

# Development of the Guideline for HIV Testing in South Korea with Low Prevalence of HIV-1 Infection Based on the Expert Consensus<sup>\*</sup>

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# ABSTRACT

**Purpose:** This study was conducted to develop a guideline for HIV testing in South Korea where the HIV prevalence is very low. It is necessary to make the recommendations presented here based on the epidemiology of opportunistic infection and cancer in the community. **Methods:** The development of a guideline for HIV testing was conducted using literature reviews and the agreement of Korean experts for HIV patients using a two-round Delphi consensus technique. Each expert was asked to independently answer to each item related to HIV risk. Ten experts participated in the two-round survey. **Results:** The individual items were determined based on the following categories: high risk behavior, symptom and diseases, colo-rectal diseases, uro-genital diseases and gynecology, skin and oral diseases. The final guideline consisted of 4-scale agreement rating (strongly recommended, recommended, not routinely recommended, no recommendation for routine provision). **Discussion:** We have developed the guideline for HIV testing in a country where the HIV prevalence is low based on a systematic investigation and expert consensus.

Keywords: HIV, Testing, Guideline, Consensus, Delphi Studies

# **1. Introduction**

The HIV prevalence of South Korea is still far less than 0.01% of its population, which is considered to be much lower than that of other countries [1]. Recommendations for HIV testing are already available from the Centers for Disease Control and Prevention (CDC), which was developed by the United States, where there is greater than 1% HIV prevalence. According to a recent survey in South Korea [2], compliance with HIV testing by Korean physicians has been relatively poor due to the low prevalence of HIV infection and insufficient experience with HIV patients in clinics in South Korea. Furthermore, tuberculosis (TB) or viral hepatitis B of general population is still more common, which are considered to be indicative diseases for HIV testing, in Korea compared to the United States statistics [3,4]. Therefore, previous recommendations by the United States may be not applicable to the country whose HIV prevalence is very low,

and a new guideline for HIV testing is required for the use by primary physicians in the community.

Although some individual guidelines for HIV testing are currently available in Korea, these guidelines have been developed by individual medical societies associated with HIV through the Korean NIH and CDC, which had been recognized by only a few physicians in Korean clinics. In addition, these are not new guidelines that were systematically developed. However, It is required to establish the recommendations that were made based on agreements by experts treating HIV patients with consideration of the Korean environment in terms of epidemiology. Accordingly, they need to be appropriately revised to reflect the current prevalence of HIV and other diseases in Korea. Due to the increasing demand and as a preparative measure, we have developed the guideline for HIV testing in South Korea based on a systematic investigation and expert consensus.

# 2. Methods

1) Selection of items for the questionnaire for HIV test-

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The statements for the HIV testing survey were extracted from the CDC recommendations and individual guidelines by Korean medical societies associated with HIV [5-7]. The references that were recently developed in Korea included the HIV/AIDS clinical guide that was published by the Korean Society of Infectious Diseases and the Korean Alliance to Defeat AIDS that focused on Korean methods of HIV testing, diagnosis and confirmation, reporting, and therapy [7]. In the questionnaires, each item was categorized into the following areas. The HIV testing requirements in the questionnaires based on high-risk behaviors were made from the CDC guideline for HIV counseling. Other items for HIV testing requested to special clinics were selected from each guideline developed by Korean Dermatological Association, Korean society of Obstetrics and Gynecology, Korean Society of Coloproctology, Korean Surgical Society, Korean Urological Association, Korean Academy of Dental Sciences, and Korean Society of Emergency Medicine [7].

2) Expert panel selection and guideline development using the two-round Delphi process

This study was conducted from January to February, 2006. Experts for the panel were composed of ten infectious disease specialists in Korea who had AIDS research experience at university hospitals and were also AIDS advisory council in the Korean CDC. To request their participation into the panel, experts were contacted by electronic mail. All ten experts agreed to participate in the survey. The questionnaires were sent to an expert panel via an attached file in an electronic mail and returned to the participants. In the first Delphi round, each panelist was asked to independently respond on a scale (Yes or No). In addition, they were asked to give comments and to suggest new items. After responses were received from the panel, their answers were collected, and the revised questionnaires containing additional items for HIV testing suggested by the panel were returned to them in the second round of the Delphi survey. The newly added items for questionnaires were as follows: homosexual man; oral candidiasis and oral hairy leukoplakia in dental clinic; syphilis; UTI due to rare organisms; prostatitis or prostatic abscess; and any STD in the uro-genital field.

