Vaccine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Cost-effectiveness of increasing cervical cancer screening coverage in the Middle East: An example from Lebanon

Monisha Sharma [a,*], Muhieddine Seoud [b], Jane J. Kim [c]

[a] University of Washington, Department of Epidemiology, 1959 NE Pacific Street, Seattle, WA 98195, USA
[b] Department of Obstetrics and Gynecology, Gynecologic Oncology, American University of Beirut, Beirut, Lebanon
[c] Harvard T. H. Chan School of Public Health, Center for Health Decision Science, Boston, MA 02115, USA

ARTICLE INFO

Article history:
Received 8 September 2016
Received in revised form 12 November 2016
Accepted 9 December 2016
Available online xxxx

Keywords:
Cervical cancer
Screening
Middle East
Lebanon
Cost-effectiveness
Modeling

ABSTRACT

Background: Most cervical cancer (CC) cases in Lebanon are detected at later stages and associated with high mortality. There is no national organized CC screening program so screening is opportunistic and limited to women who can pay out-of-pocket. Therefore, a small percentage of women receive repeated screenings while most are under-or never screened. We evaluated the cost-effectiveness of increasing screening coverage and extending intervals.

Methods: We used an individual-based Monte Carlo model simulating HPV and CC natural history and screening. We calibrated the model to epidemiological data from Lebanon, including CC incidence and HPV type distribution. We evaluated cytology and HPV DNA screening for women aged 25–65 years, varying coverage from 20 to 70% and frequency from 1 to 5 years.

Results: At 20% coverage, annual cytologic screening reduced lifetime CC risk by 14% and had an incremental cost-effectiveness ratio of I$80,670/year of life saved (YLS), far exceeding Lebanon's gross domestic product (GDP) per capita (I$17,460), a commonly cited cost-effectiveness threshold. By comparison, increasing cytologic screening coverage to 50% and extending screening intervals to 3 and 5 years provided greater CC reduction (26.1% and 21.4, respectively) at lower costs compared to 20% coverage with annual screening. Screening every 5 years with HPV DNA testing at 50% coverage provided greater CC reductions than cytology at the same frequency (23.4%) and was cost-effective assuming a cost of I$18 per HPV test administered (I$12,210/YLS); HPV DNA testing every 4 years at 50% coverage was also cost-effective at the same cost per test (I$16,340). Increasing coverage of annual cytology was not found to be cost-effective.

Conclusion: Current practice of repeated cytology in a small percentage of women is inefficient. Increasing coverage to 50% with extended screening intervals provides greater health benefits at a reasonable cost and can more equitably distribute health gains. Novel HPV DNA strategies offer greater CC reductions and may be more cost-effective than cytology.

1. Introduction

The age standardized incidence of cervical cancer in the Middle East is estimated to be 2.7 per 100,000 woman years, with higher rates in Lebanon (4.6 per 100,000 woman years) [1,2]. Overall, cervical cancer incidence is similar to that of developed countries in North America and Western Europe, but cancer mortality rates in the Middle East are disproportionately high and the majority of cases are diagnosed at later stages [3]. The mortality rates reflect barriers to accessing regular screening and treatment. Cervical cancer is largely preventable and developed countries with widespread screening coverage at regular intervals have reduced burden by 80% [4]. However, most countries in the Middle East lack organized national screening programs and rely instead on opportunistic screening at low coverage [5]. In Lebanon, most physicians practice annual screening with cytology, reaching a coverage of approximately 20% of eligible women [5]. Similar to many countries in the Middle East, cervical cancer screening is Lebanon is limited to those who can afford to pay out of pocket for pap smears. This results in a small percentage of women receiving frequent screening while the vast majority are never screened.

Abbreviations: CC, cervical cancer; ICER, incremental cost-effectiveness ratio; HPV, human papillomavirus.

