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Differential impact of cervical cancer in immigrant women: a decade-long epidemiological study in the Marche Region, Italy

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ABSTRACT

Background Cervical cancer is primarily caused by persistent human papilloma virus (HPV) infections, with significant disparities observed in its burden, especially affecting immigrant populations from high HPV prevalence regions. This study evaluates the incidence and severity of cervical cancer in immigrant women in the Marche region, Italy, from 2010 to 2019.

Methods We employed a detailed analysis of population-based data from the Marche Cancer Registry using the age-standardised incidence rates (IRs) and Poisson regression models for in situ cervical cancer (ISCC) and infiltrating cervical cancer (ICC).

Results The IRs for ICC and ISCC among immigrant women are alarmingly higher compared with their Italian counterparts; IR for ICC in immigrant women is 26.5 per 100 000 women-years, compared with 7.9 in Italian women. For ISCC, the IR is 55.1 for immigrants versus 29.2 for Italians.

Immigrant women showed a median age at diagnosis for ICC of 49 years, almost a decade younger than Italian women, and they were more likely to have squamous cell histology, which is linked to high-risk HPV strains.

Conclusions The study reveals a substantially higher incidence of both ISCC and ICC among immigrant women with ICC diagnosed 8 years previously. These findings underscore the pressing need for culturally and linguistically tailored public health interventions, including improved access to screening and vaccination for HPV, to address the elevated risk and earlier onset of cervical cancer in immigrant women in Italy. The study highlights the critical role of preventive measures in reducing health disparities and enhancing the efficacy of public health policies.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cervical cancer is the fourth most prevalent cancer among women worldwide.
⇒ Disparities in the burden affect immigrant populations from high human papilloma virus (HPV) prevalence regions.

WHAT THIS STUDY ADDS

⇒ The immigrant women are diagnosed a decade younger ages than Italian women.
⇒ The immigrant women are more likely to have squamous cell histology, which is linked to high-risk HPV strains.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The analysis emphasises the need for targeted preventive health measures among immigrant populations in Italy.
⇒ Identifying barriers to effective cervical cancer prevention within immigrant populations is necessary to mitigate avoidable disparities and to reduce costs.

INTRODUCTION

Cervical cancer (CC) is the fourth most prevalent cancer among women worldwide, with an age-standardised incidence rate (IR) of 13.3 per 100 000 women annually. The incidence of CC exhibits pronounced geographical disparities, predominantly burdening low to middle-income nations. Europe witnesses approximately 34 000 new CC cases yearly, resulting in 13 000 deaths.[1] CC is the fifth most diagnosed cancer among women aged 0–49 and the third among those aged 50–69 in Italy.[2]

Human papilloma virus (HPV) is the main etiological factor for CC, causing up to 99.7% of high-grade precarcinomas.[3] Screening programmes such as the Pap test, visual inspection, and HPV-DNA and HPV-mRNA assays are highly effective in infiltrating CC prevention through early detection of preneoplastic lesions.[4 5] HPV-DNA screening is more effective but less specific than a Pap test in preventing CC, whereas HPV-mRNA test has a similar sensitivity but a higher specificity than the HPV-DNA tests.[5]

HPV vaccination is a further aid in prevention, by controlling the disease at its source. The possibility of eradicating CC trough vaccination seems both realistic and achievable in the near future. CC is certainly a disease of inequalities.[6] Scaling up to 80–100% HPV vaccination coverage globally with a broad-spectrum HPV vaccine could avoid 6.7–7.7 million cases over the following 50 years.[7]

Italy has seen a significant rise in immigration from regions with high HPV prevalence, necessitating a focused study on CC incidence and severity among immigrant versus native populations. A large fraction of these immigrants originates from

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low- to middle-income countries in Asia, Eastern Europe and North Africa, where there is a high prevalence of HPV infections. Research indicates that immigrant women face a heightened risk of developing CC.[8]

This study analyses the incidence and severity of CC in immigrant women to pinpoint effective preventive measures in Marche Region, Italy, using cancer registry data.