After receiving the responses to the second survey from the expert panel, the final items were categorized into a 4-scale for agreement rating (strongly recommended, seven or more of the ten experts agreed on the need for an HIV screening test; recommended, four to six out of the ten experts agreed; not routinely recommended, one to three of the ten experts agreed; no recommendation for routine provision, no one agreed).

## 3. Results

1) Results of the survey of HIV testing requirement based on high-risk behaviors.

Out of the ten experts surveyed for this study, nine have commonly conducted HIV tests for patients who had unprotected intercourse with prostitutes. Additionally, six have conducted HIV tests on patients who had unprotected intercourse with those who had unknown sex partners. Although only two experts had experienced HIV testing of IV drug abusers who had shared injecting needles, all of the panel members agreed to recommend HIV testing to these individuals. In addition, all experts agreed to recommend HIV testing to patients who had unprotected intercourse with those who had multiple sex partners and to any homosexual men. Although pregnancy is not compatible with HIV-high risk behavior, all of the experts recommended HIV testing of pregnant woman.

2) Survey results of the requirements of HIV testing according to the AIDS case definition by the CDC.

These items are consistent with the opportunistic diseases of HIV and most experts agreed with the necessity of HIV testing of those items listed in Table 2. All ten experts have performed HIV testing of patients with candidiasis of the esophagus, bronchus, and lung. Moreover, nine of the ten experts agreed to recommend the HIV testing to patients with extra-pulmonary cryptococcosis, chronic fatigue, fever for more than 30 days, nonspontaneous weight loss, chronic diarrhea for more than 30 days, and pneumocystis carinii pneumonia. Although the Korean panel has limited experience with chronic cryptosporidiosis, extrapulmonary histoplasmosis, isosporosis, Kaposi sarcoma in individuals younger than 60 years old, progressive multifocal leukoencephalopathy, recurrent nontyphoid salmonellosis, and toxoplasmosis of viscera, the experts accepted the recommendation of HIV testing of patients with these diseases. Only one member of the panel had experience recommending HIV testing to a cervical cancer patient, but six panelists agreed on the need for HIV testing of individuals with invasive cervical cancer. For TB, eight panelists had experience with patients with military TB and four had experience with pulmonary TB patients. However, only four experts recommended HIV testing of patients with pulmonary TB.

3) Survey results of HIV testing of the items in colorectal clinics.

The panel did not have experience with HIV testing of colorectal diseases except for syphilis. However, all of the panel members agreed to recommend HIV testing for

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Questionnaire Items	HIV testing			
Questionnaire items	Experienced Required (1st) Requ		st) Required (2nd)	
A patient who had unprotected intercourse with someone that might be infected STD	5	9	10	
A patient who had unprotected intercourse with someone that has had anonymous sex partners	6	9	10	
A patient who had unprotected intercourse with persons who exchange sex for money or drugs	9	9	10	
A patient who had unprotected intercourse with someone that has had multiple sex partner	3	9	10	
A patient who had shared IV drugs or injecting needle	2	10	10	
A patient who has been diagnosed for viral hepatitis B or C	2	3	1†	
Any homosexual men*	1	1	7	
All pregnant women	1	5	6	

## Table 1. Agreement with items describing HIV testing requirement based on high-risk behaviors.

All items were evaluated by a panel of ten experts; \*Added item following the 1st Survey; †required only for viral hepatitis C.

#### Table 2. Agreement with items describing the requirements for HIV testing according to the AIDS case definition by CDC.