* Corresponding author.
E-mail address: msharma04@gmail.com (M. Sharma).

http://dx.doi.org/10.1016/j.vaccine.2016.12.015
0264-410X/

HPV-16/18 vaccination offers promising primary prevention against cervical cancer [6,7]. Although both the bivalent (Cervarix) and quadrivalent (Gardasil) vaccines are licensed in Lebanon and many countries in the Middle East, they are not widely implemented. In Lebanon, HPV vaccination is not publically financed and therefore only available to those who can pay $70 per dose for Cervarix or $178 per dose for Gardasil [8]. A recent cost-effectiveness analysis found that HPV vaccination at 70% coverage is cost-effective up to a cost of I$27 per dose in most countries in the Middle East, including Lebanon, indicating that the market price would have to be reduced substantially before scale-up of vaccination provides good value for money [9]. Additional challenges with HPV vaccine implementation include competing priorities including measles and polio eradication, strained immunization programs, lack of pre-adolescent/adolescent immunization platform, and social stigma around vaccination for a sexually transmitted disease in Middle Eastern countries [10].

Given the challenges associated with scaling up HPV vaccination and the many cohorts of older women who are past the eligible age of vaccination, implementing efficient screening strategies can be a successful approach to reducing cervical cancer burden. Cervical cancer incidence has remained relatively stable in the Middle East with low rates that reflect the region's conservative attitudes toward sexual behavior [11]. However, younger generations are less confined to cultural norms and increases in sexual activity are reflected in the increasing HPV prevalence [8]. Therefore cervical cancer rates may rise in the absence of effective interventions [11].

In this analysis, we evaluate the impact of different screening strategies to identify efficient ways to reduce cervical cancer burden in the Middle East. Using the setting of Lebanon, we estimate the health and economic impacts of current screening practice and evaluate the cost-effectiveness of increasing screening coverage at various screening intervals. Since many Middle Eastern countries lack infrastructure for widespread cytology screening, we also assess the impact of screening strategies implementing HPV DNA testing, which relies less heavily on infrastructure [12]. As the cost of HPV DNA testing is uncertain in Lebanon, we performed a threshold analysis to determine the cost at which HPV DNA testing would provide good value for money.

2. Methods

2.1. Mathematical model

We adapted an existing individual-based first-order Monte Carlo microsimulation model of HPV infection and cervical carcinogenesis [13–16]. The model simulates the natural history of cervical cancer in individual women using transitions between clinically relevant health states. Girls enter the model at age 9 in a healthy state, and face monthly probabilities of HPV incidence and clearance, progression and regression of lesions, and progression to cancer; transition probabilities are a function of HPV type, age, and clinical history. Females with invasive cancer can be detected at different stages either through symptoms or screening. All women face a risk of background mortality, while women with invasive cancer face excess mortality rates that differ by stage. The model tracks health status and resource use of individuals to estimate the health and economic outcomes associated with each screening strategy.

We calibrated the model to epidemiological data, including age-specific cervical cancer incidence and HPV type distribution in cervical cancer using primary data from Lebanon. We allowed baseline natural history parameters to vary over plausible ranges. Using a likelihood-based approach, we identified unique sets of parameter values that achieved a close fit to the empirical data, and conducted the analysis using a sample of 20 good fitting parameter sets. Model outcomes included reductions in lifetime risk of cancer, life expectancy and lifetime costs associated with each strategy. Details of the calibration process have been previously described [14,15,17–19] and additional information on calibration data, methods, and results are provided in Supplemental Appendix.

2.2. Cost estimates

Societal costs associated with screening, diagnosis, and treatment for cervical lesions and cancer were based on estimates from primary sources, published literature, and similar countries as previously described [9,14]. Costs included both direct medical (e.g., staff, supplies, equipment, specimen transport and processing) and non-medical (e.g., patient transportation) costs. Costs for patient time spent traveling to, waiting for, and receiving services were estimated based on procedure times and female wages in Lebanon [20]. Additional information on cost estimates, methods, and assumptions are provided in the Appendix.