METHODS

This retrospective population-based study analysed CC incidence during 2010–2019 in the Marche Region, a territory of the central Italy divided into five provinces: Pesaro e Urbino, Ancona, Macerata, Ascoli Piceno and Fermo. The population at risk was all Italian and foreign citizenship female, aged 20 years old and over. Resident population were retrieved from the Italian National Institute of Statistics database[9]; specifically, population for the years 2010–2018 came from the Intercensuary Reconstruction of the resident population by age, sex and municipality, whereas for the year 2019, data are from census source.

CC incidence data were sourced from the Marche Cancer Registry (Registro Tumori Marche (RTM)). The RTM covers a population of 1 512 672 inhabitants (as of 1 January 2020) across all provinces in the Marche Region. The registry has been systematically collecting cancer diagnosis data for the regional population since 1 January 2010; it adheres to data quality standards recommended by the Italian Network of Cancer Registries (Associazione Italiana Registri Tumori) and the International Agency for Research on Cancer.

The demographic and clinical characteristics of the participants included date of birth, gender, province of residence and country of origin, date of diagnosis, tumour characteristics, treatments and vital status. Immigrants were defined as women born outside Italy based on the most commonly used criterion for identifying immigrant populations.[10]

CC diagnoses were classified according to ICD-O-3.2 codes (International Classification of Diseases for Oncology, Third Edition 2022), and the disease's severity was gauged on staging criteria. Advanced disease is defined as all cases classified as stage ≥IIB according to the FIGO (International Federation of Obstetrics and Gynecology) 2018 classification, or cases where the patient underwent chemotherapy and radiotherapy.

Data analysis focused on demographic details, tumour characteristics and treatments. We analysed the cancer characteristics (in situ cervical cancer (ISCC) and infiltrative cervical cancer (ICC)), histological type, pathological stage, presence of metastases and the application of surgical and adjuvant/curative therapies (ie, radiotherapy and chemotherapy).

For descriptive analysis, we used absolute and relative frequencies to represent categorical variables and χ^2 test or Fisher's exact test for group comparisons. Continuous variables were summarised using medians and ranges. The Kaplan-Meier analyses with the log-rank test assessed the hypothesis that there was no significant difference in the age at diagnosis between the two groups of women.

We calculated crude and direct age-standardised IRs per 100 000 women per year for females aged 20 years and older using the European Standard Population (2013) in 5-year age intervals as reference. To assess variability, 95% CIs were calculated using the Gamma Method.[11] This analysis was performed for both Italian and immigrant women and stratified by CC type.

To estimate the relative risk of cervical neoplasm development in immigrant compared with Italian women, a Poisson regression model was employed with age group as a covariate. The analysis revealed that the nationality's effect on IRs varied across age groups, indicated by the statistical significance of the nationality-age interaction term. Consequently, the model was reparameterised to directly compute the Incidence Rate Ratio (IRR) for immigrant versus Italian women across each age category.

All statistical tests were conducted as two-tailed, with a significance level set at 0.05.

Data analysis was performed using RStudio, V.2023.03.0.

Table 1 Distribution of women's nationalities diagnosed with ICC and ISC. Marche Region, 2010–2019

	Total	ICC	ISC
Nationality	N (%)	N (%)	N (%)
Overall	2570 (100)	651 (25.3)	1919 (74.7)
Italian	2017 (78.5)	500 (24.8)	1517 (75.2)
Foreign	553 (21.5)	151 (27.3)	402 (72.7)

ICC, infiltrating cervical cancer; ISC, in situ cancer.

RESULTS

The average annual population of the Marche region between 2010 and 2019 was 1 541 100, with females comprising 52%. Among women aged 20 years and older; approximately 91% were Italian, and 9% were immigrants. Over the 10-year study period, this population contributed 6 046 386 and 582 873 person-years at risk, respectively.

We identified 2570 new cases of CC during 2010–2019 period; among them, 553 (22%) were immigrant women (table 1). The overall crude IR was 38.77 per 100 000 women/years (95% CI 37.28 to 40.3), and the standardised rate was 41.07 (95% CI 39.49 to 42.71), with ISCC accounting for 75% (1919 cases) and ICC for 25% (651 cases).

