Table 3. Case–control studies dealing with cervical cancer screening using conventional cytology

Authors	Published year	Research area	Target age	Numbers		Screening rate		Endpoint	Odd ratio (95% CI) Relative protection (95% CI)[a]
				Case	Control	Case	Control		
Macgregor et al. (8)	1994	Scotland	25–60 years	15	150	35%	73%	Cervical cancer mortality	Reference: women with a negative screening result obtained within 5 years; screening history in past 5–10 years, 1.63 (90.62–4.25)[a]; screening history in past 10 years or more, 2.20 (0.86–5.60)[a]; no screening history, 6.75 (3.43–13.41)
Sobue et al. (9)	1988	Japan	≤80 years	15	150	6.7%	53.3%	Cervical cancer mortality	0.22 (0.33–1.95)
Macgregor et al. (10)	1985	Scotland	Unclear	(i) Symptomatic cancer 35 and (ii) Stage 1 50	(i) 139 and (ii) 250	Unclear	Unclear	(i) Symptomatic cancer and (ii) Stage 1	Reference: women with a negative screening result obtained 10 or more years previously (i) 30–47 months, 3.5 (1.1–2.2)[a]; 48–71 months, 1.9 (0.8–6.5)[a]; 72–79 months, 1.0 (0.4–3.9)[a]; (ii) 30–47 months, 6.6[a]; 48–71 months, 10.5[a]; 72–119 months, 2.1[a]
Yang et al. (11)	2008	Austo	20–69 years	877	2614	33.3%	87.3%	Invasive cancer	Reference: women without Pap test One time screening history 0.152 (0.119–0.194); two times screening history 0.043 (0.033–0.057)
Hernández-Avila et al. (12)	1998	Mexico	Average case: CIS, 44.7 years; invasive cancer, 47.7 years; control, 48 years	CIS, 233; invasive cancer, 397	1005	CIS, 42.4%; invasive cancer, 42.4%	50.70%	CIS and invasive cancer	CIS, 0.68 (0.45–1.00); invasive cancer, 0.38 (0.28–0.52)
Sato et al. (13)	1997	Japan	35–79 years; average: case, 49.0 years; control, 48.8 years	109	218	55.0%	88.5%	Invasive cancer	0.16 (0.090–0.278)
Jiménez-Prez and Thomas (14)	1999	Mexico	≤70 years; average: case, 49.5 years; control, 49.1 years	143	311	54.6%	81.7%	Invasive cancer	0.3 (0.2–0.4)
Palli et al. (15)	1990	Italy	≤75 years	191	540	18.8%	47.7%	Invasive cancer	0.15 (0.09–0.25)
Herrero et al. (16)	1992	Colombia, Mexico, Costa Rica and Panama	≤70 years	759	1430	50.1%	71.0%	Invasive cancer	No screening history, 2.5 (2.1–3.3)[a]
Celentano et al. (17)	1989	USA	21–84 years	153	(i) Neighborhood 153; (ii) random selection 392	153	(i) 92.8%; (ii) 91.1%	Invasive cancer	(i) 4.30 (1.46–12.7)[a]; (ii) 3.63 (1.38–9.57)[a]
Makino et al. (18)	1995	Japan	35–79 years	198	396	48.4%	83.8%	Invasive cancer	0.14 (0.088–0.230)

[a]Relative protection (inverse of relative risk).

Table 4. Accuracy of cervical cancer screening (conventional and liquid-based cytology, HPV testing)

Authors	Published year	Target age group	Definition of true-positive cases	Method for follow-up	Follow-up years	Conventional cytology			Liquid-based cytology			HPV testing (alone)		Combination of HPV testing and liquid -based cytology	
						Cut -off point	Sensitivity	Specificity	Cut -off point	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Yoshida et al. (38)	2001	Unclear	COI	Cancer registry	1 year	LSIL	94.7	98.7	–	–	–	–	–	–	–
Strander et al. (47)	2007	23–60 years	CIN2	Regional database for prevention of cervical cancer	2 years 9 months	–	–	–	–	Relative sensitivity compared conventional cytology Follow-up 1.5 years 1.60 (1.12–2.28); follow-up 3–7 years 1.51 (1.13–2.01)	–	–	–	–	–
Taylor et al. (39)	2006	35–64 years	CIN1	Diagnostic tests (Coloposcopy)	–	ASCUS	83.6 (71.2–92.2)	94 (92–96)	ASCUS	70.6 (58.3–81.0)	84.8 (83.5–86.1)	–	–	–	–
						LSIL	69.1 (55.2–80.9)	94.5 (93.5–95.4)	LSIL	60.3 (47.7–71.9)	94.1				
Cochand-Priollet et al. (40)	2005	High-risk group average 37.8 years	CIN1	Diagnostic tests (Coloposcopy)	–	ASCUS	85 (81–89)	92 (89–94)	ASCUS	78 (73–83)	94 (93.2–94.9)	80 (74–86)	54 (49–60)	80 (74–86)	93 (90–96)
		Screening group average 33.3 years					60 (45–75)	99 (99–99)		65 (50–80)	98 (98–99)	96 (88–100)	85 (83–87)	76 (59–93)	97 (97–98)
Cecchini et al. (41)	1989	18–60 years	Invasive cancer	Cancer registry	9 years	–	Screening interval: 1 year, 0.9; 3 years, 0.78; 5 years, 0.68	–	–	–	–	–	–	–	–
Belinson et al. (48)	2002	35–45 years	CIN2	Cancer registry	–	–	–	–	(i) ASCUS; (ii) LSIL; (iii) HSIL	(i) 94; (ii) 87; (iii) 77	–	–	–	–	–
			CIN3						(i) ASCUS; (ii) LSIL; (iii) HSIL	–	(i) 78; (ii) 94; (iii) 98				

CIN, cervical intraepithelial neoplasia; ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.

cytology (so called relative sensitivity) was calculated. The relative sensitivity was reported to be 1.60 (95% CI: 1.12–2.28) compared with that of conventional cytology based on 1.5 years of follow-up (40). In a systematic review of 24 studies using Thin Prep, the sensitivity was 68% for conventional cytology and 76% for liquid-based cytology, and the specificity was 79% and 86%, respectively (45).

HPV Testing (Level of Evidence: 2−)

There have been no studies that evaluated the reduction in mortality from cervical cancer. Although RCTs were performed, the defined outcomes were sensitivity, specificity and positive predictive value (PPV); the reductions in cervical cancer incidence and mortality are unclear. To detect CIN2 or worse, the sensitivity of HPV testing is always higher than that of conventional cytology. When the target lesion is changed to detect CIN3 or worse, the sensitivity of HPV testing is equal to or higher than that of conventional cytology. The high CIN detection rate does not lead to an absolute reduction in the incidence of invasive cancer because there is a high possibility of no progression. Both the specificity and PPV are lower than those of conventional cytology. The high sensitivity of HPV testing suggests the possibility of reducing mortality from cervical cancer. At present, there is insufficient evidence to determine its role based on studies that reported test accuracy alone.

Test Accuracy: Randomized Controlled Trials

The RCTs that compared HPV testing and conventional cytology were conducted in three countries (Canada, Italy and Finland; Table 5) (42,43,49–52). The design of these studies differed based on each country's current system of cervical cancer screening. In the Swedish study, accuracy was calculated in the experimental arm within the RCT (43).

