

## MINI-REVIEW

# Gastric Cancer in Asian American Populations: a Neglected Health Disparity

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### Abstract

Gastric cancer incidence rates vary dramatically by world region with East Asia having the highest rate. The Asian population of the United States (US) is growing rapidly and over 17 million Americans are of Asian descent. A majority of Chinese, Korean and Vietnamese Americans are immigrants. Americans of East and Southeast Asian descent experience marked gastric cancer disparities and the incidence rate among Korean men in the US is over five times higher than the incidence rate among non-Hispanic white men. Randomized controlled trials have provided evidence for the effectiveness of helicobacter pylori identification and eradication in preventing gastric cancer. Additionally, Japan and South Korea have both experienced improvements in gastric cancer mortality following the implementation of programs to detect early stage gastric cancers. There are currently no clear US guidelines regarding the primary and secondary prevention of gastric cancer in high-risk immigrant populations. However, it is likely that a proportion of US physicians are already recommending gastric cancer screening for Asian patients and some Asian immigrants to the US may be completing screening for gastric cancer in their native countries. Surveys of US primary care physicians and Asian American communities should be conducted to assess current provider practices and patient uptake with respect to gastric cancer prevention and control. In the absence of clinical guidelines, US health care providers who serve high-risk Asian groups could consider a shared decision-making approach to helicobacter pylori identification and eradication, as well as gastric endoscopy.

**Keywords:** Asian Americans - gastric cancer - health disparity - primary prevention - secondary prevention

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### Introduction

Worldwide, gastric cancer is the fifth most commonly occurring cancer and third leading cause of cancer death (Ferlay et al., 2013). Gastric cancer incidence rates vary dramatically by world region with East Asia having the highest rate (Ferlay et al., 2013; Fock, 2014). Currently, three East Asian countries (China, Japan and Korea) account for 60% of all gastric cancer cases (Fock, 2014). As shown in Figure 1, the age-adjusted incidence rates in South Korea, Japan and China are 41.8, 29.9 and 22.7 per 100,000, respectively (compared to 3.9 per 100,000 in the US) (Ferlay et al., 2013). Gastric cancer incidence rates increase progressively with age (Crew and Neugot, 2006; Brenner et al., 2009). Gender is strongly associated with gastric cancer risk and men have markedly higher incidence rates than women (Crew and Neugot, 2006; Brenner et al., 2009; Ferlay et al., 2013).

About 90% of gastric cancers are adenocarcinomas originating in the gastric mucosa (Crew and Neugot, 2006; Brenner et al., 2009). The main tumor locations of

gastric adenocarcinomas are proximal (cardia) and distal (non-cardia) (Crew and Neugot, 2006). There are two main histologic types of gastric adenocarcinomas: intestinal (well-differentiated) and diffuse (undifferentiated) (Crew and Neugot, 2006; National Cancer Institute, 2014). Distally located and intestinal type tumors (which are primarily associated with helicobacter pylori infection) predominate in high-risk geographic areas such as East Asia, and account for much of the regional variation in gastric cancer incidence rates (Crew and Neugot, 2006). Histological precursors of gastric cancer include atrophic gastritis, gastric intestinal metaplasia and gastric dysplasia (Gomez and Wang, 2014; Lin, 2014).

The Asian population of the US is growing rapidly and over 17 million Americans are of Asian descent (Hoefell et al., 2012). The six largest Asian American sub-groups are Chinese, Filipinos, Indians, Japanese, Koreans and Vietnamese which all number over one million. Table 1 provides data for these sub-groups and shows a majority of Chinese, Indian, Korean and Vietnamese Americans were foreign-born (Gryn and Gambino, 2012; Hoefell

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et al., 2012).

This review article summarizes the gastric cancer disparities experienced by Asian American populations. Additionally, it provides relevant information about the primary prevention of gastric cancer through helicobacter pylori identification and eradication, as well as the secondary prevention of gastric cancer through the use of screening tests. Our goal is to draw attention to gastric cancer as a neglected health disparity among some Asian American sub-groups, and promote discussion about potential gastric cancer prevention and control strategies for Americans who are at high risk for gastric cancer because of their Asian ethnicity. While we focused on

Asian Americans for this review, many of the issues that we address are also relevant to US immigrant populations from other regions of the world with high gastric cancer incidence rates (e.g. countries in Central America and Eastern Europe) as well as Asian immigrants to other Western countries (e.g. Australia and Canada) (Ferlay et al., 2013).