Predominant nationalities among immigrants included Romanians, Albanians, Moroccans and Chinese. Table 2 categorised CC cases by the foreign women's country of birth, differentiating between ICC and ISCC.

A total of 553 cases of CC were observed among immigrants in 2010–2019 period; in particular, 151 (27%) were infiltrating and 402 (73%) in situ. The data reveal that Romanian women were the largest group among the foreign women diagnosed with both types of CC, highlighting a significant representation of Eastern European women in the immigrant population affected by CC in the Marche region.

Table 3 showed the comparative analysis of both crude and age-standardised IR of ICC and ISCC per 100 000 women per year in the Marche Region that was categorised by Italian and Immigrant women, with their respective 95% CIs. This table

Table 2 Distribution of immigrants' country of birth diagnosed with ICC and ISC. Marche Region, 2010–2019

	Total	ICC	ISC
Immigrants' country of birth	N (%)	N (%)	N (%)
Overall	553 (100)	151 (27.3)	402 (72.7)
Romania	183 (33.1)	55 (30.1)	128 (69.9)
Ukraine	38 (6.9)	18 (47.4)	20 (52.6)
Moldova	39 (7.1)	10 (25.6)	29 (74.4)
Morocco	16 (2.9)	9 (56.3)	7 (43.8)
Albania	32 (5.8)	9 (28.1)	23 (71.9)
Other	245 (44.3)	50 (20.4)	195 (79.6)

ICC, infiltrating cervical cancer; ISC, in situ cancer.

Table 3 Crude and age-adjusted (European standard population) incidence rates per 100 000 women with 95% CI for infiltrating and in situ neoplasm for Italian and immigrant women. Marche Region, 2010–2019

	Crude IR		Age-adjusted IR	
Neoplasm	**Italian**	**Immigrant**	**Italian**	**Immigrant**
	(95% CI)	**(95% CI)**	**(95% CI)**	**(95% CI)**
ICC	8.3	25.9	7.9	26.5
	(7.6–9.0)	(21.9–30.4)	(7.2–8.6)	(21.9–31.9)
ISCC	25.1	69.0	29.2	55.1
	(23.8–26.4)	(62.4–76.1)	(27.7–30.7)	(48.9–61.9)

ICC, infiltrating cervical cancer; IR, incidence rate; ISCC, in situ cervical cancer.

revealed higher crude IR of both ICC and ISCC among immigrant women compared with Italian women (25.9 (95% CI 21.9 to 30.4) vs 8.3 (95% CI 7.6 to 9.0)). Immigrant women had a significantly higher crude IR for ISCC than Italian women (69.0 (95% CI 62.4 to 76.1) vs 25.1 (95% CI 23.8 to 26.4)).

Age-standardised IR for ICC was 7.9 (95% CI 7.2 to 8.6) per 100 000 women/year for Italian women and 26.5 (95% CI 21.9 to 31.9) for immigrant women, after adjusting for age differences between the Italian and immigrant female populations. The age-standardised IR for ISCC was 55.1 (95% CI 48.9 to 61.9) for immigrant women and 29.2 (95% CI 27.7 to 30.7) for Italian women. The non-overlapping CIs for ICC and ISCC IRs between Italian and immigrant women highlight the statistically significant difference in cancer risk, confirming the disparity observed in crude and age-adjusted rates. These adjusted rates further underlined the significantly higher risk of CC among immigrant women, independent of age distribution.

Results of Poisson regression, adjusted for age, confirmed higher risk of immigrant vs Italian for ICC (IRR=3.80; 95% CI 3.13 to 4.59) and ISCC (IRR=1.77; 95% CI 1.58 to 1.97); however, the significance of interaction term for nationality by age (results not showed) suggests a possible effect modification by age. Figures 1 and 2 showed the age-standardised IR of ICC and ISCC, respectively, comparing Italian and immigrant women across different age groups.