2.3. Strategies and assumptions

The baseline screening strategy was cytology, which varied in frequency from annual to every five years between ages 25 and 65 years. We assumed the entire screening process occurred in three visits: initial screening (visit 1), colposcopy and possible biopsy for screen-positive women (visit 2), and if necessary, treatment of precancerous lesions or invasive cancer (visit 3) [13,21]. As key opinion leaders in Lebanon are considering implementation of HPV DNA testing at intervals of every 3, 4, or 5 years, we also evaluated screening with HPV DNA testing between ages 30 and 65 years. HPV DNA testing was assumed to occur in two visits: the initial screen (visit 1) and a return visit for results and treatment if HPV positive [13]. We assume 15% loss to follow up at each clinical contact [16]. Screening coverage was varied from 20 to 50% and we assumed repeated screening of the same women; for example in the scenario of 20% coverage, we assumed the same 20% of women would undergo screening while the remaining 80% were never screened. In sensitivity analyses, we evaluated screening scale up to 70% coverage of a random subset of women (as oppose to the same women screened throughout their lifetime). We also assessed the effect of reducing colposcopy and biopsy costs by 50%.

2.4. Cost effectiveness analysis

We conducted a cost-effectiveness analysis from the societal perspective. Following health economic guidelines, costs and benefits were discounted at an annual rate of 3% [22]. Incremental cost-effectiveness ratios (ICERs) are reported as the ratio of the difference in mean costs divided by the difference in mean effects across the good-fitting parameter sets for one strategy compared with the next best alternative [23,24]. Strategies that were more costly and less effective (i.e. 'strongly dominated') or less costly and less cost-effective (i.e. 'weakly dominated') than an alternative strategy were considered inefficient and as is standard practice, were eliminated from the calculations. We used Lebanon's 2014 gross domestic product (GDP) per capita (I$17,462) as a threshold for cost-effectiveness [25].

3. Results

Lebanon's current screening practice of annual cytology at 20% coverage of eligible women was associated with a 14.2% (range

Please cite this article in press as: Sharma M et al. Cost-effectiveness of increasing cervical cancer screening coverage in the Middle East: An example from Lebanon. Vaccine (2016), http://dx.doi.org/10.1016/j.vaccine.2016.12.015

11.4–16.5%) reduction in the lifetime risk of cervical cancer relative to no screening and had an ICER of $80,670 per YLS, which greatly exceeded the cost-effectiveness threshold of Lebanon's GDP per capita (I$17,462) (Table 1). By comparison, increasing screening intervals to every two years reduced the ICER to more than half that of annual cytology (I$35,040 per YLS), with a reduction in lifetime cervical cancer risk of 12% (9.2–14.8%). Further extending screening intervals to 3 and 5 years were associated with lower ICERs, although they also had lower cancer reductions. Cytology screening every 5 years at 20% coverage had a cancer reduction of 8.6% (range 5.7–12.0%) and was the only strategy with an ICER under the threshold of Lebanon's GDP per capita (I$7710 per YLS). Results were robust to lowering colposcopy and biopsy costs by 50% (Table S14).

Compared to Lebanon's current screening practice of annual cytology at 20% coverage, increasing coverage to 50% and extending screening intervals to 5 years yielded a greater cervical cancer reduction (21.4%) at a lower lifetime cost per woman (reduced by 41%) (Table 2). At 50% coverage, cytology screening every 5 years was also the most efficient strategy with an ICER under Lebanon's GDP per capita. Increasing screening frequency to every 3 years provided nearly twice the cancer reduction of Lebanon's current practice and had a lower lifetime cost per woman. However, it was associated with an ICER slightly higher than Lebanon's per capita GDP ($19,704 per YLS). Scaling up annual cytology was not found to be cost-effective.

Fig. 1 displays the efficiency frontier associated with cytology screening strategies at various coverage and frequency. Annual cytology at 20% is to the right of the curve (i.e., inefficient), with a lifetime cost per woman of $57; cytology every 3 years yields a similar cancer reduction and is much closer to the efficacy frontier. Screening every 5 years at 50% coverage provides a greater cancer reduction than the current practice of annual cytology and is less costly ($34 per woman). Similarly, cytology every 3 years at 50% coverage is more effective than current practice and is $6 less per woman. Scaling up annual cytology to 50% is shown to the far this should say "far right" not far left. Left of the curve.