When the cut-off point was changed, the relative sensitivity decreased in the Finnish study (52) and the Italian study (49). The Italian study compared HPV testing to conventional cytology, and the relative sensitivity of HPV testing to detect CIN2 or worse was 1.92 (95% CI: 1.28–2.87) in the 35–60 years age group and 3.50 (95% CI: 2.11–5.82) in the 25–34 years age group (49). When the target disease was changed to CIN3 or worse, the relative sensitivity of HPV testing was higher in the younger group: 2.06 (95% CI: 1.16–3.68) in the 35–60 years age group and 2.61 (95% CI: 1.21–5.61) in the 25–34 years age group. However, the sensitivity and the specificity were similar to both cut-off points in the Swedish study.

Test Accuracy: Otiher Designs

In the systematic review, the sensitivity to detect CIN2 or worse was 96.1% (95% CI: 94.2–97.4) for HPV testing and 53.0% (95% CI: 48.6–57.4) for conventional cytology (45). When the target disease was changed to CIN3 or worse, the sensitivity of HPV testing was 96.1% and that of conventional cytology was 55.0%. However, the specificity for excluding CIN2 or worse was higher for conventional cytology than for HPV testing. In this study, methods of HPV testing were combined with HC 1 and 2, and polymerase chain reaction.

In split-sampling studies that compared sensitivity between HPV testing and conventional cytology, the sensitivity to detect CIN2 or worse was higher with HPV testing than with conventional cytology, but the specificity was the opposite (53–56). The most serious problem when comparing both the methods was that the test accuracy differed among countries. Cuzick et al. (57) calculated the sensitivity and the specificity limited to the 35 years and over age group based on the diagnostic test for positive results. When the target disease was changed to CIN3 or worse, the sensitivity of HPV testing was 96.0% and that of conventional cytology was 82.4%. However, the specificity of both methods was almost equal: 95.4% for HPV testing and 96.4% for conventional cytology. In this study, the results suggested that HPV testing may be a possible screening method when the target age group is limited to 35 years and over.

Combination of HPV Testing and Cytology (Level of Evidence: 2−)

HPV Testing with Cytology Triage (Level of Evidence: 2−)

Although RCTs were performed with defined outcomes of sensitivity, specificity and PPV, no studies evaluated the reduction in mortality from cervical cancer. The sensitivity of both methods was higher than that of conventional cytology, and the specificity was lower. The high sensitivity of the combination with HPV testing suggests that it may reduce mortality from cervical cancer. Increased sensitivity reflects the inclusion of regressing lesions. Although the specificity is lower than that of conventional cytology, the PPV could be improved by using HPV testing with cytology triage. There is insufficient evidence to determine the role of this approach based on the studies that reported test accuracy only.

Test Accuracy: Combination of HPV Testing and Cytology

Two RCTs were conducted in the Netherlands and in Italy (Table 6) (51,58,59). In the studies conducted in Sweden, sensitivity was calculated within the intervention arm in the RCT (42,43). The methods in these studies included several options using HPV testing compared with conventional cytology.

The Dutch study involved subjects in the 29–56 years age group who participated in regular screening programs (58). The incidence of CIN3 or worse was 70% higher at baseline with the combination method than with cytology screening (68 of 8575 vs. 40 of 8580, $P = 0.007$). In the subsequent round, the numbers of cases of CIN3 and invasive cancer reversed between the groups (24 of 8413 vs. 54 of 8456, $P = 0.007$). The total numbers of cases of CIN3 and

Table 5. Accuracy of HPV testing alone

Authors	Country/study	Published year	Target age	Numbers in target population		Cut-off point of cytology	Target disease: CIN2			Target disease: CIN3		
				Conventional cytology	HPV testing		Sensitivity/ relative sensitivity	Specificity	Positive predictive value/relative positive predictive value	Sensitivity/ relative sensitivity	Specificity	Positive predictive value/relative positive predictive value
Kotaniemi-Talonen et al. (52)	Finland	2008	30–60 years	30 585	30 564	LSIL	1.64[a] (95% CI: 1.08–2.49)	HPV testing, 92.9% (95% CI: 92.6–93.3)	HPV testing, 5.4%: (95% CI: 4.3–6.6)	1.10[a] (95% CI: 0.57–2.12)	HPV testing, 92.7% (95% CI: 92.3–93.0)	HPV testing1.5% (95%CI:0.9–2.2)
								Conventional cytology, 99.3% (95% CI: 99.1–99.4)	Conventional cytology, 27.6% (95% CI: 21.5–34.4)		Conventional cytology, 99.0% (95% CI: 99.0–99.2)	Conventional cytology, 10.1% (95% CI: 6.2–15.1)
Mayrand et al. (42)	Canada	2007	30–69 years	5059	5055	ASCUS	HPV testing, 94.6% (95% CI: 84.2–100.0)	HPV testing, 94.1% (95% CI: 93.4–94.8)	HPV testing, 6.4% (95% CI: 5.0–8.0)	–	–	–
	Canadian Cervical Cancer Screening Trial Study Group						Conventional cytology, 55.4% (95% CI: 33.6–77.2)	Conventional cytology, 96.8% (95% CI: 96.3–97.3)	Conventional cytology, 7.1% (95% CI: 4.8–10.3)	–	–	–
Ronco et al. (49)	Italy	2008	25–60 years	24 535	24 661	ASCUS	25–34 years: 3.50[a] (95% CI: 2.11–5.82)	–	25–34 years: 0.89[b] (95% CI: 0.55–1.44)	25–34 years: 2.61[a] (95% CI: 1.21–5.60)	–	25–34 years: 0.66[b] (95% CI: 0.31–1.40)
	New Technologies for Cervical Cancer Screening Working Group						35–60 years: 1.92[a] (95% CI: 1.28–2.87)		35–60 years: 0.80[b] (95% CI: 0.55–1.18)	35–60 years: 2.06[a] (95% CI: 1.16–3.68)	–	35–60 years: 0.86[b] (95% CI: 0.49–1.52)
Naucler et al. (43)	Sweden	2009	32–38 years	–	6257	ASCUS	HPV testing 95.4% (95% CI: 88.6–98.7)	HPV testing 94.2% (95% CI: 93.5–94.7)	HPV testing 19.2% (95% CI: 15.6–23.2)	HPV testing 96.0% (95% CI: 86.3–99.5)	HPV testing 93.6% (95% CI: 93.0–94.2)	HPV testing 11.1% (95% CI: 8.3–14.4)
							Conventional cytology 71.3% (95% CI: 60.6–80.5)	Conventional cytology 98.6% (95% CI: 98.3–98.5)	Conventional cytology 42.5% (95% CI: 34.6–50.9)	Conventional cytology 74.0% (95% CI: 59.7–85.4)	Conventional cytology 98.2% (95% CI: 97.9–98.5)	Conventional cytology 25.3% (95% CI: 18.5–33.2)

[a]Relative sensitivity.
[b]Relative positive predictive value.