ICC incidence was consistently higher among immigrant women compared with Italian women across almost all age categories except in the 20–29 age group. The Poisson regression analysis confirmed this result (table 4). This indicated a higher vulnerability of immigrant women to infiltrating CC across the lifespan, with the exception of the youngest age group. Immigrant women had also higher ISCC IRs than Italian women in all age groups.

Table 5 provided detailed clinical and demographic characteristics associated with ISCC and ICC cases. The analysis focused on age at diagnosis, pathological stage, presence of metastases and treatment approaches, contrasting the findings between Italian and immigrant women. The median age at diagnosis for ISCC was comparable between Italian and immigrant women, positioned at 40 years. This similarity suggested an early disease detection across both groups.

The distribution of ISCC predominantly affected the uterine cervix, with no significant difference between the two populations, indicating similar disease manifestation patterns.

Treatment for ICC, primarily involving surgical interventions, showed no significant variance between Italian and immigrant women, reflecting equitable treatment access once diagnosed.

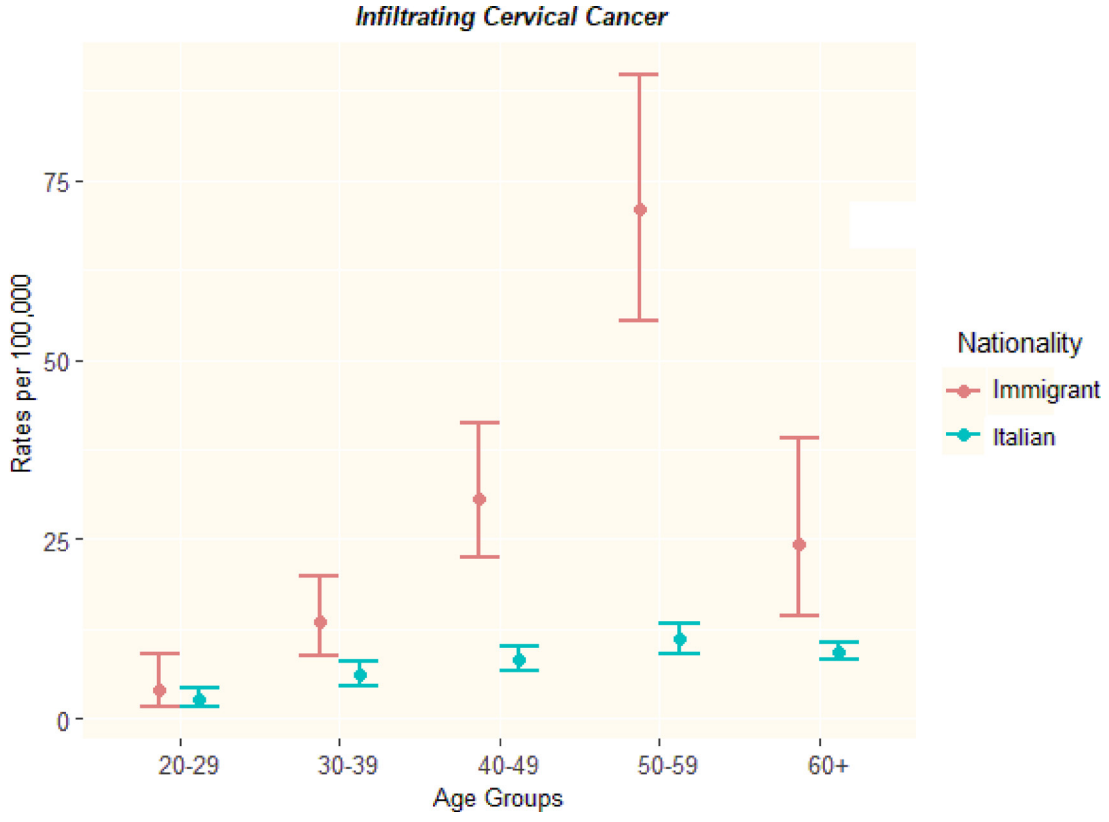

Figure 1 Age-standardised incidence rate for infiltrating cervical cancer and 95% CIs for italian and immigrant women. Marche Region, 2010–2019.