We also explored the effectiveness of implementing HPV DNA testing every 3, 4, and 5 years (Table 3) and performed a threshold analysis to determine the cost at which HPV DNA testing falls below Lebanon's per capita GDP (Supplemental Appendix). At 50% coverage, HPV DNA testing at 3 and 5 year intervals provided a greater cancer reduction than cytology at the same interval and coverage. At a composite cost of $19 for test administration, strategies of HPV DNA testing every 4 and 5 years testing had ICERs that fell below the cost-effectiveness threshold (I$12,210 and I$16,340 per YLS, respectively). HPV DNA testing every 3 years yielded even greater cervical cancer reductions but exceeded the cost-effectiveness threshold with an ICER of I$25,390 per YLS. Cytology screening every three years at 50% coverage was less cost-effective than HPV DNA screening every 3 years (dominated). Annual and biannual cytology screening strategies had ICERs that exceeded Lebanon's GDP per capita.

Assuming random screening of eligible women with cytology at 50% coverage yielded greater cancer reductions and more attractive ICERs compared to repeated screening of the same 50% of

Table 1
Health and economic impact of Lebanon's current cervical cancer screening strategy.

Screening strategy and frequency	Screening coverage[a] (%)	Mean cancer reduction[b], % (range)	Lifetime costs per woman[c]	Discounted life expectancy[d]	ICERs (I$/YLS)[e]
No screening	–	–	6.30	38.0909	–
Cytology (5 year)	20	8.6 (5.7–12.0)	17.30	38.0923	**7680**
Cytology (3 year)	20	10.3 (7.6–14.2)	23.70	38.0927	20,420
Cytology (2 year)	20	12.0 (9.2–14.8)	32.10	38.0929	35,040
Cytology (1 year)	20	14.2 (11.4–16.5)	56.90	38.0932	80,670

[a] Cytology screening is assumed to occur between the ages of 25–65 years.
[b] Shown is the mean cancer reduction for the best-fitting parameter sets from the empirically calibrated model. Cancer reductions are calculated for each strategy compared to no screening.
[c] Lifetime costs are discounted annually at 3%.
[d] Average life expectancy for women under each strategy, discounted at 3% annually.
[e] ICER: Incremental cost-effectiveness ratio; YLS: Year of life saved. ICERs represent the ratio of the difference in mean-costs divided by the difference in mean-effects of one strategy compared to the next most costly strategy among non-dominated strategies across the best-fitting parameter sets, and are expressed as international dollars per year of life saved (I$/YLS). Bolded strategies fall below the threshold of Lebanon's GDP per capita.

Table 2
Health and economic impact of increasing cytology screening coverage to 50%.

Screening strategy and frequency	Screening coverage[a] (%)	Mean cancer reduction [b], % (range)	Lifetime costs per woman [c]	Discounted life expectancy [d]	ICERs (I$/YLS) [e]
No screening	–	–	6.30	38.0909	–
Cytology (1 year)	20	14.2 (11.4–16.5)	56.90	38.0932	Dom[f]
Cytology (5 year)	**50**	**21.4 (14.9–30.5)**	**33.80**	**38.0945**	**7680**
Cytology (3 year)	50	26.1 (18.9–35.6)	49.70	38.0953	19,700
Cytology (2 year)	50	30.3 (23.8–37.8)	70.70	38.0959	34,590
Cytology (1 year)	50	35.7 (29.8–41.5)	132.60	38.0966	86,730

[a] Cytology screening is assumed to occur between the ages of 25–65 years.
[b] Shown is the mean cancer reduction for the best-fitting parameter sets from the empirically calibrated model. Cancer reductions are calculated for each strategy compared to no screening.
[c] Lifetime costs are discounted annually at 3%.
[d] Average life expectancy for women under each strategy, discounted at 3% annually.
[e] ICER: Incremental cost-effectiveness ratio; YLS: Year of life saved. ICERs represent the ratio of the difference in mean-costs divided by the difference in mean-effects of one strategy compared to the next most costly strategy among non-dominated strategies across the best-fitting parameter sets, and are expressed as international dollars per year of life saved (I$/YLS). Bolded strategies fall below the threshold of Lebanon's GDP per capita.
[f] These strategies are either more costly and less effective, or less costly and less cost-effective, than alternative options, and are thus considered (strongly or weakly) dominated.

