J Med* 2010;362:1597-604.
- Chiba N. Treating *Helicobacter pylori* infection in primary care patients with uninvestigated dyspepsia: the Canadian adult dyspepsia empiric treatment—*Helicobacter pylori* positive (CADET-Hp) randomised controlled trial. *BMJ* 2002;324(7344):1012.
- World Gastroenterology Organization. Global guideline—*Helicobacter pylori* in developing countries. *J Digest Dis* 2011;12:319-26.
- World Health Organization. *Helicobacter pylori: immunization, vaccines and biologicals*, 2008 Jan 5. Available: www.who.int/immunization/topics/helicobacter_pylori/en/ (accessed Jan. 8, 2019).
- IARC Working Group on the Evaluation of Carcinogenic Risk to Humans. Schistosomes, Liver Flukes and *Helicobacter pylori*. Lyon (FR): International Agency for Research on Cancer; 1994. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 61.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK487782/>
- Asante M, Lord J, Mendall M, et al. Endoscopy for *Helicobacter pylori* seronegative young dyspeptic patients: an economic evaluation based on a randomized trial. *Eur J Gastroenterol Hepatol* 1999;11(8):851-6.
- Moayyedi P. The health economics of *Helicobacter pylori* infection. *Best Pract Res Clin Gastroenterol* 2007;21(2):347-61.
- Ford AC, Forman D, Hunt RH, et al. A community screening program for *Helicobacter pylori* saves money: 10-year follow-up of a randomized controlled trial. *Gastroenterology* 2005;129:1910-7.
- Eusebi LH, Zagari RM, Bazzoli F. Epidemiology of *Helicobacter pylori* infection. *Helicobacter* 2014;19(1):1-5.
- Graham D, Rugge M. Clinical practice: diagnosis and evaluation of dyspepsia. *J Clin Gastroenterol* 2010;44(3):167-72.
- BTNX Inc. Rapid Response Test Cassette. Product monograph. Updated 2014. Available: <https://www.btnx.com/Product?id=1986> (accessed Feb. 12, 2019).
- Patel SK, Pratap CB, Jain AK, et al. Diagnosis of *Helicobacter pylori*: What should be the gold standard? *World J Gastroenterol* 2014;20(36):12847-59.
- Jensen K. Current management recommendations for *Helicobacter pylori* infections in adults. *Pharm Pract Plus* 2017;4(6):15-9.
- Towards optimized practice: diagnosis and treatment of *Helicobacter pylori* infection in adults. Clinical Practice Guidelines. 2009. Available: www.topalb.ertadoctors.org/download/362/h_pylori_guideline.pdf?_20170531132925 (accessed Feb. 12, 2019).
- Canadian Pharmacists Association. Pharmacists' scope of practice in Toronto. 2016 January. Available: https://www.pharmacists.ca/cpha-ca/assets/File/pharmacy-in-canada/Scope%20of%20Practice%20in%20Canada_JAN2016.pdf (accessed Jan. 7, 2019).
- Papastergiou J, Rajan A, Diamantouros A, et al. HbA1c testing in the community pharmacy: a new strategy to improve care for patients with diabetes. *Can Pharm J (Ott)* 2002;145(4):165-7.
- Papastergiou J, Folkins C, Li W, et al. Community pharmacy rapid influenza A and B screening: a novel approach to expedite patient access to care and improve clinical outcomes. *Can Pharm J (Ott)* 2016;149(2):83-9.
- Papastergiou J, Trieu CR, Saltmarche D, et al. Community pharmacist-directed point-of-care group A *Streptococcus* testing: evaluation of a Canadian program. *J Am Pharm Assoc* 2018;58(4):450-6.
- Farrell B, Pottie K, Thompson W, et al. Deprescribing proton pump inhibitors: evidence-based clinical practice guideline. *Can Fam Phys* 2017;63(5):354-64.
- Nardino RJ, Vender RJ, Herbert PN. Overuse of acid-suppressive therapy in hospitalized patients. *Am J Gastroenterol* 2000;95(11):3118-22.
- Naunton M, Peterson GM, Bleasel MD. Overuse of proton pump inhibitors. *J Clin Pharm Ther* 2008;25(5):333-40.
- Trifan A, Stanciu C, Irinia G, et al. Proton pump inhibitors therapy and risk of *Clostridium difficile* infection: systematic review and meta-analysis. *World J Gastroenterol* 2017;23(35):6500-15.

24. Lam JR, Schneider JL, Zhao W, et al. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. *JAMA* 2013;310(22):2435-42.
25. Gisbert JP. The recurrence of *Helicobacter pylori* infection: incidence and variables influencing it: a critical review. *Am J Gastroenterol* 2005;100(9):2083.
26. Panteghini M. The future of laboratory medicine: understanding the new pressures. *Clin Biochem Rev* 2004;25(4):207-15.
27. Osborn R, Squires D, Doty MM, et al. In new survey of 11 countries, US adults still struggle with access to and affordability of health care. *The Commonwealth Fund*. 2016 November. Available: <https://www.commonwealthfund.org/publications/journal-article/2016/nov/new-survey-11-countries-us-adults-still-struggle-access-and> (accessed May 8, 2019).
28. Fashner J, Gitu AC. Diagnosis and treatment of peptic ulcer disease and *H. pylori* infection. *Am Fam Physician* 2015;91(3):236-42.
29. Fallone CA, Chiba N, Van Zanten SV, et al. The Toronto consensus for the treatment of *Helicobacter pylori* infection in adults. *Gastroenterology* 2016;151(1):51-69.
30. Chey WD, Leontiadis GI, Howden CW, et al. Treatment of *Helicobacter pylori* infection. *Am J Gastroenterology* 2017;112:212-38.
31. Agah S, Khedmat H, Ghamar-Chehred ME, et al. Female gender and *Helicobacter pylori* infection, the most important predisposition factors in a cohort of gastric cancer: a longitudinal study. *Caspian J Intern Med* 2016;7(2):136-41.