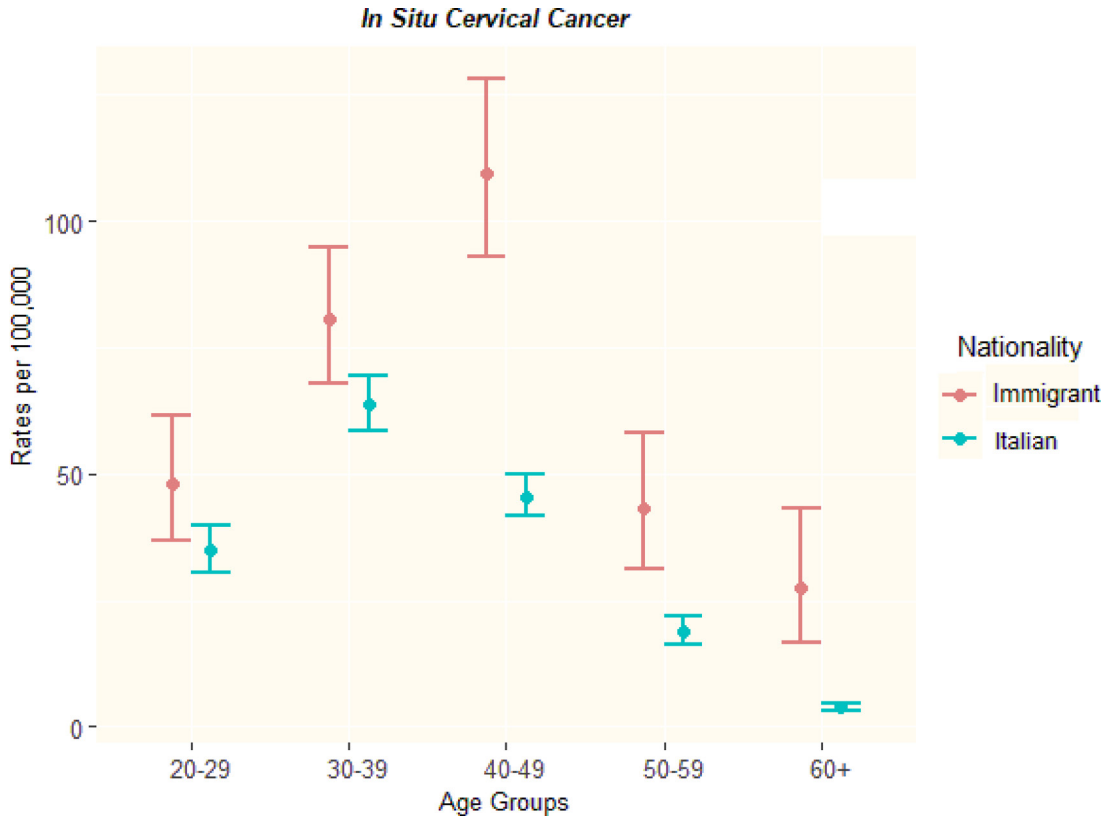

Figure 2 Age-standardised incidence rate for in situ cervical cancer and 95% CIs for Italian and immigrant women. Marche Region, 2010–2019.

Notably, immigrant women had ICC at a median age of 49 years, significantly lower than their Italian counterparts, who were diagnosed at a median age of 59 years (p<0.001).

ICC cases were primarily located at the uterine cervix for both groups. However, immigrant women were more frequently diagnosed at advanced stages (stage>IIB).

A marginally higher incidence of metastatic disease was observed at diagnosis among immigrant women, though treatments involving chemotherapy and surgery were similarly applied across both demographics.

Immigrant women had a higher prevalence of squamous histology in ICC cases (86%) compared with Italian women (67%), with a statistically significant difference (p<0.001).

DISCUSSION

Migration has become an important phenomenon in Western Europe, in terms of population changes during the past decades, causing major challenges to healthcare systems and policies.[12] The immigrant female population in the Marche region is 9% total female population in the period between 2010 and 2019.