Please cite this article in press as: Sharma M et al. Cost-effectiveness of increasing cervical cancer screening coverage in the Middle East: An example from Lebanon. Vaccine (2016), http://dx.doi.org/10.1016/j.vaccine.2016.12.015

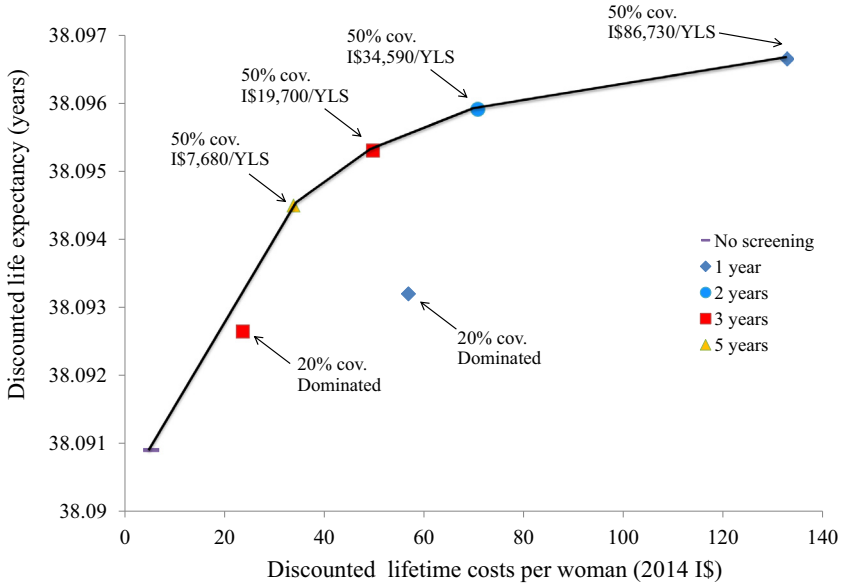

Fig. 1. Each shape on the graph represents the average life expectancy and costs per woman associated with cytology screening strategies at different screening intervals and coverage levels.

Table 3
Health and economic impact of implementing HPV DNA testing (I$19 per test).

Screening strategy and frequency	Screening coverage[a] (%)	Mean cancer reduction[b], % (range)	Lifetime costs per woman[c]	Discounted life expectancy[d]	ICERs (I$/YLS)[e]
No screening	–	–	6.30	38.0909	–
Cytology (1 year)	20	14.2 (11.4–16.5)	56.90	38.0932	Dom[e]
Cytology (5 years)	**50**	**21.4 (14.9–30.5)**	**33.80**	**38.0945**	**7680**
HPV DNA (5 years)	**50**	**23.4 (15.5–32.6)**	**36.30**	**38.0947**	**12,210**
HPV DNA (4 years)	**50**	**24.7 (17.1–33.7)**	**41.60**	**38.0950**	**16,340**
Cytology (3 years)	50	26.1 (18.9–35.6)	49.70	38.0953	Dom[f]
HPV DNA (3 years)	50	27.7 (20.9–36.4)	52.80	38.0955	25,390
Cytology (2 years)	50	30.3 (23.8–37.8)	70.70	38.0959	40,000
Cytology (1 year)	50	35.7 (29.8–41.5)	132.60	38.0966	86,720