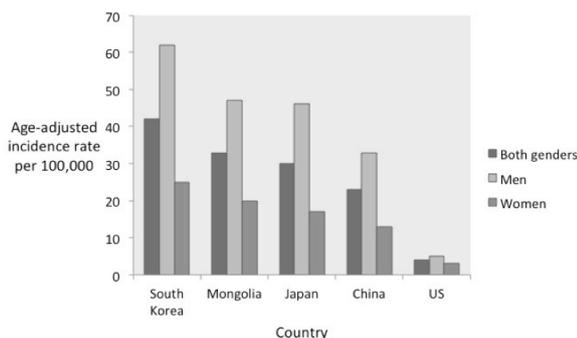
## Gastric Cancer among Asian Americans

### Overview

Asian Americans as an aggregate group have higher gastric cancer incidence rates than US blacks, Hispanics and non-Hispanic whites (Lui et al., 2014). Additionally, multiple studies have shown marked variations in gastric cancer incidence and mortality rates among Asian American populations (McCracken et al., 2007; Miller et al., 2008; Gomez et al., 2013; Huang et al., 2013). Table 2 provides gastric cancer incidence and mortality rates for selected population sub-groups (Miller et al., 2008). Americans of East Asian (i.e. Chinese, Japanese and Korean) and Southeast Asian (e.g. Vietnamese) origin have high incidence and mortality rates compared to non-Hispanic whites, but Americans of Indian and Filipino origin do not.

### Temporal trends

A recent analysis examined temporal trends in gastric cancer incidence rates among Asian Americans. Table 3 provides age-adjusted rates among Asian sub-groups that experience gastric cancer disparities for three time periods between 1990 and 2008 (Gomez et al., 2013). Incidence rates have remained relatively constant among Korean American men and women over the last two decades. For example, the rates among Korean American men in 1990-1994, 1998-2002 and 2004-2008 were 55.9, 49.2 and 52.5 per 100,000, respectively. In contrast, rates have decreased over time among Japanese American men and women.



**Figure 1. Gastric Cancer Incidence Rates: East Asia and Use**

**Table 1. Largest Asian American Sub-groups**

Asian group	Total number 2010*	Number of foreign-born 2011**
Chinese	4,010,000	2,231,000
Filipino	3,417,000	1,814,000
Indian	3,183,000	1,857,000
Japanese	1,304,000	318,000
Korean	1,707,000	1,083,000
Vietnamese	1,737,000	1,259,000

\*Data are from the 2010 US Census and include individuals reporting more than one race \*\*Data are from the 2011 American Community Survey

**Table 2. Age-adjusted Gastric Cancer Incidence and Mortality Rates – US, 1998-2002 (Miller et al., 2008)**

Group	Incidence rate per 100,000 men*	Incidence rate per 100,000 women*	Mortality rate per 100,000 men**	Mortality rate per 100,000 women**
Asian Indian	8.2	4.7	3.7	2.4
Chinese	18.3	11.1	11.7	7.3
Filipino	9.4	5.6	4.9	3.2
Japanese	29.3	15	16.6	10.2
Korean	50	26.3	31.5	14.5
Vietnamese	25.6	13.8	12.7	7
Non-Hispanic white	9.9	4.3	5.8	2.8

\*SEER registry areas (Metropolitan Atlanta, Metropolitan Detroit, Seattle/Puget Sound, California, Connecticut, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah) \*\*States that require specification of Asian sub-groups on death certificates (California, Hawaii, Illinois, New Jersey, New York, Texas, and Washington)

**Table 3. Age-adjusted Gastric Cancer Incidence Rates by Time Period-US, 1990-2008 (Gomez et al., 2013)**

Group	Incidence rate per 100,000 men			Incidence rate per 100,000 women		
	1990-1994	1998-2002	2004-2008	1990-1994	1998-2002	2004-2008
Chinese	19.2	17.7	16.3	11.3	10.9	Not reported*
Japanese	37.7	28.5	24.2	19.1	14.6	11.1
Korean	55.9	49.2	52.5	26	26.6	27.4
Vietnamese	30.8	24.6	21.2	22.6	Not reported*	Not reported*