Table 6. Accuracy of combination of HPV testing and cytology

Authors	Country/study	Published year	Target age	Cut-off point of cytology	Numbers in target population		Target disease: CIN2		Specificity	Target disease: CIN3	
					Conventional cytology	Combination of HPV testing and conventional cytology	Sensitivity/relative sensitivity	Positive predictive value/relative positive predictive value		Sensitivity/relative sensitivity	Positive predictive value/relative positive predictive value
Naucler et al. (43)	Sweden	2009	32–38 years	ASCUS	–	6257	HPV testing + cytology 100% (95% CI: 95.8–100.0)	HPV testing + cytology 38.1% (95% CI: 31.6–44.9)	–	HPV testing + cytology 100% (95% CI: 92.9–100.0)	HPV testing + cytology 22.0% (95% CI: 16.7–44.9)
							Cytology 71.3% (95% CI: 60.6–80.5)	Cytology 42.5% (95% CI: 34.3–50.9)		Cytology 74.0% (95% CI: 59.7–85.4)	Cytology 25.3% (95% CI: 18.5–33.2)
Bulkmans et al. (58)	The Netherland	2007	29–56 years	ASCUS	9196	9207	First round 1.56[a]	–	–	First round 1.70[a]	–
							Second round 0.53[a]			Second round 0.45[a]	
Ronco et al. (59)	Italy	2006	25–34 years	ASCUS	6002	5808	1.61[b] (95% CI: 1.05–2.48)	0.55[b] (95% CI: 0.37–0.82)	–	0.70[b] (95% CI: 0.37–1.34)	0.24[b] (95% CI: 0.13–0.45)
	New Technologies for Cervical Cancer Screening Working Group		35–60 years		16 658	16 706	1.47[b] (95% CI: 1.03–2.09)	0.40[b] (95% CI: 0.23–0.66)		1.25[b] (95% CI: 0.78–2.01)	0.34[b] (95% CI: 0.21–0.54)

[a]Relative sensitivity.
[b]Relative positive predictive value.

invasive cancer did not differ between the groups ($P = 0.89$). The increased incidence in the intervention group at the baseline was based on the lead time.

The Italian studies reported two age groups: 25–34 and 35–64 years. Although CIN2 or worse was detected more often with a combination of HPV testing and cytology than with cytology alone in both age groups (1.47 for 25–34 years and 1.61 for 35–64 years), the PPV was lower than with cytology alone (51,59). When the target lesion was limited to CIN3 or worse, the relative sensitivity of combined HPV testing and cytology was higher than with cytology alone in the 35–64 years age group only (1.58, 95% CI: 1.03–2.44). The PPV for CIN3 or worse was lower in both age groups. However, the results of first and subsequent rounds were consistent in both age groups.

Test Accuracy: HPV Testing with Cytology Triage

Three RCTs were conducted in Finland, Sweden and Italy (Table 7) (43,50–52,59). In the Swedish study, the detection of CIN2 or worse using HPV testing with cytology triage was increased by 51% (relative risk = 1.51, 95% CI: 1.13–2.02) compared with the control group using cytology alone for prevalence screening (50). However, in subsequent screening, the incidence was reduced by 42% (relative risk = 0.58, 95% CI: 0.36–0.96). The increased incidence of CIN2 diagnosed at the initial screening in the intervention group was not followed by a statistically significant reduction in CIN2 at later screening. Although HPV testing as an adjunct to cytology increased sensitivity, the lesions might regress spontaneously.

In the Finnish study, compared with conventional cytology, the relative sensitivity of HPV screening with cytology triage for CIN2 or worse was 1.64 (95% CI: 1.08–2.49), but that for CIN3 or worse was equal (1.10, 95% CI: 0.57–2.12) (52). The specificity for CIN2 or worse was 99.1% (95% CI: 99.0–99.2) and that for CIN3 or worse was 98.8% (95% CI: 98.7–99.0). Compared with conventional cytology, the specificity was lower when the target disease was changed.

In the Italian study, which targeted the 35–60 years age group, the relative sensitivity compared with cytology for CIN2 or worse was 1.02 (95% CI: 0.69–1.50), and it was 0.96 (95% CI: 0.58–1.59) for CIN3 or worse (51). The PPV was improved: 1.66 (95% CI: 1.16–2.36) for CIN2 or worse and 1.57 (95% CI: 0.97–2.54) for CIN3 or worse.

Harms of Cervical Cancer Screening

Cervical cancer screening is not associated with serious adverse effects. However, three major points must be considered as harms of cervical cancer screening.

Overdiagnosis

Increasing detection of CIN is likely to result in overdiagnosis, since most mild lesions regress. Within 10 years, mild and moderate dysplasia regressed by 87.7% and 82.9%, respectively (60). On the other hand, mild and moderate dysplasia progressed to severe or worse by 9.9% and 32.0%, respectively. Although the sensitivity of HPV screening is higher than that of cytology, the high detection rate of CIN could lead to overdiagnosis (49–52).

Diagnostic Examinations

Colposcopy with and without punch biopsy is used as the standard diagnostic examination. Although some bleeding may occur following biopsy, there are no serious adverse effects.

Loop Electrosurgical Excision Procedure

LEEP including conization is used to exclude CIN lesions. For maintenance of fertility, LEEP is often performed for young females. There were ambivalent reports about whether LEEP was associated with preterm delivery or not (61–66). It is difficult to make conclusions about the adverse effects of LEEP, since both increases and no effect on pregnancy loss in the early gestation period have been reported.

DISCUSSION

In the present systematic review, sufficient evidence for cervical cancer screening using conventional and liquid-based cytology was identified. Although the technique for transferring the cellular materials to a microscope slide differs between the two methods, collecting cells from the uterine cervix and the microscopic analysis was the same. The results of evaluation studies using conventional cytology have been conducted worldwide, and these results have been consistent. Although there were limitations because of the potential bias of ecological studies, the studies of conventional screening were sufficient to sustain the evidence for reduced mortality from cervical cancer. In addition, both the sensitivity and the specificity of liquid-based cytology were similar to those of conventional cytology based on many studies that included important factors that were part of the analytic framework for cervical cancer screening. Therefore, we decided that the evidence for liquid-based cytology was at a 2+ level, because the mortality reduction was as valid as that for conventional cytology. On the other hand, HPV testing is a new technology that is different in its basic concept and its procedure for measurement. To date, the effect of HPV testing on mortality reduction in cervical cancer has not been properly evaluated. The results of five RCTs concerning HPV testing have been published, but the outcomes of these studies were sensitivity, specificity and PPV for CIN2 or worse. Three methods using HPV testing were evaluated based on these studies. Although the sensitivity is increased with all methods, the specificity is not improved compared with conventional cytology alone. An