[a] Cytology screening is assumed to occur between the ages of 25–65 years. HPV DNA testing is assumed to occur between the ages of 30 and 65.
[b] Shown is the mean cancer reduction for the best-fitting parameter sets from the empirically calibrated model. Cancer reductions are calculated for each strategy compared to no screening.
[c] Lifetime costs are discounted annually at 3%.
[d] Average life expectancy for women under each strategy, discounted at 3% annually.
[e] Cytology screening strategies assume that cytology is conducted at the first visit, and results provided at the second visit along with colposcopy and biopsy of screen-positive women, with treatment provided in a third visit. 15% loss to follow-up is assumed at each subsequent visit. We do not include the costs associated with improving quality of care, enhancing infrastructure needs, or reducing loss to follow-up. Bolded strategies fall below the threshold of Lebanon's GDP per capita.
[f] These strategies are either more costly and less effective, or less costly and less cost-effective, than alternative options, and are thus considered (strongly or weakly) dominated.

women (Supplemental Appendix). With random screening, cytology at 2 and 3 year intervals were now below Lebanon's GDP per capita (I$9470 and I$14,750 per YLS respectively). Differences in cervical cancer reduction between screening a random subset compared to the same women with the same strategy were greater with higher coverage and screening frequency. For example, cytology screening at 50% every 5 years yielded 4.7% higher cervical cancer reductions when a random subset of women were screened while cytology ever 3 years at 50% coverage had 8.7% larger reduction with random screening. Screening a random subset of women at 70% coverage yielded even greater health benefits; cytology screening every 5 years had a cervical cancer reduction of 33.2% (range 21.1–51.6%) (Supplemental Appendix). Increasing screening frequency to every 3 years at 70% coverage had a reduction of 42.6% (range 28.5–63.1) and was the most efficient strategy under Lebanon's GDP per capita. Scale up of annual or biannual cytology were not found to be cost-effective.

4. Discussion

Lebanon's current screening practice of annual screening at 20% coverage is highly inefficient, with only a 14% cancer reduction and an ICER over 4 times higher than the country's GDP per capita. Larger health gains can be achieved at lower costs by increasing screening coverage to 50% and extending intervals to every 3 or 5 years. Specifically, cytology screening every 5 years was the most efficient strategy under Lebanon's GDP per capita. Since Lebanon currently lacks infrastructure for widespread cytology screening (adequate healthcare facilities, trained healthcare providers, cytopathologists) [11], the lifetime costs saved by extending screening intervals to every 5 years ($23 per woman) may be utilized for capacity building and demand creation. Additional health gains can be achieved at even lower costs if screening could be offered to a random subset of women at 50% coverage instead of repeatedly screening the same women. Further increasing cytology

Please cite this article in press as: Sharma M et al. Cost-effectiveness of increasing cervical cancer screening coverage in the Middle East: An example from Lebanon. Vaccine (2016), http://dx.doi.org/10.1016/j.vaccine.2016.12.015

screening to 70% coverage produced similar findings, but extended screening intervals to 3 or 5 years was found to be cost-effective under the assumption that a random subset of women were screened. However, achieving such high coverage may not be feasible without additional infrastructure or demand creation.

When we evaluated strategies of HPV DNA testing, we found that screening every 3 and 5 years at 50% coverage yielded a greater cervical cancer reduction than cytology with the same coverage and screening interval. In particular, HPV DNA testing every 4 and 5 years were efficient strategies with ICERs that were under Lebanon's GDP per capita at a cost of I$19 for HPV testing administration, with similar results at 70% coverage. Recent technology advancements have allowed for the development of low-cost HPV tests such as careHPV and OncoE6, which require less processing time than traditional tests [26]. Additionally, HPV-self sampling is a promising strategy that relies less heavily on infrastructure and may be preferable in conservative countries such as Lebanon where women can be reluctant to undergo pelvic examinations. Studies have shown that both novel molecular-based HPV tests as well as HPV self-sampling have good sensitivity and specificity in low and middle resource settings [27–29]. Less reliance on infrastructure and trained healthcare providers can facilitate scale up and provide greater population coverage [30].