This study presents the analysis of the incidence and severity of CC among immigrant women in the Marche Region of Italy over 10-year period (2010–2019), using statistical models to adjust for demographic differences. The prevalence of CC among women from Eastern Europe reflects the higher incidence of the disease in their countries of origin.[13] The results highlight a significantly higher burden of both ISCC and ICC among immigrant women compared with their Italian counterparts, even after adjusting for age differences. In cases of ICC, immigrant women exhibited higher crude and age-standardised IRs compared with their Italian counterparts, with figures of 25.9 versus 8.3 and 26.5 versus 7.9, respectively (table 3). Our evidence of ICC excess of risk associated with the immigrant women (IRR=3.80; 95% CI 3.13 to 4.659) is supported by Collatuzzo *et al*, showing a high risk of CC in migrants in Southern Italy (OR=3.54, 95% CI 2.99 to 4.20).[8] Migrant females (from Eastern Europe) show a higher IR for ICC (IRR 2.02, 95% CI 1.57 to 2.61) also in Veneto Region.[14]

Table 4 Results of multivariate Poisson regression models, with reparameterisation of interaction effect, infiltrating and in situ cervical cancer. Immigrant versus Italian women. Marche Region, 2010–2019

Nationality/age		Infiltrating cervical cancer		In situ cervical cancer	
Group	Reference	IRR (95% CI)	P value	IRR (95% CI)	P value
Immigrant 20–29	Italian 20–29	1.54 (0.51 to 3.90)	0.400	1.37 (1.02 to 1.82)	0.032
Immigrant 30–39	Italian 30–39	2.22 (1.33 to 3.60)	0.002	1.26 (1.04 to 1.52)	0.015
Immigrant 40–49	Italian 40–49	3.76 (2.58 to 5.39)	<0.001	2.41 (2.00 to 2.88)	<0.001
Immigrant 50–59	Italian 50–59	6.43 (4.72 to 8.69)	<0.001	2.27 (1.60 to 3.16)	<0.001
Immigrant 60+	Italian 60+	2.60 (1.48 to 4.23)	<0.001	7.35 (4.23 to 12.0)	<0.001

IRR, incidence rate ratio.

Table 5 Sample description of infiltrating cervical cancer and in situ cervical cancer cases. Marche Region, 2010–2019

	All	Italian	Immigrant	
Characteristics	**N (%)**	**N (%)**	**N (%)**	**p Value**
In situ cervical cancer				
Total	1919 (100)	1517 (79)*	402 (21)*	
Age at diagnosis				
Median (range)	40 (18–80)	40 (18–80)	40 (20–78)	0.2000
Tumour site				0.3601
Uterine cervix	1512 (79)	1193 (79)	319 (79)	
Endocervix	119 (6)	101 (7)	18 (18)	
Exocervix	264 (14)	205 (14)	59 (15)	
Bordering lesion of the cervix	24 (1)	18 (1)	6 (1)	
Infiltrating cervical cancer				
Total	651 (100)	500 (77)[1]	151 (23)[1]	
Age at diagnosis				
Median (range)	55 (20–93)	58 (20–93)	50 (24–79)	<0.0001
Tumour site				0.3828
Uterine cervix	285 (44)	220 (44)	65 (43)	
Endocervix	120 (18)	95 (19)	25 (17)	
Exocervix	240 (37)	182 (36)	58 (38)	
Bordering lesion of the cervix	6 (1)	3 (1)	3 (2)	
Disease stage				0.6463
Advanced (stage >IIB or chemo)	384 (59)	292 (58)	92 (61)	
Mild (no chemo, stage <IIB)	267 (41)	208 (42)	59 (39)	
Metastases				0.7002
Presence	235 (36)	178 (36)	57 (38)	
Tumour type				<0.0001
Squamous cell	466 (72)	336 (67)	130 (86)	
Adenocarcinoma	106 (16)	91 (18)	15 (10)	
Other	79 (12)	73 (15)	6 (4)	
Type of therapy				
Chemotherapy	377 (58)	287 (57)	90 (60)	0.6920
Surgery	424 (65)	327 (65)	97 (64)	0.8648

*Row percentages. All other percentages in the table are column percentages.