AIDS Case Definition Items	HIV testing		
AIDS Case Definition items	Experienced	Required (1st)	Required (2nd)
Candidiasis of Esophagus, Trachea, bronchus or lung	10	10	10
Invasive cervical cancer	1	6	6
Extrapulmonary cryptococcosis	9	10	10
Cryptosporidiosis, chronic diarrhea (greater than 1 mo)	2	10	10
Cytomegalovirus disease (other than liver, spleen, or nodes)	7	10	10
Herpes simplex: chronic ulcer (greater than 1 month); or bronchitis, pneumonitis or esophagitis	4	10	10
Histoplasmosis, disseminated or extrapulmonary	0	9	9
Dementia of unknown cause	2	8	8
Chronic fatigue and unknown origin of fever more than 1 month	9	10	10
Involuntary weight loss of more than 10%, chronic diarrhea	9	10	10
Isosporiasis, chronic intestinal disease (greater than 1 month)	0	10	10
Kaposi's sarcoma developed in individuals less than 60 years old	2	10	10
Brain lymphoma developed in individuals less than 60 years old	4	10	10
Non-Hodgkin's B cell lymphoma	3	8	6
Disseminated Mycobacterium avium or M. cansasii Infection	7	10	10
Disseminated tuberculosis	8	9	9
Pulmonary tuberculosis	4	6	4
Pneumocystis carinii pneumonia	9	10	10
Recurrent bacterial pneumonia	2	7	7
Progressive multifocal leukoencephalopathy	3	10	10
Recurrent salmonella septicemia	3	8	9
Toxoplasmosis, internal organ	3	9	10

gonococcal infection of the lower rectum and anus, Chlamydia, CMV colitis, Lymphogranuloma venereum, Herpes simplex viral (HSV) infection, syphilis (Chancre, condyloma lata), anal papilloma, anal dysplasia, squamous carcinoma of anorectum, Non-Hodgkin's B cell lymphoma, and Kaposi's sarcoma (**Table 3**).

4) Survey results of HIV testing of the items in urogenital fields.

All ten experts agreed on recommending HIV testing to any patients with syphilis seen in urological or gynecological exams, and of patients with recurrent genital HSV, recurrent Herpes simplex genitalis, severe genital Herpes or candidiasis, other genital ulcers, and refractory or multiple condyloma accuminata. Eight of the ten experts agreed with HIV testing of patients with persistent or recurrent candida vaginitis. In the first survey, HIV testing of patients with pelvic inflammatory disease or abnormal findings upon Pap smear was required by four experts, but in the second survey testing of these individuals was not required by any of the experts. Urinary tract infection and prostatitis or prostatic abscess by rare organisms were newly posted after the first survey, but only two experts agreed with HIV testing of individuals with these items in the second survey.

5) Survey results regarding HIV testing requirements for the items in dermatology and dental clinics

Herpes zoster was found to be the disease for which HIV testing was most often recommended among dermatology diseases, with all ten experts reporting they had performed testing on such individuals. This was followed by recurrent oral candidiasis patients, who have been tested for HIV by seven experts, and patients with anal or genital ulcers, who were tested by six experts. It was also suggested that HIV testing of herpes zoster patients be limited to more specific subjects, such as those who are younger than 50 years old. Some of the items in the dental field overlapped with those in other fields that were removed in the first survey. However, some experts proposed that patients with oral hairy leukoplakia and oral candidiasis be tested for HIV; therefore, they were included in the second survey.

All ten experts agreed to test for HIV in herpes zoster patients that were younger than 50 years old, as well as in patients with anal or genital ulcer, Kaposi's sarcoma, genital warts, bacillary angiomatosis, and oral hairy leukoplakia. It was recommended that patients with molluscum contagiosum of the face or genitalia be tested for HIV by nine of the experts. Moreover, patients with persistent generalized lymphadenopathy, which are lymph nodes more than 1 cm in diameter that are located at more than two sites excluding inguinal areas without other distinct diseases and patients with recurrent oral candidiasis were recommended for HIV testing by eight experts. Six of the experts recommended that patients with bartonellosis and severe eosinophilic purulent folliculitis undergo HIV testing, while five experts recommended that individuals with non-Hodgkin's lymphoma and four of the experts recommended that those with skin T cell lymphoma and recurrent aphthous ulcer undergo HIV testing. Five experts responded that severe gingivitis

Diseases Items		HIV testing	
Diseases items	Experienced	Required (1st)	Required (2nd)
Gonorrhea	2	10	10
Chlamydial infection in recto-anal area	1	10	10
Nonspecific proctitis	2	7	6
CMV proctitis/colitis	4	10	10
Lymphogranuloma venereum	2	10	10
Herpes simplex infection	4	10	10
Syphilis	7	10	10
Idiopathic rectal-anal ulcer	3	8	9
Conlyloma	3	10	10
Anal dysplasia, squamous cancer	1	10	10
Non-Hodgkin's B cell lymphoma, Kaposi's sarcoma	0	10	10
Rare anal cancer; adenocarcinoma, basal cell carcinoma	0	8	7