Our results should be interpreted within the context of several limitations. Epidemiologic data on HPV and cervical cancer are limited in the Middle East. We chose the setting of Lebanon since we had access to cervical cancer registry data and primary cost estimates. However, we did not have data on age-specific prevalence of precancerous lesions or HPV type distribution in lesions, which are useful for model calibration. Similarly, there was large variation in cost estimates for screening, diagnosis, and treatment for precancerous lesions and cancer across payers (e.g., Ministry of Public Health vs. patient) and healthcare facility. Since the accuracy of mathematical models depend strongly on high quality epidemiological and economic data, our results can only be interpreted as qualitative assessments of the differing impacts of various screening strategies, rather than exact estimates of cancer reduction or ICERs. We aimed to provide broad insights to policy-makers regarding the relative efficiency of annual screening compared to extended intervals with cytology, as well as the potential value of HPV DNA testing. As more data become available, this analysis should be revisited to provide quantitative assessments of cervical cancer screening strategies, which are important for planning and healthcare allocation.

The strengths of our analysis include the use of a well-published cervical cancer model calibrated to the natural history of HPV pathogenesis using the best available data [13,17,18,21]. We employed a multi-parameter calibration approach to maximize model fit to the available epidemiologic endpoints and used a subset of good-fitting parameter sets to increase robustness of analyses. We found that greater health gains can be achieved at more reasonable costs by increasing cytology screening coverage while also extending intervals to every 5 years. HPV DNA testing is also a promising strategy that can allow for equal or greater cervical cancer reduction. Further, with trends toward higher and earlier sexual activity in the Middle East, increasing screening coverage will likely have even greater impact on disease burden. Results from this exploratory analysis can contribute to ongoing policy discussion regarding how best to maximize cervical cancer prevention in the Middle East.

Disclosed potential conflicts of interest

MS and JJK have disclosed no potential conflicts of interest. MS (Dr. Seoud) is on the medical advisory board of GSK, has received honoraria and travel grants for lecturing from GSK, MSD and Roche diagnostics and has received research grant money from GSK and MSD.

Acknowledgement

The authors would like to acknowledge the contributions of the cervical cancer prevention team at the Center for Health Decision Science (Harvard T.H. Chan School of Public Health). This study received no specific grant from a funding agency.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.12.015.

References

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:69–90.
[2] National Cancer Registry. Lebanese ministry of public health. <http://www.moph.gov.lb/en/> [accessed 10.15.16].
[3] Ferguson L, Grant AD, Lewis J, Kielmann K, Watson-Jones D, Vusha S, et al. Linking women who test HIV-positive in pregnancy-related services to HIV care and treatment services in Kenya: a mixed methods prospective cohort study. PLoS ONE 2014;9:e89764.
[4] Franco EL, Schlecht NF, Saslow D. The epidemiology of cervical cancer. Cancer J 2003;9:348–59.
[5] Sancho-Garnier H, Khazraji YC, Cherif MH, Mahnane A, Hsairi M, El Shalakamy A, et al. Overview of cervical cancer screening practices in the extended Middle East and North Africa countries. Vaccine 2013;31(Suppl 6):G51–7.
[6] Group FIS. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. N Engl J Med 2007;356:1915–27.
[7] Schiller JT, Castellsague X, Garland SM. A review of clinical trials of human papillomavirus prophylactic vaccines. Vaccine 2012;30(Suppl 5):F123–38.
[8] Dany M, Chidiac A, Nassar AH. Human papillomavirus vaccination: assessing knowledge, attitudes, and intentions of college female students in Lebanon, a developing country. Vaccine 2015;33:1001–7.
[9] Kim JJ, Sharma M, O'Shea M, Sweet S, Diaz M, Sancho-Garnier H, et al. Model-based impact and cost-effectiveness of cervical cancer prevention in the Extended Middle East and North Africa (EMENA). Vaccine 2013;31(Suppl 6):G65–77.
[10] Jumaan AO, Ghanem S, Taher J, Braikat M, Al Awaidy S, Dbaibo GS. Prospects and challenges in the introduction of human papillomavirus vaccines in the extended Middle East and North Africa region. Vaccine 2013;31(Suppl 6):G58–64.
[11] Seoud M. Extended Middle East and North Africa: cervical cancer and human papillomavirus: can we make the case for prevention in this "relatively" low prevalence region? Vaccine 2013;31(Suppl 6):vii–viii.
[12] Sullivan T, Sullivan R, Ginsburg OM. Screening for cancer: considerations for low- and middle-income countries. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. Cancer: disease control priorities, third ed., vol. 3. Washington (DC); 2015.
[13] Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahe C, et al. Cost-effectiveness of cervical-cancer screening in five developing countries. N Engl J Med 2005;353:2158–68.
[14] Goldie SJ, Kim JJ, Kobus K, Goldhaber-Fiebert JD, Salomon J, O'Shea MK, et al. Cost-effectiveness of HPV 16, 18 vaccination in Brazil. Vaccine 2007;25:6257–70.
[15] Kim JJ, Kuntz KM, Stout NK, Mahmud S, Villa LL, Franco EL, et al. Multiparameter calibration of a natural history model of cervical cancer. Am J Epidemiol 2007;166:137–50.
[16] Sharma M, Ortendahl J, van der Ham E, Sy S, Kim JJ. Cost-effectiveness of human papillomavirus vaccination and cervical cancer screening in Thailand. BJOG 2011;119:166–76.
[17] Campos NG, Kim JJ, Castle PE, Ortendahl JD, O'Shea M, Diaz M, et al. Health and economic impact of HPV 16/18 vaccination and cervical cancer screening in Eastern Africa. Int J Cancer 2011;130:2672–84.
[18] Diaz M, de Sanjose S, Ortendahl J, O'Shea M, Goldie SJ, Bosch FX, et al. Cost-effectiveness of human papillomavirus vaccination and screening in Spain. Eur J Cancer 2010;46:2973–85.
[19] Diaz M, Kim JJ, Albero G, de Sanjose S, Clifford G, Bosch FX, et al. Health and economic impact of HPV 16 and 18 vaccination and cervical cancer screening in India. Br J Cancer 2008;99:230–8.
[20] World Bank: Occupational wages around the world. <http://data.worldbank.org/data-catalog/occupational-wages> [accessed 09.01.16].
[21] Goldhaber-Fiebert JD, Goldie SJ. Estimating the cost of cervical cancer screening in five developing countries. Cost Eff Resour Alloc 2006;4:13.