\*Incidence rates were only reported for the five most commonly occurring cancers

### Generational level

No recent studies have examined gastric cancer incidence rates among foreign-born versus US-born Asian Americans. However, one previous study examined incidence rates among Japanese immigrants and their descendants using 1973-1986 US cancer registry data (Kamineni et al., 1999). Japanese Americans, regardless of birthplace, experienced higher gastric cancer incidence rates than US-born whites. The incidence rate in Asia-born Japanese men was about four times higher than in US-born white men, and the incidence rate in Asia-born Japanese women was about six times higher than in US-born white women. While the incidence rate was lower among US-born Japanese than Asia-born Japanese, it was still almost three times that of US-born whites.

## Modifiable Gastric Cancer Risk Factors

Smoking is a causal risk factor for gastric cancer and it is estimated that about one in six gastric cancers are attributable to smoking (Gonzalez et al., 2003; Ladeiras-Lopez et al., 2008; Brenner et al., 2009; Moore, 2014). There is also an established link between a high dietary salt intake and gastric cancer and a recent meta-analysis of prospective studies found a relative risk of 1.68 (95% confidence interval: 1.17-2.41) for high versus low salt intakes (D'Elia et al., 2012; D'Elia et al., 2014; Moore, 2014).

A large-scale European prospective investigation into cancer and nutrition study found that a high intake of red and processed meat is associated with an increased risk of gastric cancer, but a high fruit and vegetable intake is not associated with a decreased risk (Gonzalez et al., 2006; Bradbury et al., 2014).

## Helicobacter Pylori Identification and Eradication

### Overview

Helicobacter pylori infection is a well-established risk factor for gastric cancer, and the International Agency for Research on Cancer has classified it as a class I carcinogen for gastric cancer (Brenner et al., 2009; Ford et al., 2014; Moore, 2014). As would be expected, helicobacter pylori infection is generally more prevalent in countries with high gastric cancer incidence rates than countries with low gastric cancer incidence rates (Fock, 2014).

There are several non-invasive tests for helicobacter pylori that can be used in routine clinical practice. These include C urea breath tests, stool antigen tests, and serologic antibody-based tests (Canadian Cancer Society, 2014; Tonkic et al., 2014). Infection with helicobacter pylori can be treated with various combination therapies such as triple therapy with a proton-pump inhibitor, amoxicillin and clarithromycin (Canadian Cancer Society, 2014; Heo and Jeon, 2014). Eradication can be documented through follow-up urea breath or stool antigen testing (serologic tests can remain positive after eradication and are not useful for this purpose) (Attumi and Graham, 2014).

### Evidence for effectiveness

Several meta-analyses have assessed whether testing for helicobacter pylori and treating infected individuals with eradication therapy leads to a reduction in the incidence of gastric cancer (Leung et al., 2008; Fock, 2014; Ford et al., 2014). The most recent meta-analysis identified six randomized controlled trials that examined the effect of at least seven days of eradication therapy on subsequent occurrence of gastric cancer in asymptomatic adults who tested positive for helicobacter pylori. Five of these trials were conducted in Asia (China or Japan). The analysis yielded a summary relative risk of subsequent occurrence of gastric cancer with eradication therapy versus placebo or no treatment of 0.66 (95% confidence interval: 0.46-0.95) (Ford et al., 2014).

### Clinical guidelines

The Asia Pacific consensus guidelines on gastric cancer prevention specify that populations in Asia at high risk for gastric cancer should receive helicobacter pylori testing and eradication therapy (Fock et al., 2008; Fock et al., 2009). Both the Canadian helicobacter study group and Canadian Cancer Society recommend testing for and treating helicobacter pylori infection in immigrants from geographic areas of the world where the incidence of gastric cancer is high (Hunt et al., 2004; Canadian Cancer Society, 2014). The American Society of Gastrointestinal Endoscopy recognizes that helicobacter pylori identification and eradication has the potential to reduce the risk for gastric cancer in groups at high risk for the disease but does not suggest ethnicity-based deviations from usual care (American Society of Gastrointestinal Endoscopy, 2010; 2014).