Table 3. The requirements for HIV testing in colorectal clinics.

should lead to HIV testing in the first survey, but only three experts agreed with this recommendation for the second survey. Other items including squamous cell carcinoma of the skin, melanoma, refractory seborrheic dermatitis, maculopapular rash, recurrent bacterial folliculitis, and generalized Tinea corporis were considered to necessitate HIV testing by four or five experts, but only one or two experts recommended HIV testing of individuals with those diseases in the second survey. Moreover, none of the panel recommended HIV testing of individuals with scabies, atopic dermatitis, drug eruption, pyoderma, skin abscess, cellulitis, and necrotizing fasciitis in the second survey. One expert pointed out that HIV testing was required for patients older than 20 years who developed atopic dermatitis for the first time and for young males who developed maculo-papular rash.

6) Guideline endorsed by the expert panel for HIV testing recommendation in Korea.

All of the questionnaire items considered by the ten experts in Korea are shown in **Tables 1-5**. These items were integrated and developed into a guideline (**Table 6**). The recommendations were categorized into the following four different levels as described in the methods: Strongly-recommended, Recommended, Not routinely recommended, and Not recommended.

## 4. Discussion

The number of HIV-infected patients has been increasing in South Korea since the first HIV-infected person was confirmed in 1985. Indeed, the number of reported cases was more than 6000 in 2009. However, the prevalence of HIV in Korea is still only 0.01% of the national population, which is lower than the average prevalence of the world, which was 0.8% in 2008 [1].

In 2001, the United States CDC recommended routine HIV screening of persons aged 13 - 64 years in medical settings in which the HIV sero-prevalence exceeds 1% [5]. This recommendation was broadened in 2006 to include routine HIV testing for all persons aged 13 - 64 years in all healthcare settings [6]. However, the UK guideline recommends that HIV testing should only be conducted for high-risk groups and in medical settings in local areas in which the prevalence exceeds 0.2% [8]. The European guideline for HIV testing was updated to provide advice for sexually transmitted infection services in 2008 [9]. The WHO recommends HIV testing in countries in which HIV is prevalent, but they clarified that health care providers should not recommend HIV testing to all persons attending health facilities in settings with low-level epidemics [10]. Therefore, it is necessary

Diseases items	HIV testing		
Diseases items	Experienced	Required (1st)	Required (2nd)
Syphilis	2	2	10
Any STD	1	1	9
UTI due to rare organisms	0	1	2
Prostatitis or prostatic abscesses	0	1	2
Recurrent Herpes simplex genitalis*	3	8	10
Severe genital Herpes or candidiasis	1	9	10
Other genital ulcer	3	9	10
Refractory or multiple Condyloma accuminata	2	9	10
Abnormal findings in Pap smear	0	4	0
Any PID	1	4	0
Any STD	3	8	10
Persistent or recurrent candida vaginitis**	1	7	8

Table 4. Agreement with items describing HIV testing requirements in uro-genital field.

\*Twice during six months or more than four times per year, the cases occurring two times in frequency though one year; \*\*Persistent diseases after two rounds of treatment, twice during six months or more than four times per year, the cases occurring two times in frequency through one year; <sup>†</sup>All items in the Urology department were suggested by experts following the first survey.