[22] Memiah P, Makokha V, Mbuthia W, Kiiru GW, Agbor S, Odhiambo F, et al. Epidemiology of Cervical Squamous Intraepithelial Lesions in HIV Infected Women in Kenya: a cross-Sectional Study. Afr J Reprod Health 2015;19:133–9.
[23] Gold MR. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
[24] Drummond M. Methods for the economic evaluation of health care programmes, second ed.
[25] World Bank Development indicators. <http://data.worldbank.org/indicator/PA.NUS.FCRF?page=1> [accessed 11.07.15].
[26] Belinson SE, Belinson JL. Human papillomavirus DNA testing for cervical cancer screening: practical aspects in developing countries. Mol Diagn Ther 2010;14:215–22.
[27] Labani S, Asthana S. Age-specific performance of careHPV versus Papanicolaou and visual inspection of cervix with acetic acid testing in a primary cervical cancer screening. J Epidemiol Community Health 2016;70:72–7.
[28] Valdez M, Jeronimo J, Bansil P, Qiao YL, Zhao FH, Chen W, et al. Effectiveness of novel, lower cost molecular human papillomavirus-based tests for cervical cancer screening in rural china. Int J Cancer 2016;138:1453–61.
[29] Chen W, Jeronimo J, Zhao FH, Qiao YL, Valdez M, Zhang X, et al. The concordance of HPV DNA detection by Hybrid Capture 2 and careHPV on clinician- and self-collected specimens. J Clin Virol 2014;61:553–7.
[30] Gravitt PE, Belinson JL, Salmeron J, Shah KV. Looking ahead: a case for human papillomavirus testing of self-sampled vaginal specimens as a cervical cancer screening strategy. Int J Cancer 2011;129:517–27.

Please cite this article in press as: Sharma M et al. Cost-effectiveness of increasing cervical cancer screening coverage in the Middle East: An example from Lebanon. Vaccine (2016), http://dx.doi.org/10.1016/j.vaccine.2016.12.015