## Gastric Cancer Screening

### Overview

Several screening tests have been used in Asia for the early detection of gastric cancer and its precursors, either alone or in combination (Hamashima et al., 2008; Leung et al., 2008; Lin, 2014). These tests include measurement of serum pepsinogen I and II levels (the level of pepsinogen I and ratio of pepsinogen I/II are decreased in the presence of atrophic gastritis, a gastric cancer precursor), upper gastrointestinal barium series and gastric endoscopy (Lin, 2014; National Cancer Institute, 2014).

### Evidence for effectiveness

No randomized controlled trials have evaluated the impact of gastric cancer screening (using pepsinogen levels, upper gastrointestinal barium series or gastric endoscopy) on mortality (National Cancer Institute, 2014). However, multiple Japanese studies have evaluated the effectiveness of screening for gastric cancer with upper gastrointestinal series using non-randomized designs (Hamashima et al., 2008; Leung et al., 2008; National Cancer Institute, 2014). Case-control studies consistently found significant decreases in mortality from gastric cancer (of between 40% and 60%) in those who had been screened with upper gastrointestinal series (Hamashima

et al., 2008; Leung et al., 2008). While prospective cohort studies that defined death from gastric cancer as the endpoint have mostly shown a protective effect of upper gastrointestinal series, their results have been inconsistent (Leung et al., 2008). Little research has evaluated the effectiveness of other gastric cancer screening tests (i.e. pepsinogen levels and gastric endoscopy) in reducing mortality using case-control or cohort designs (Hamashima et al., 2008).

#### *Clinical guidelines*

While the physician data query screening and prevention editorial board has concluded that population-based gastric cancer screening is not appropriate in areas with a relatively low incidence of gastric cancer such as the US, it has also concluded that there may be justification for screening some groups of Americans at high risk of gastric cancer such as immigrants from countries with high rates of the disease (National Cancer Institute, 2014). Similarly, the American Society for Gastrointestinal Endoscopy suggests screening with gastric endoscopy for US immigrants from high-risk countries (e.g. Korea), especially if there is a family history of gastric cancer in a first-degree relative (American Society of Gastrointestinal Endoscopy, 2010; 2014).

### **Asian Gastric Cancer Control Programs**

#### *Japanese programs*

Japan first implemented a screening program for gastric cancer in Miyagi prefecture over 50 years ago and has had a national screening program since 1983 (Hamashima et al., 2008; Leung et al., 2008). For many years, the national program was based on annual upper gastrointestinal series (photofluorography) for people ages 40 and older to detect early cancers (Hamashima et al., 2008; Leung et al., 2008; Lin, 2014). The introduction of mass screening coincided with a decline in gastric cancer mortality in Japan (Hamashima et al., 2008; Leung et al., 2008). For example, the male age-adjusted mortality rate decreased from 69.9 to 34.5 per 100,000 between 1980 and 2003 (Hamashima et al., 2008).

A new strategized and comprehensive gastric cancer control approach was implemented in Japan during 2013 and has multiple components targeting people in specific age groups (Fock, 2014). First, people younger than 20 years are tested for helicobacter pylori and infected people receive eradication therapy. Second, people ages 50 and older are tested for helicobacter pylori and infected people receive both eradication therapy and endoscopic screening. Surveillance is offered to people with pre-malignant gastric changes at endoscopy (Asaka et al., 2014; Fock, 2014; Lin, 2014).

#### *South Korean program*

Gastric cancer screening was implemented in Korea during 1999 as part of the national cancer screening program (Kim et al., 2011; Choi et al., 2012; Shin and Lee, 2012; Cho et al., 2013; Kim et al., 2013). Screening every two years is recommended for people ages 40 years and older via either gastric endoscopy or upper

gastrointestinal series (Kim et al., 2011; Choi et al., 2012). Since implementation of this program, the proportions of early (versus late) stage gastric cancers have increased, gastric cancer mortality rates have decreased, and gastric cancer survival rates have increased (Jung et al, 2013; Kim et al., 2014). For example, the 5-year survival rate for both genders combined increased from 43% in 1993-1995 to 67% in 2006-2010 (Jung et al., 2013).