Migrant women have higher age-standardised IR than Italian women for both ICC and ISCC across all age groups, except for those aged 20–29 years for ICC.

Our study show also that immigrant women are diagnosed at younger ages and more advanced stages of CC compared with Italian women (50 vs 58 years, p<0.001). High ICC IRs in immigrant women >40 years may reflect inadequate screening in the previous decade. On the contrary, ISCC are diagnosed at the same age (40 years) in immigrants and Italian women. This may be due to clinical examinations for pregnancy or subsequent follow-ups; these kind of controls stop after this period. The results therefore reflect differences in health-seeking behaviour, awareness and access to healthcare, emphasising the need for targeted educational and screening programmes to effectively reach these at-risk populations. These findings are in alignment with previous studies, which have demonstrated elevated risks of CC in immigrant due lower sociocultural levels, higher prevalence of HPV infections in their countries of origin, disadvantages in accessing services and consequent negative effects on adherence to screening and vaccination programmes.[15 16] Key social determinants that influence European parents' decisions to vaccinate their children against HPV are: immigrant status, unemployment and religiosity.[17] Immigrant parents, moreover, have a 39% lower likelihood of vaccinating their children compared with native parents in their respective countries.[18]

Immigrant women have a higher prevalence of squamous histology than Italian women in our study (86% vs 67%, p<0.001). This variation in histological type may be explained by different prevalences of HPV strains across various population subgroups.[19 20] It is important to note that 35% of ISCC and 36% of ICC are in Romanian immigrant. A recent study conducted in Romania emphasises the importance of implementing an integrated diagnostic algorithm in screening that incorporates HPV genotype, Pap smear and p16/Ki-67 staining to enhance the accuracy of CC screening and management strategies. This approach is particularly crucial for women from regions with a high disease burden.[3]

Finally, it is worth noting that ICC results in high costs, in particular, when diagnosed in advanced stages and requires expensive treatments such as chemo-radiotherapy and immunotherapy. This without considering the high human cost of suffering and death and the significant loss of women in their most productive years.

Although the study is representative of the CC incidence in the central Italy in the period 2010–2019, the limitation concerns the reporting delay to the cancer registry that affects the efficiency of health system. Another limitation of our study is that we were unable to analyse IR by region of origin due to unavailability of immigrant population data by country of birth. The population of immigrants used for the denominators, moreover, is related to the legal immigrants, and this may have inflated the incidence in immigrants compared with the native population.

The implications of these findings suggest some reflections: first, they underscore the necessity for culturally and linguistically appropriate health interventions that address the specific needs of immigrant communities. Enhancing accessibility to CC screening and vaccination programmes for HPV is pivotal in reducing the incidence and severity of this disease among immigrant women. We should remember that this disease is preventable. Second, the distinct pattern of disease presentation in immigrant women suggests that modifications to existing screening guidelines might be warranted to better detect and manage CC in this population at an earlier stage. Otherwise, the global cost of disease will increase steadily in next years, if we consider factors as lower pap test screening during COVID pandemic, increase of immigrant women in the last years (eg, with arrival of Ukranian women due to war) and higher costs of new treatments.

Current findings also show persistent challenges in cancer care among migrant population, including long waiting lists and regional disparities and highlighting the need for inclusive healthcare strategies in Italy.[16 21 22] The practice of asking individuals to make choices that their circumstances do not allow almost inevitably perpetuates health inequalities. It is globally acknowledged that health is inherently political; although it transcends party politics, politicians from any faction have the opportunity to act based on the extensive evidence at their disposal.[23] Enhancing population health and minimising avoidable health disparities should be prioritised at the national level in Italy, where the right to health is enshrined in the Constitution.[24]

CONCLUSIONS

Continued monitoring of incidence and outcomes of CC will be essential to assess the effectiveness of such interventions and to ensure equity in healthcare outcomes across all segments of the population. Future research should focus on identifying barriers to effective CC prevention (both primary and secondary) within immigrant populations and developing tailored interventions with policymakers. These strategies aim to mitigate avoidable disparities and potentially reduce costs for individuals and the National Health System.

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