Table 7. Accuracy of HPV testing with cytology triage

Authors	Country/study	Published year	Target age	Cut-off point of cytology	Numbers in target population		Target disease: CIN2			Target disease: CIN3		
					Conventional cytology	HPV testing with cytology triage	Sensitivity/ relative sensitivity	Specificity	Positive predictive value/relative positive predictive value	Sensitivity	Specificity	Positive predictive value
Kotaniemi-Talonen et al. (52)	Finland	2008	30–60 years	LSIL	30 585	30 564	1.64[a] (95% CI: 1.08–2.49)	HPV testing with cytology triage 99.1% (95% CI: 99.0–99.2) Cytology 99.3% (95% CI: 99.1–99.4)	HPV testing with cytology triage 32.4% (95% CI: 26.6–38.6) Cytology 27.6% (95% CI: 21.5–34.4)	1.10[a] (95% CI: 0.57–2.12)	HPV testing with cytology triage 99.1% (95% CI: 99.0–99.2) Cytology 99.3% (95% CI: 99.1–99.4)	HPV testing with cytology triage 8.9% (95% CI: 5.7–13.2) Cytology 10.1% (95% CI: 6.2–15.1)
Naucler et al. (43)	Sweden	2009	32–38 years	ASCUS	6270	6257	Prevalence screening 1.51 (95% CI: 1.31–2.02) Interval screening 0.58 (95% CI: 0.36–0.96)	–	–	Prevalence screening 1.31 (95% CI: 0.92–1.87) Interval screening 0.53 (95% CI: 0.29–0.98)	–	–
Ronco et al. (51)	Italy	2006	25–34 years	ASCUS	6002	5808	HPV testing ≥1 pg/ml 1.58[a] (95% CI: 1.03–2.44)	–	HPV testing ≥1 pg/ml 0.78[b] (95% CI: 0.52–1.16)	HPV testing ≥1 pg/ml 0.66 (95% CI: 0.34–1.27)	–	HPV testing ≥1 pg/ml 0.33[b] (95% CI: 0.17–0.61)
	New Technologies for Cervical Cancer Screening Working Group						HPV testing ≥2 pg/ml 1.58[a] (95% CI: 1.03–2.44)		HPV testing ≥2 pg/ml 0.84[b] (95% CI: 0.56–1.25)	HPV testing ≥2 pg/ml 0.66 (95% CI: 0.34–1.27)		HPV testing ≥2 pg/ml 0.35[b] (95% CI: 0.19–0.66)
Ronco et al. (51)	Italy New Technologies for Cervical Cancer Screening Working Group	2006	35–60 years	ASCUS	16 658	16 706	1.02[a] (95% CI: 1.16–2.36)	–	1.66[b] (95% CI: 1.16–2.36)	0.96[a] (95% CI: 0.58–1.59)	–	1.57[b] (95% CI: 0.97–2.54)

[a]Relative sensitivity.
[b]Relative positive predictive value.

appropriate method that includes HPV testing may reduce the incidence and mortality of cervical cancer. However, at present, there is no conclusive evidence of the effect of HPV testing.

After the guideline draft was completed, the cluster RCT in India and the results of the second round of the ARTISTIC (A Randomized Trial in Screening to Improve Cytology) study were published. In the HPV testing group, mortality from cervical cancer was reduced by 48% compared with the control group that received standard care (hazard ratio = 0.52, 95% CI: 0.33–0.83) (67). No significant reductions in advanced cancer and death from cervical cancer were observed in the cytology and visual inspection groups. This is the first report to evaluate mortality reduction in cervical cancer by HPV testing. However, the Indian RCT had several limitations that need to be considered. Although cervical cancer was detected more in the cytology group than in the HPV testing group, there was no decrease in invasive cancer and death in the cytology group. Since there is little screening for cervical cancer in India, few women had previous screening histories (67,68). Although the characteristics of the four clusters were nearly equal, smoking habit and medical services use were unclear. It might be suggested that there were differences in the incidence of cervical cancer among the four clusters. On the other hand, in the ARTISTIC study, for the first and second round combined, the proportion of women with CIN3 or worse was similar for liquid-based cytology screening and for the combination of liquid-based cytology screening and HPV testing (69). The result was nearly equal to those of the Dutch and Swedish studies, which were selected as the evidence for our guideline. In addition, to detect CIN3 or worse, the sensitivity of liquid-based cytology alone was only slightly higher than that of HPV testing with cytology triage and of cytology with HPV triage. Although the effect of HPV testing was only shown by the Indian clustered RCT, changing the current recommendation is not warranted, given the limitations of the study and the different healthcare system in Japan.

Around 1960, cervical cancer screening using the Pap smear was started in Miyagi Prefecture, and this approach was adopted nationwide. In 1983, under the Health Service Law for the Aged, cervical cancer screening was introduced for all residents aged 40 years and over. Previous guidelines published in 2001 recommended cytology screening using the conventional method, not liquid-based cytology. HPV testing was not recommended because of insufficient evidence (2). There was no change in the implementation of cervical cancer screening because new technologies were not common in 2001. In 2003, the target age and screening interval were changed based on changes in the age distribution of both cancers and the limited resources available for screening programs. The target age group was expanded from 30 years and over to 20 years and over, and the screening interval was prolonged from 1 year to every 2 years (70). The purpose of this change was to increase the opportunities for testing for women who had never participated in cervical cancer screening. However, screening uptake increased slightly after the change in the screening interval in 2004. In 2006, 3.3 million women participated in population-based screening for cervical cancer; the screening uptake has been around 18% (71).

In developed countries, population-based screening for cervical cancer has been conducted since the 1960s. Nordic countries and the UK have organized screening systems to reduce mortality from cervical cancer. A well-organized screening program could achieve high coverage of the target population and demonstrate good quality at all levels. European guidelines recommended 3–5-year screening intervals depending on available resources (72). The USPSTF (US Preventive Services Task Force) recommended at least a 3-year interval, but others recommended annual screening in the USA. The target group differs among the countries, but mainly includes the 30–60 years age group (73). The IARC handbook concluded that organized programs should not include women aged less than 25 years (4). On the other hand, American guidelines, including the USPSTF, recommended that screening should begin within 3 years of starting sexual activity or at 21 years (73–78). In 2009, the American College of Obstetricians and Gynecologists revised the guideline and starting age was changed to 21 years of age regardless of sexual history to avoid unnecessary and harmful diagnostic tests and treatment (79). In a recent study in the UK, compared with the substantial reduction in mortality in older women, cervical screening in women aged 20–24 years has little or no impact on the rate of invasive cancer up to age 30 years (80). Although we could find several studies including the 20–29 years age group, the mortality reduction in this age group was uncertain. At the next revision of the guidelines, we have to reconsider the appropriate target age group based on the balance of benefits and harms.

The main method for cervical screening is the Pap smear (conventional cytology), except in Denmark and the UK, which mainly used liquid-based cytology. In the UK, based on the systematic review by NICE, liquid-based cytology was used to decrease inadequate samples (81). Cervical screening using HPV testing has not been conducted at the community level. However, a guideline published by the American Cancer Society, the American College of Obstetricians and Gynecologists and the American Society for Colposcopy and Cervical Pathology recommended the method including HPV testing (74–78). In the USA, HPV testing has been used in combination with cytology or triage in clinical settings. European Guidelines concluded that new primary screening programs should not be introduced without first performing RCTs to investigate the effect at the population level (72). If new technologies are used in clinical settings, shared decision-making based on appropriate information relating to the benefits and harms should be performed.

Genital HPV infection is common and acquired soon after onset of sexual activity. However, persistent HPV infection with a high-risk HPV type causes cervical cancer. Although

HPV types 16 and 18 are common high-risk types worldwide (82), the distribution of HPV types in Japan differs from that in Western countries. In Japan, HPV type 16 and 18 infection accounts for 69.3% of invasive cancer cases lower than in other countries (83). Two prophylactic HPV vaccines have been licensed in Europe and the USA: the quadrivalent vaccine and the bivalent vaccine. Both vaccines protect against the high-risk HPV types 16 and 18, which could reduce CIN by over 90% (84,85). HPV vaccination programs have been introduced in several countries, including Australia (86–90). At present, antibody persistence and protection against persistent infection have been shown for up to 5 years after vaccination. The main target age group of vaccination is before the start of sexual activity. However, vaccination does not eliminate the need for cervical cancer screening. Based on the introduction of HPV vaccination in Canada in 2007, Howlett et al. (91) outlined the short-, medium-, and long-term requirements of an evaluation strategy related to HPV vaccination and cervical cancer screening. The European Center for Disease Prevention and Control (ECDC) recommended that organized screening should continue, and the coverage and quality of screening programs should be improved (92). In addition, monitoring of vaccination is needed.