Issues for Description and Description	HIV testing		
Items for Dermatology and Dental Clinics	Experienced	Required (1st)	Required (2nd)
Herpes zoster, age <50 years old	10	9	10
Ulcer of anal or genital area	6	10	10
Molluscum contagiosum in face, genitalia	2	8	9
Scabies	0	4	0
Bartonellosis	0	7	6
Kaposi's sarcoma	4	10	10
Non-Hodgkins's lymphoma	1	6	5
Skin T cell lymphoma	0	6	4
Squamous cell carcinoma	0	5	2
Melanoma	0	5	2
Severe eosinophilic purulent folliculitis	1	6	6
Psoriasis	1	2	0
Refractory seborrheic dermatitis	1	5	2
Atopic dermatitis	0	2	0
Drug eruption	1	1	0
Maculopapular rash	2	4	2
Persistent generalized lymphadenopathy*	2	9	8
Generalized Tinea corporis	2	4	1
Genital condyloma	2	7	10
Recurrent bacterial folliculitis	1	4	2
Pyoderma, abscess, cellulitis, necrotizing fasciitis	1	2	0
Bacillary angiomatosis	1	7	10
Recurrent oral candidiasis	7	10	8
Oral hairy leukoplakia	2	9	10
Recurrent aphthous ulcer	2	4	4
Severe gingivitis, periodontitis	3	5	3

#### Table 5. Agreement with items describing HIV testing requirements in dermatology and dental clinics.

\*Lymph nodes more than 1 cm in diameter located in more than two sites except inguinal areas without other distinct diseases.

to establish a Korean national recommendation for HIV testing that reflects the prevalence of infectious diseases in Korea. This is the first study to integrate evidence available in the literature, several recommendations for other countries, and Korean expert consensus using a Delphi survey [11].

The experts agreed on an HIV testing requirement for all high-risk behaviors, except for viral hepatitis B or C. The United States guideline recommends HIV testing of hepatitis B positive patients, but the Korean guidelines do not consistently adopt this recommendation. This is likely due to the difference in the prevalence of viral hepatitis B. The sero-prevalence of chronic hepatitis B was about 3.7% in South Korea in 2005 [3]. In contrast, the prevalence of hepatitis B in the United States was about 0.3% - 0.5% in 2006 [12]. The physicians who participated in the present survey considered viral hepatitis B to be too common to recommend HIV testing in

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### Table 6. The guideline endorsed by the expert panel for HIV testing recommendation in Korea.

Strongly recommended		
A. High risk behaviors		
A patient who had unprotected intercourse with someone that might be infected with an STD		
A patient who had unprotected intercourse with someone that has had an anonymous sex partner		
A patient who had unprotected intercourse with someone that has exchanged sex for money		
A patient who had unprotected intercourse with someone that has had multiple sex partners		
A patient who has shared IV drug or injecting needle		
Any homosexual men		
B. Symptom and Diseases		
Candidiasis in esophagus, trachea, bronchus or lung		
Extrapulmonary cryptococcosis		
Cryptosporidiosis accompanying chronic diarrhea for more than 1 month		
Cytomegalovirus disease (other than liver, spleen, or nodes)		
Herpes simplex viral infections: chronic ulcer (s) (duration greater than 1 month)		
HSV bronchitis, pneumonitis, or esophagitis		
Extrapulmonary Histoplasmosis		
Dementia, unknown origin		
Involuntary weight loss greater than 10% and unknown fever for greater than 30 days		
Isosporiasis, chronic intestinal (duration greater than 1 month)		
Kaposi's sarcoma in individual less than 60 years old		
Brain lymphoma in individual less than 60 years old		
Disseminated Mycobacterium avium or M. cansasii		
Disseminated tuberculosis		
Pneumocystis carinii pneumonia		
Recurrent bacterial pneumonia		
Progressive multifocal leukoencephalopathy		
Recurrent salmonella bacteremia		
Toxoplasmosis of internal organ		
C. Colo-rectal Diseases		
Gonorrheal diseases in rectum and anal canal		
Chlamydial infection, CMV colitis in rectum and anal canal		
Lymphogranuloma venereum		
Herpes simplex infection		
Syphilis		
(diopathic rectal ulcer		
Condyloma		
Dysplasia		
Non-Hodgkin's B cell lymphoma, Kaposi samcoma		
Rare anal cancer; adenocarcinoma, small cell cancer, basal cell carcinoma		
D. Uro-genital Diseases/Gynecology		
Syphilis		
Sexually Transmitted Diseases		
Recurrent Herpes simplex genitalis (Twice during six months or more than four times per year,		
Severe genital Herpes or candidiasis		