#### *Choice of gastric cancer screening test*

The performance of gastric endoscopy and upper gastrointestinal series has been compared using 2002-2005 data from the South Korea national cancer screening program (Choi et al., 2012). Overall, gastric endoscopy performed better than upper gastrointestinal series with respect to gastric cancer detection and sensitivity. Gastric cancer detection rates for endoscopy and upper gastrointestinal series were 2.61 per 1,000 and 0.68 per 1,000 screenings, respectively. Japanese data from a program in Niigata city (that allowed people to choose their gastric cancer screening method) also suggest that gastric endoscopy is superior to upper gastrointestinal series as a cancer screening method (Tashiro et al., 2006). Therefore, both Japan and South Korea are now emphasizing use of gastric endoscopy rather than upper gastrointestinal series as the screening test of choice for gastric cancer (Lin, 2014).

### **Provider Gastric Cancer Screening Practices**

In 2006, Kwon and colleagues surveyed a random sample of 100 primary care physicians who practiced in New York and New Jersey zip codes where more than 25% of the population was Asian (Kwon et al., 2013). The physicians were asked to indicate how often they recommended gastric cancer screening to Asian patients during routine check-ups on a scale of 1 to 5, with 1 being never and 5 being always. The mean score was 2.7 (standard deviation: 1.5). In 2007-2008, Won and Hwang surveyed a convenience sample of 56 members of the American Geriatrics Society (Won and Hwang, 2012). Respondents were asked if they would recommend gastric cancer screening to a healthy 67 year old Korean American man who had never been screened for gastric cancer, had emigrated from South Korea a year earlier and had no risk factors for gastric cancer. Nearly one-third (30%) said they would recommend gastric cancer screening for this hypothetical patient.

### **Potential Impact of Medical Tourism**

The medical tourism industry in South Korea offers preventive care packages that include gastric cancer screening and aggressively markets its health care services to Korean communities in the US (Oh et al., 2014). Ko and colleagues recently surveyed a convenience sample of 193 Koreans ages 50-75 who lived in the Puget Sound area of Washington State, and found nearly one-third (31%) of the respondents had travelled to South Korea for medical services within the previous five years (Ko et al., 2014). It is likely that some Korean immigrants to the

US are receiving gastric endoscopy in their native country, and this is potentially problematic for people who have abnormal findings and then need follow-up surveillance or treatment (Oh et al., 2014).

## Discussion

Gastric cancer is one of the five most commonly occurring malignancies among Chinese, Japanese, Korean, and Vietnamese American men (Gomez et al., 2013). The incidence rate among Korean men in the US is over five times higher than the rate among non-Hispanic white men, is only slightly lower than the rate among men in South Korea, and is not decreasing over time (McCracken et al., 2008; Ferlay et al., 2013; Gomez et al., 2013). Gastric cancer and hepatic cancer both represent marked health disparities experienced by Asian American sub-groups (McCracken et al., 2007; Miller et al., 2008; Gomez et al., 2013). While much attention has been paid to hepatic cancer control in Asian American communities over the last decade, relatively little attention has been paid to gastric cancer control (Chao et al., 2009; Nguyen et al., 2012).

Approximately one-quarter of Korean men (23%) and Vietnamese men (27%) in California are current smokers, and New York city data indicate that over one-third (36%) of Korean men in some geographic areas of the US smoke (Li et al., 2013; University of California Los Angeles, 2014). Additionally, traditional Asian diets often include foods that have a high salt content (e.g. soy sauce) or were preserved in salt (e.g. salt-preserved fish) and many Asian immigrant families continue to eat traditional diets after settling in the US (Satia et al., 2001; Brown et al., 2009; Jasti et al., 2011; D'Elia et al., 2012). The role of smoking and dietary factors in the development of gastric cancer should be addressed in health education programs for US Asian communities.