Although the effect of conventional cytology has already been proven, the quality assurance system for cervical cancer screening is immature in Japan. To reduce the mortality from cervical cancer, improvements in screening uptake and appropriate management are required. In addition, to achieve its aims, the preferred target age group and the screening interval must be considered. The effects of new technologies, including liquid-based cytology and HPV testing, must be evaluated at the community level in Japan. Liquid-based cytology is expected to decrease unsatisfactory samples compared with conventional cytology. Akamatsu et al. (93) reported unsatisfactory samples with both methods in Japan: 0.95% with liquid-based cytology and 11.54% with conventional cytology, recalculated based on the definition of the Bethesda system. If liquid-based cytology is introduced, its cost-effectiveness compared with conventional cytology must be considered based on original Japanese data. Furthermore, sensitivity and specificity should be examined at the community level. Although HPV testing has the possibility to decrease invasive cancer, the appropriate use of this approach has not been determined. The RCTs conducted in Finland and the UK have been continued to evaluate incidence and mortality reduction using HPV testing (94,95). As for liquid-based cytology, Japanese studies evaluating its sensitivity and specificity are needed. When HPV vaccine will be introduced in the near future, comprehensive programs to prevent cervical cancer should be considered. For planning new screening programs, original Japanese studies including evaluation of HPV vaccines should be required. We have a schedule to revise the guideline within 5 years, given that new evidence may become available.

Table 8. Recommendations for cervical cancer screening

Screening method	Recommendation grade	Recommendations for language	
		Population-based Screening	Opportunistic Screening
Conventional cytology	B	Recommend	Recommend
Liquid-based cytology	B	Recommend	Recommend
HPV testing (alone)	I	Not recommend[a]	Decision-making at individual[b]
Combination of HPV testing and cytology	I	Not recommend[a]	Decision-making at individual[b]
HPV testing with cytology triage	I	Not recommend[a]	Decision-making at individual[b]

[a]There is insufficient evidence to recommend for or against.
[b]If required, the health professional should explain that the evidence regarding mortality and incidence reduction by cancer screening is unclear. In addition, information about the harms is required. In such situations, the decision regarding cancer screening should be made on the individual level.

RECOMMENDATIONS

On the basis of the balance of benefits and harms, recommendations were formulated for population-based and opportunistic screening (Table 8). Benefits were defined as evidence that mortality from a specific cancer was reduced by a cancer screening program.

Cervical cancer screening using conventional and liquid-based cytology is recommended for population-based and opportunistic screening because of sufficient evidence (Recommendation Grade B). However, to introduce liquid-based cytology, it is necessary to identify the volume of adequate samples in conventional cytology and investigate the sensitivity compared with conventional cytology in Japan. Cervical cancer screening using either HPV testing alone or a combination of HPV testing and cytology including the triage method is not recommended for population-based screening due to insufficient evidence (Recommendation Grade I). With respect to opportunistic screening, if individuals request screening, they should be given appropriate information and decision-making is required at the individual level.

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Conflict of interest statement

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APPENDIX 1

PEER REVIEW COMMITTEE FOR THE JAPANESE CERVICAL CANCER SCREENING GUIDELINE

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JAPANESE RESEARCH GROUP FOR DEVELOPMENT OF CERVICAL CANCER SCREENING GUIDELINES

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APPENDIX 2

KEY QUESTIONS: THE NUMBERS IN THE ANALYTIC FRAMEWORK REFER TO THE KEY QUESTIONS AS FOLLOWS

(i) Compared to no screening (or other screening strategy), is there direct evidence that following screening, the incidence and/or mortality are reduced?
  (a) Conventional cytology
  (b) Liquid-based cytology
  (c) Combination of HPV testing and cytology
  (d) HPV testing

To determinate the level of evidence appropriately, the primary outcomes of mortality from cervical cancer and incidence of invasive cancer were differentiated.

Method for combination of HPV testing and cytology included the following;

- Combination of HPV testing and cytology is used for screening
- HPV testing is used for screening and subsequently cytology is used as triage to decide necessity of coloposopy

(ii) What is the prevalence of cervical cancer in the target group? What strategy can reliably identify a high-risk group from among average- risk persons?

(iii) Can the screening test accurately detect the target cancer? The screening methods are conventional cytology, liquid-based cytology, combination of HPV testing and cytology and HPV testing alone.
  (a) What are the sensitivity and specificity of the test?
  (b) Is there significant variation between examiners in how the test is performed?
  (c) In actual screening programs, how much earlier are patients identified and treated?

(iv) Does screening result in adverse effects compared to no screening?
  (a) Is the test acceptable to patients?
  (b) What are the potential harms, and how often do they occur?

(v) Can the diagnostic test accurately detect the target cancer? The diagnostic method is LEEP (loop electrosurgical excision procedure).
  (a) What are the sensitivity and specificity of the test?
  (b) Is there significant variation between examiners in how the test is performed?
  (c) In actual screening programs, how much earlier are patients identified and treated?

(vi) Does the diagnostic test result in adverse effects compared to no test?
  (a) Is the test acceptable to patients?
  (b) What are the potential harms, and how often do they occur?

(vii) For cervical cancer patients, does any treatment reduce the incidence of an intermediate outcome compared to no treatment (or other treatment)?
  (a) Does treatment work under ideal, clinical trial conditions?
  (b) How do the efficacy and effectiveness of treatments compare in community settings?

(viii) Does any treatment result in adverse effects?

その他：編集委員会依頼原稿（原著）

コンセンサスパネルを用いた肺がん検診チェックリストの適切性検討と改訂案作成

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国のがん対策の一つの柱にがん検診受診率向上があげられているが、検診の効果を確保するには適切な精度管理が必要である。厚生労働省「がん検診に関する検討会」では検診機関に対して「事業評価のためのチェックリスト」を策定・普及を図っているが、継続的な精度向上のためにはチェクリストもまた適切性の検証と改善を繰り返すことが望まれる。今回、評価基準を定める際の国際的な標準的手法を用い、全国各地の検診従事医師8名のコンセンサスパネルでチェックリスト検証と改訂案策定を行った。結果、現行のチェックリストは、一項目（「1日あたり実施可能な人数を明らかにしている」）以外は適切という評価であったが、さらなる改善のため検討会議では様々な修正・追加が行われた。本過程は現段階では研究上の試みであるが、地域的に多様な委員による検討と定型的な手順に基づく合意がまとめられており、次回の公式的な改訂時に活用可能と考えられる。

キーワード：　肺がん検診、事業評価、精度管理、コンセンサスパネル、ヘルスサービス研究
J Thorac CT Screen 2010;17:106-114

平成19年施行されたがん対策基本法[1]に基づき発行された国のがん対策推進基本計画では、5年以内にがん検診受診率を50％とすることが目標とされている[2]。現状では平成19年国民生活基礎調査によると肺がん検診の受診率は40歳以上男性25.7％、女性21.1％[3]と目標へは隔たりがあり、検診の必要性の認知を広げていくことが望まれる。

検診の受診率向上の一方で、検診の効果を確保するためには検診受診者が適切な検診を受けられるよう検診提供体制の質・精度管理も重要である。その認識のもと、厚生労働省「がん検診に関する検討会」では、自治体が実施する住民検診を対象とし、「事業評価のための点検表（チェックリスト）」を乳がん、子宮がん、大腸がん、胃がん、肺がんと順次策定した[4]。このチェックリストは、都道府県、市町村、検診実施機関版が設けられ、それぞれ満たすべき事項が評価基準として定められており、主に検診の技術・体制的指標の達成度の自己点検を図るための基準である。これらの周知徹底により検診の質の向上、精度管理が図られている。