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Other genital ulcer
Refractory or multiple Condyloma accuminata
Persistent or recurrent candida vaginitis (Occurring after two rounds of treatment, twice during six months or more than four times per year)
E. Skin and Oral Diseases
Herpes zoster in individuals less than 50 years old
Ano-genital ulcer
Molluscum contagiosum on face, genitalia
Generalized persistent lymphadenopathy (Lymph nodes greater than 1 cm in diameter
located in more than two sites except inguinal areas without other distinct diseases)
Genital warts
Bacillary angiomatosis
Recurrent oral candidiasis
Oral hairy leukoplakia

Recommended		
A. High-risk Behavior	C. Colorectal Diseases	
Pregnancy	Nonspecific proctitis	
B. Symptom and Diseases	D. Skin and Oral Diseases	
Invasive cervical cancer	Bartonellosis	
Non-Hodgkin's B cell lymphoma	Non-Hodkin's lymphoma	
Pulmonary tuberculosis	Skin T cell lymphoma	
	Severe eosinophilic pustular folliculitis	
	Recurrent aphthous ulcer	

Not routinely recommended

A. Symptom and Diseases
Viral Hepatitis C
B. Uro-genital Diseases
Urinary Tract Infection by rare organisms
Prostatitis or prostatic abscess
C. Skin and Oral Diseases
Squamous cell carcinoma
Melanoma
Refractory seborrheic dermatitis
Maculopapular rash
Generalized Tinea corporis
Recurrent bacterial folliculitis
Severe periodontitis, gingivitis

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No recommendation for routine provision

A. Symptom and Diseases
Viral hepatitis B
B. Uro-genital Diseases
Abnormal Pap smear findings
Pelvic inflammatory diseases
C. Skin & Oral Diseases
Scabies
Psoriasis
Atopic Dermatitis
Drug eruption
Pyoderma, abscess, cellulitis, necrotizing fasciitis

Korea.

In 2001, the CDC recommended all pregnant women undergo an HIV test as part of routine screening for prenatal care [13]. The universal HIV screening for the prenatal period and HAART therapy demonstrated that 20% of the perinatal transmission cases decreased to less than 2% due to the recommendation for HIV testing [14,15]. Therefore, despite the low HIV prevalence among Korean women, experts recommended routine screening of pregnant women for HIV based on evidence for the reduction of perinatal HIV transmission when it was detected early.

As shown in Table 2, most of the panel members agreed to the recommendation for screening of individuals with the opportunistic diseases mentioned in the AIDS-surveillance case definition [16]. The prevalence of TB is relatively high in Korea, with 18,000 (0.039%) smear positive and 224,000 (0.32%) radiologically active TB patients being present in 2006 [4]. In contrast, the United States reported only 4.2 cases of TB per 100,000 in 2008, which was 10-fold lower than that of the Korean smear-positive cases [17]. TB prevalence is also decreasing in Korea, but it is an important opportunistic infection of HIV patients. Therefore, although TB is still prevalent in Korea, our expert panel recommended HIV testing of individuals diagnosed with TB. Meanwhile, in the uogenital and anorectal field, most experts in this study agreed to recommend HIV testing of individuals with well-known AIDS defining opportunistic infections or cancer. However, it was not recommended that individuals with nonspecific diseases of the skin such as scabies, atopic dermatitis, drug eruption, and psoriasis undergo HIV testing. All the recommendations were integrated, scaled and completed to a guideline.

Since 2006, the CDC has recommended universal HIV testing at hospitals, but it was reported that many physicians did not routinely provide HIV tests [18], and only 35.8% of residents of internal medicine in New York administered HIV tests [19]. The CDC recommends HIV testing of newly diagnosed TB patients. In the United States, 63% of TB patients were tested for HIV in 1993, but only 37% of such patients were tested in Singapore in 2006 [20,21]. This discrepancy suggests that the guide-line should be publicized to practicing doctors. This guideline could help Korean physicians properly apply HIV testing to their patients.

In summary, this literature review and Korean expert consensus conducted through the Delphi process resulted in the development of guideline for HIV testing reflecting national epidemiology of HIV-indicating diseases, which were different points compared with both CDC in US recommending universal HIV testing at hospital. The guideline presented here should be revised again according to the change of HIV-prevalence.

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#### 6. Author Disclosure Statement

Hee Jung Choi, Kyoung Ae Kong, Jung Won Min, Hun-Jae Lee and Hae-Sook Park have no potential conflicts of interest to disclose.

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