Available randomized controlled trial data provide limited, moderate quality evidence that testing for and treating helicobacter pylori reduces the incidence of gastric cancer in Asian countries but these findings are not necessarily generalizable to non-Asian countries (Ford et al., 2014). No randomized controlled trials have addressed the effectiveness of gastric cancer screening (using pepsinogen levels, upper gastrointestinal barium series or gastric endoscopy) in reducing mortality (National Cancer Institute, 2014). Japan and South Korea have both experienced improvements in gastric cancer mortality following the implementation of gastric cancer screening programs. However, it is unclear whether these improvements are due to the implementation of protocols to identify helicobacter pylori infection and early gastric cancers or improved gastric cancer treatment methods (e.g. endoscopic sub-mucosal dissection) (Hamashima et al., 2008; Leung et al., 2008; Jung et al., 2013; Fock et al., 2014; Gomez and Wang., 2014). Ideally, randomized controlled trials would be conducted to evaluate the effectiveness of helicobacter pylori identification and eradication, as well as screening with gastric endoscopy in high-risk Asian American populations (Talley et al., 2008; Ford et al., 2014).

There is a consensus that neither helicobacter pylori identification and eradication nor gastric cancer screening are appropriate for the general populations of low-risk countries (Hillier et al., 2009; Fock, 2014; Lin, 2014; National Cancer Institute, 2014). However, individuals who contributed to the Asia Pacific consensus guidelines on gastric cancer prevention have suggested that guidelines for the identification and eradication of helicobacter pylori infection in Asia should be applied to Asian communities with high gastric cancer rates in Western countries (such as Korean immigrants to the US) (Talley et al., 2008). Additionally, Canadian Cancer Society guidelines already call for helicobacter pylori identification and eradication for Asian immigrants from high-risk countries (Canadian Cancer Society, 2014; Hunt et al., 2004). Both the physician data query screening and prevention editorial board and American society of gastrointestinal endoscopy have suggested that gastric cancer screening be considered for Asian immigrants from geographic areas with high gastric cancer incidence rates (American Society of Gastrointestinal Endoscopy, 2010; 2014; National Cancer Institute, 2014).

Endoscopy has emerged as the preferred gastric cancer screening method in the two Asian countries with national gastric cancer screening programs (Japan and South Korea) (Lin, 2014). Training during gastrointestinal fellowships in the US has not traditionally focused on endoscopic screening to identify pre-malignant gastric lesions and early gastric cancers (Gomez and Wang, 2014). It is unclear how many US gastroenterologists have the expertise to effectively use conventional endoscopy (or newer techniques such as magnification endoscopy and narrow band imaging) to screen for early gastric cancer and its precursors (Fock, 2014; Gomez and Wang, 2014; Lin, 2014). The endoscopic screening capacity would need to be assessed prior to the implementation of any US gastric cancer screening programs for Asian American or other high-risk groups. Additionally, newer endoscopic techniques to treat early gastric cancer such (e.g. endoscopic sub-mucosal dissection) would need to be widely disseminated to optimize screening efforts.

Two studies suggest that a proportion of US physicians are already recommending gastric cancer screening for at least some of their Asian patients. However, both of these studies had small sample sizes and relatively low response rates (Won and Hwang, 2012; Kwon et al., 2013). Population-based needs assessment surveys of primary care physicians and Asian community members (in geographic areas with large Asian populations) should be conducted to examine current provider practices and patient uptake with respect to helicobacter pylori identification and eradication, as well as gastric cancer screening.

The US rice has recommended a shared decision-making approach between clinicians and patients when the evidence is insufficient to guide a decision for or against the execution of a chemoprevention or screening strategy. Clinicians can use decision aids (e.g. video tapes) to ensure that balanced, evidence-based information about a service (including the potential benefits and harms, alternatives, and uncertainties) is available to patients (Sheridan et

al., 2004). In the absence of national guidelines from organizations such as the American Cancer Society and US Preventive Services Task Force, health care providers who serve high-risk Asian groups could consider a shared decision-making approach to the primary (helicobacter pylori identification and eradication) and secondary (gastric endoscopy) prevention of gastric cancer.

## Conclusions

The gastric cancer disparities experienced by some Asian American groups could potentially be impacted through primary prevention programs that promote lifestyle modification and provide treatment to individuals who are infected with helicobacter pylori, as well as secondary prevention programs that identify individuals with gastric cancer precursors and asymptomatic gastric cancers. There is a need for research focusing on the potential outcomes, costs and benefits of alternative approaches to gastric cancer control in Korean and other Asian American populations. Health care providers who serve Asian American patients would benefit from clear national guidelines about shared decision-making versus other approaches to primary and secondary gastric cancer prevention for high-risk Asian communities.

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