チェックリストなど一般に評価指標を策定する際には、その妥当性を確保し、かつ現場での順守を促す意味でも現場の視点により評価することが重要である。しかも、その評価と改善の作業は継続的な改善を旨として繰り返し行うことが望ましい。今回、その手始めとして実際に検診実施機関に勤務して検診業務に従事してい

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る医師の意見によりチェックリストの適切性の評価を行い、さらに、次回改訂する場合の案を作成したので報告する。

対象と方法

＜概　要＞

本研究は、米国RAND/UCLAで開発された適切性評価法（デルファイ変法）と呼ばれる方法に従ってコンセンサスパネルによりチェックリストの検証を行った[5,6]。この方法は質評価の指標作成など、客観的な合意に基づく項目選択に使用され、判定の再現性[7]や、本手法により作成された医療の質評価基準においてはその基準を用いた測定結果の予後予測における妥当性[8]が示されている。本手法の一般的な全体の流れをFig. 1に示す。今回の具体的手順としては、まず様々な背景を持つ委員を8名選定、現行のチェックリストを各委員に送付し1～9のスケールで各項目の適切性の評価を依頼した。この第1回の評価は、原稿のチェックリストに対する委員の評価として機能する。さらに、その集計を元に3時間超の検討会議を行い、チェックリストとして改善すべき点については修正を加え、またそれらの適切性に関する議論をおこなった。これらの過程をふまえて再評価を行い、合意が得られた項目がチェックリスト改訂案として決定された。ただし、この改訂案は即公的なチェックリストに反映されるものではなく次回改訂が提起された際の資料として扱われることは始めに確認した。

＜検診専門家パネルの選定＞

多様な意見を収集するために地理的に東日本と西日本を幅広く含めた関連各者を専門家委員会（以下パネル）に選定し、また、検診実施機関および大学関係者も選定した。実際のパネルのメンバーは以下の通り（敬称略、勤務先所在地順）となった。

国立病院機構北海道がんセンター	原田真雄
東北大学加齢医学研究所	遠藤千顕
ポートスクエア柏戸クリニック	瀧澤弘隆
化学療法研究所附属病院	小中千守
（初回評価のみ）	
石川県予防医学協会	木部佳紀
岐阜環境医学研究所	松井英介
岡山県健康づくり財団附属病院	西井研治
香川県立保健医療大学	佐藤　功

＜現行のチェックリスト＞

今回評価対象としたチェックリスト項目は、がん検診に関する検討会で作成された肺がん検診のためのチェックリスト（検診機関用）26項目[4]であり、それぞれ、受診者への説明に関して4項目、問診および撮影の精度管理に関し

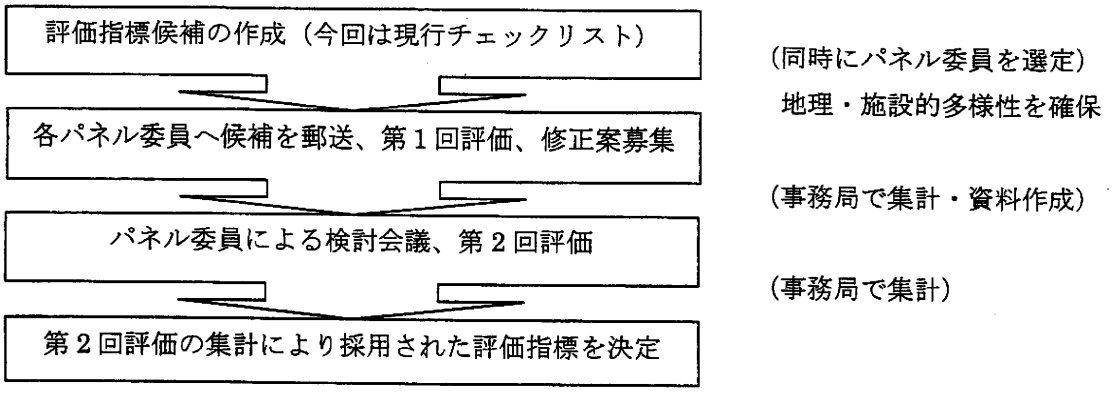

Fig. 1　The flow of the RAND/UCLA appropriateness method

て6項目、X線撮影の精度管理に関して5項目、喀痰細胞診の精度管理に関して7項目、システムとしての精度管理に関して4項目からなっていた。それぞれの項目は、第1回の評価対象となっており、Table 1に示す。

＜評価過程＞

各パネル委員に会議の約2週間前に、Table 2

Table 1　Current checklist for lung cancer screening provider facilities, proposed revisions, and appropriateness ratings

	現行チェックリスト	評価*	会議後、チェックリスト改訂案	評価*
1	受診者への説明			
(1)	要精密検査となった場合には、必ず精密検査を受ける必要があることを事前に明確に知らせているか	9, A	受診者全員に対して、肺がん検診が有効であるためには、要精密検査となった場合には必ず精密検査を受ける必要があることを検査前に明確に知らせているか	9, A
(2)	精密検査の方法や内容について説明しているか	8, A	受診者全員に対して、検査前に精密検査の方法や内容について説明しているか	9, A
(3)	精密検査の結果の市町村への報告などの個人情報の取り扱いについて、受診者に対し十分な説明を行っているか	8, A	修正なし	9, A
(4)	禁煙及び防煙指導等、肺がんに関する正しい知識の啓発普及を行っているか	7, I	修正なし	9, A
2	問診および撮影の精度管理			
(1)	検診項目は、問診、胸部X線検査、および喀痰細胞診を行っているか	9, A	検診項目として、問診、胸部X線検査、および喀痰細胞診を行っているか	9, A
(2)	問診は喫煙歴および血痰の有無を聴取しているか	9, A	問診の中で喫煙歴および血痰の有無を聴取しているか	9, A
(3)	問診記録は少なくとも5年間は保存しているか	9, A	修正なし	9, A
(4)	肺がん診断に適格な胸部X線撮影を行っているか注1)	9, A	修正なし	9, A
(5)	撮影機器の種類（直接・間接撮影、ミラー・I.I.方式等）、フィルムサイズを明らかにしているか注2)	9, A	撮影機器の種類（直接・間接撮影、デジタル方式等）に応じた撮影法を行っているか（注2参照）	9, A
(6)	[redacted]	[redacted]	[redacted]	[redacted]
3	胸部X線読影の精度管理			
(1)	2名以上の医師によって読影し、うち一人は十分な経験を有した呼吸器または放射線の専門医を含めているか	9, A	2名以上の医師によって読影し、うち一人は十分な経験を有し熟練した呼吸器科または放射線科の医師を含めているか	9, A
(2)	2名のうちどちらかが「要比較読影」としたものは、過去に撮影した胸部X線写真と比較読影しているか	9, A	修正なし	9, A
(3)	比較読影した症例数を報告しているか	8, I	[redacted]	
(4)	X線写真は少なくとも3年間は保存しているか	9, A	[redacted]	
(5)			胸部X線写真は少なくとも5年間は保存しているか	9, A
(6)	X線検査結果は少なくとも5年間は保存しているか	9, A	胸部X線検査結果は少なくとも5年間は保存しているか	9, A
4	喀痰細胞診の精度管理			
(1)	喀痰細胞診は、年齢50才以上喫煙指数400もしくは600以上、あるいは年齢40才以上6ヶ月以内に血痰を有したもの、その他職業性など高危険群と考えられるものに行っているか	9, A	修正なし	9, A
(2)	細胞診の業務を委託する場合は、その委託機関（施設名）を明記しているか	9, A	修正なし	9, A
(3)	採取した喀痰は、2枚のスライドに塗沫し、湿固定の上、パパニコロウ染色を行っているか	9, A	修正なし	9, A
(4)	固定標本の顕微鏡検査は、日本臨床細胞学会の認定を受けた細胞診専門医と細胞検査士が連携して行っているか注3)	9, A	修正なし	9, A

Table 1　Current checklist for lung cancer screening provider facilities, proposed revisions, and appropriateness ratings

(5)	がん発見例は、過去の細胞所見の見直しを行っているか	9, A	修正なし	9, A
(6)	標本は少なくとも3年間は保存しているか	9, A		
(6)'			標本は少なくとも5年間は保存しているか	9, A
(7)	喀痰細胞診検査結果は少なくとも5年間は保存しているか	9, A	修正なし	9, A
5	システムとしての精度管理			
(1)	精密検査結果及び治療結果の報告を、精密検査実施機関から受けているか注4)	9, A	精密検査結果(組織型や病期等) 及び治療結果の報告を、精密検査実施機関から追跡収集する体制があるか	9, A
(2)	診断のための検討会や委員会 (第三者の肺がん専門家を交えた会)を設置しているか	8. 5, A	診断のための検討会や委員会 (外部の肺がん専門家を交えた会)を設置・参加しているか	9, A
(3)	都道府県がプロセス指標 (受診率、要精検率、精検受診率、がん発見率、陽性反応適中度) に基づく検討ができるようデータを提出しているか	9, A	都道府県がプロセス指標 (受診率、要精検率、精検受診率、がん発見率、陽性反応適中率) に基づく検討ができるようデータを提出することができるか	9, A
(4)	実施主体へのがん検診の集計・報告は、地域保健・健康増進事業報告に必要な項目で集計しているか	9, A	修正なし	9, A
(5)			要精検者に対して、結果通知時に精密検査の重要性を個別に知らせているか	9, A
(6)			検診結果の通知を実施する場合には、正確な通知を行うためのチェック体制があるか (責任者の明確化を含む)	9, A

注1) 肺がん診断に適格な胸部X線撮影：日本肺癌学会編集、肺癌取り扱い規約　改訂第6版より
背腹一方向撮影1枚による場合、適格な胸部X線写真とは、肺尖、肺野外側縁、横隔膜、肋骨横隔膜角などを含むように正しく位置づけされ、適度な濃度とコントラストおよび良好な鮮鋭度をもち、中心陰影に重なった気管、主気管支の透亮像ならびに心陰影及び横隔膜に重なった肺血管が観察できるもの
注2) 撮影法：日本肺癌学会編集、肺癌取り扱い規約　改訂第6版より
1：間接撮影の場合は、100mm ミラーカメラと、定格出力 150kV 以上の撮影装置を用いて 120kV 以上の管電圧により撮影する。やむを得ず定格出力 125kV の撮影装置を用いる場合は、110kV 以上の管電圧による撮影を行い縦隔部の感度を肺野部に対して高めるため、希土類 (グラデーション型) 蛍光板を用いる。定格出力 125kV 未満の撮影装置は用いない
2：直接撮影の場合は、被検者一管球間距離を 1.5m 以上とし、定格出力 150kV 以上の撮影装置を用い、120kV 以上の管電圧及び希土類システム (希土類増感紙＋オルソタイプフィルム) による撮影がよい。やむを得ず 100～120kV の管電圧で撮影する場合も、被曝軽減のために希土類システム (希土類増感紙＋オルソタイプフィルム) を用いる
3：CR の場合は、120kV 以上の管電圧及び散乱線除去用格子比 12:1 以上を使用して撮影し、適切な階調処理、周波数処理、ダイナミックレンジ圧縮処理などを施した画像として出力する事が望ましい
注3) 日本臨床細胞学会　細胞診精度管理ガイドライン参照
注4) 組織や病期把握のための治療など
＊ (中央値、一致度：A: 一致、D: 不一致、I:どちらでもない)
注5) 太字部分は変更点、灰色は評決により不採用となった項目

Table 2　Excerpt of the rating sheet

	チェックリスト候補	チェックリストとしての適切性	コメント
1	受診者への説明		
(1)	要精密検査となった場合には、必ず精密検査を受ける必要があることを事前に明確に知らせているか	1 2 3 4 5 6 7 8 9	
(2)	精密検査の方法や内容について説明しているか	1 2 3 4 5 6 7 8 9	
(3)	精密検査の結果の市町村への報告などの個人情報の取り扱いについて、受診者に対し十分な説明を行っているか	1 2 3 4 5 6 7 8 9	

に例示したような評価スケールを評価過程と評価基準の説明書と共に電子メールで送付した。チェックリストの適切性としては、妥当性（現状の予算構成や状況においても検診実施機関はチェックリストを100％満たすべきか、また、その通りしていない場合に何らかの指導などが必要といえるか）、と明確性（要求されている事項の内容に曖昧さがないか）の2軸を定義して、その総合点として各パネル委員が判断して適切性を評価するように依頼した。評価結果は国立がんセンターがん予防・検診研究センター検診研究部に設けられた事務局で検討会議の1週間前までに回収し、会議当日までに集計結果を用意した。評価はこれまでのRAND/UCLA適切性評価法に従い各項目の「チェックリスト」としての適切性を「1＝きわめて不適切、9＝きわめて適切」のスケールで定量的な評価を依頼した（Table 2）。さらに、それぞれのチェックリストに関してコメント記入欄を設け、新しい意見、チェックリストの表現改訂案、また新しいチェックリストの追加の提案などの意見を収集し、検討資料としてまとめる作業を行った。検討会議の資料としては検討パネル委員の評点の分布およびコメントの一覧を示したが、どの委員が、何点の評点を付けたのか、またどのコメントを出したのかはわからないようにしてまとめた。

検討会議では、一つ一つのチェックリストについて評点の分布とコメントを吟味しながら検討した。検討が終わる毎に再度1～9のスケールでそのチェックリストとしての適切性を評価した。検討の過程でチェックリストの修正が提起された場合にはその場で反映させ、第2回の評価は反映後のチェックリストを対象とした。また、同時に追加が提案された項目についても検討し同様のスケールで評価した。

第2回の評点を集計し、中央値が7以上であり反対意見（1～3の評点）を付けた委員が3名以上でない項目を採用チェックリスト項目とした。また、同じ内容で期間のみが異なる場合など両方成り立たない複数の項目が採用された場合には、より高い中央値のあるもの、またはより合意の度合いが高いものを採用とした。最終的な結果は委員全員に回覧して承認を得た。

結　果

＜現状チェックリストに対する評価＞

現行チェックリストへの評価の中央値と一致度をTable 1左欄に示し、チェックリスト改訂案とその評価について右欄に示す。第1回目の評価において、基準に従って不適とされた現行チェックリストは1項目あり、2-(6)「1日あたりの実施可能人数を明らかにしているか」であった。検討会議では1日あたりの実施可能人数は様々な条件によって変化するものであり、このような数字を公表・報告しても正確さに疑問があるとされた。この項目は、関連項目として修正することも困難と判断され、そのまま第2回の評価を行い不採用となった。

＜現状に対する議論＞

まず受診者に対する説明の章のなかで、受診者へのインフォームドコンセントを行う責任は検診対象者に受診を促す役割をもつ市町村にあるのか、実際の検診を提供する検診実施機関にあるのかが議論された。本来住民検診の実施主体は市町村であり、市町村が説明を行うべきものである。しかし検診対象者への連絡の時点から検診実施機関が委託を受けて実施している例も多く、実務的には説明を検診実施機関が行わざるを得ない。そもそも説明を行う責任の所在がどこにあるのか、統一的な結論を出すことの難しさが明らかになった。

また、検診対象者全員への説明と、要精検と判定されたものへの説明を概念的に区別することの必要性が議論された。前者はインフォームドコンセントという対象者保護や人権の尊重と

しての意味合いが強いのに対して、後者は精検受診勧奨という検診の精度管理という意味合いが強い。検診の確実な実施という意味での必要性は後者の方が強い意味をもつが、この点は現行のチェックリストに含まれていなかったため、この要精検者への重要性の説明が、「システムとしての精度管理」という章の中に追加された。

＜チェックリストの修正・追加と第2回評価＞

当初の26項目のチェックリストのうち12項目に対して何らかの修正が入り、4項目が追加されて、計30項目が第2回評価を受けた。そのうち4項目については不採用となり、最終的に26項目が採用された。検討中の議論は良く収束しており、採用された項目は全て半数以上の評価委員が「9＝きわめて適切」と評価しており、6以下の評点を付けたものは全て2名以下であった（Table 1）。

考　察

本研究ではRAND/UCLA適切性評価法に従い、様々な地域の検診医師によるコンセンサスパネルの手法で肺がん検診事業評価のためのチェックリストの適切性評価と改訂案作成を行った。第1回の評価においては、現状のチェックリストは概ね適切と評価されたが、検討会議の過程で約半数のチェックリスト項目に関して表現の修正が提案され、また4項目が追加された。採用されたチェックリストは現行のチェックリストに現場の医師の意見を反映したものとなっており、次回改訂時にはその貴重な基礎資料となると考えられる。

議論の過程では、検診が非常に多様な制度の下で行われていることが再認識され、一律のチェックリストを設定することの難しさが明らかになった。まず、様々な地域のなかで検診には大きく分けて市町村の事業として行われる一般住民を対象とした住民検診と、職域で労働安全衛生法に基づく健康診断に付加して行われる職域検診がある。概念上はこの両者を区別されるものであるが、実際市町村、職域共に検診の実施については検診実施を専門とする検診実施機関へ委託することも多く、その委託に際して責任の分担が不明瞭であることも多い。職域において行われる胸部X線検診が、がん検診なのか結核検診なのか、などが明確に区別されることも少ない。しかし、今回は、チェックリストの使用が行政的な文脈を想定されているため、住民検診を対象とすることで一致した。

しかし、市町村検診のなかでも、検診対象者に受診勧奨を通知する部分を市町村が行う地域や、検診実施機関が委託されて行う地域など様々である。そのため、チェックリストの最初の検診受診者への説明の中で、例えば「要精密検査となった場合に精検を受ける必要があることを説明する」が誰の責任かという点について、まず問題とされた。本来、これは検診受診勧奨を行う際に説明するのが妥当であり、市町村が受診勧奨を行っている場合には、すでに検診を受けようとの意思をもって検診現場に来院した受診者に対して、検診実施機関がインフォームドコンセントを行うことは順序が不適切ではないかという考え方もあった。しかし、これらの説明は非常に重要であることから、市町村の責任であると同時に検診実施機関の責任があっても良いという考え方で概ね一致した。

次にX線写真の読影をどのような資格を持った医師が行うのかという項目に対して問題が明らかになった。現行のチェックリストは「呼吸器又は放射線科の専門医」となっているが、学会の認定した専門医なのか、どの学会の専門医なのか、専門医を取得していないと問題なのか、などが議論になり、結局は「専門医」の言葉は取り除かれ「医師」となった。議論のなかではこのような読影のための「専門医」制度を作ってこなかったのは我々関連学会の責任という意見もあ

り、今後の制度整備の必要性が明らかになった。

今回の結果で引き続き課題となる可能性のあるものは、胸部X線写真および細胞診標本の保存期間である。医療法施行規則第21条の5ではX線写真の保存期間は、一般の医療機関において2年とされている[9]。また、保険医療機関及び保険医療養担当規則9条では、「療養の給付の担当に関する帳簿及び書類その他の記録」として3年保存とされている[10]。細胞診標本については、結果記録は診療録に準じた扱いを受けると解釈できるものの、標本そのものに関しては、特に法的に定められたものは無い。今回現行のチェックリストでは両方とも保存期間を3年としていたが、専門家パネルではそれが5年とすべきであると言う結果になっている。これらは検診機関においてはその精度管理上、たとえば過去のX線写真との比較読影の上で必要性が高く特に必要な事項であると考えられること、また電子的な保存が可能になったことで以前よりも延長して医療の役に立てることが可能になったためとも考えられるが、実行可能性などとの関連で、今後の議論が必要となると考えられる。

RAND/UCLA適切性評価法と呼ばれる今回の定式手順には、定式化されない通常の会議に比していくつかの利点がある。まず、スケールを使った準備と決定の手順をとることで、主観的でわかりにくい思考内容が具体化される点である。もちろん各評価者のスケールのとらえ方が異なるために基礎的なばらつきや誤差が存在するのは否めないが、一定の傾向や意見の分布を示すには十分な可視化と考えられる。また、スケール化するためには、何を評点としているのかを必然的に明確化しなければならないため、チェックリスト項目とは何か、という点が最初に定義されその点でも議論の方向性が明確化される。次に、事前の評価により問題点について各委員が独自に考慮する機会が持たれ、さらにそれらが事前に明らかになって効率的に検討会が進められる点である。さらに、委員の構成を意識的に多様化することで様々な視点からの意見を集約することが出来る。また評価の集計や個別コメントの提示の際には各委員がどの評点・コメントを出したのかを知らせないことで自由な議論や評価が可能になり不本意な他人からの影響のない自立した意見を表出することが可能である。結論の決定方法もあらかじめ定められており恣意性が入る余地はない。

逆に、このような試みの限界としては、検討パネル委員の構成や人選によって結果が変わる懸念がある。そのような懸念を解消するためには検討する人の数を増やして多くの意見を集めるのが良いかもしれない。しかし、そうすると逆に検討会で一人一人が意見を表明する責任や機会が薄れてしまうため議論の深みが生まれないリスクが出てくる。そのため先行研究では多様性を確保したうえで10名前後の検討委員にとどめることが通例となっている。また広い意見を収集するために一旦10名前後の検討委員で結論を出した後に、別の場で再度承認を取られることもある。今回作成されたチェックリスト改訂案も最終結論ではなく、今後全国的に使われる前に厚生労働省の検討会などでの最終検討が行われるものであると期待される。

本手法の最終効果としての死亡率減少については、検診における精度管理のためにチェックリストを使用する経験自体が新しいため、改訂の効果はもとよりチェックリストの順守による効果を検証した報告もまだみられていない。しかし、宮城県において肺がん検診の精度管理について市町村に対して質問紙による調査を繰り返したところ、市町村における肺がん検診の精度管理が向上したことが報告されており[11, 12]、このようなチェックリストの公表は有用であると考えられる。また、海外においてはコンセンサスパネルの手順により医療の質指標を作成し、その指標により測定された医療の質がその後の