Immigrants and cancer in Italy: a literature review

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Abstract
Immigration is a growing flow in Italy. Also specific health needs could be imported. We focused on cancer. A systematic search for literature in PubMed was performed on 10th March 2016, limited to articles published between 1st March 1996 and 1st March 2016. Papers were reviewed focusing on: specific risks, prevention and care. Cancer incidence is generally lower for immigrants than for natives, also for the health immigrant effect. However, cancers with an infective etiology may have, among some groups of immigrants, a great relevance. Primary or secondary cancer prevention could be greatly improved among immigrants. Moreover, another specific aspect of immigration is at seeking cancer care for children. Specific preventive strategies should be customized for immigrants to get higher compliance, e.g. for those at high risk for cervical cancers. Moreover, the capability of the Italian health system to cope more comprehensively with sick immigrated children and their families should be improved.

INTRODUCTION
Italy is a country with a long past of emigration but in quite recent years has become one of the most carved and crowded doors for those immigrants who want to enter Europe.

Immigration has among the political, humanitarian, social and cultural perspectives also health implications. Migrants may share some characteristics which affect their health status, for example the “natural” selection of those people strong enough to get through the ordeals of migrating. Moreover, any different migrants’ group, may have a different risk pattern related to specific cultural life styles which steer risky exposures (e.g. diet, fecundity, etc.) [1].

Therefore, immigrated populations may have specific characteristics, needs, susceptibilities, risks, which have to be known, documented, and considered, to offer them, and make easily usable, the same services available for the Italian natives together with customized assistance, if necessary.

The aim of this study was to review the literature for papers published in the last twenty years focusing on cancer in immigrants in Italy, to underline those topics which need to be addressed by specific health interventions.

METHODS
We searched in PubMed publications, published between 1st March 1996 and 1st March 2016, matching the following search terms: ((immigrant* and (Italy or Italian) and cancer) or (migrant* and cancer and (Italy or Italian)) or (immigrant* and (Italy or Italian) and tumor) or (migrant* and tumor and (Italy or Italian)) or (immigrant* and (Italy or Italian) and tumour) or (migrant* and tumour and (Italy or Italian)) or (immigrant* and (Italy or Italian) and neoplasia) or (migrant* and neoplasia and (Italy or Italian)) or (immigrant* and (Italy or Italian) and neoplasm*) or (migrant* and neoplasm* and (Italy or Italian)) or (immigrant* and (Italy or Italian) and in-situ) or (migrant* and in-situ and (Italy or Italian)))). The search was performed on 10th March 2016.

The search identified 85 papers. We went through the titles and the abstracts to identify pertinent articles: 31 were about non pertinent topics (e.g. infectious diseases among immigrants), 16 were not related to migration in Italy (e.g. migration of Italians within Italy, or of Italians abroad), 1 was a case-report (on a migrant lesion), 1 was written in Hungarian. After the exclusions, 36 papers were left. For one of them neither the abstract nor the full text was available.

Full texts of the remaining 35 studies were evaluated and three main general topics were presented: cancer risk factors, cancer prevention and cancer care.

RESULTS
Migration in Italy
In 2015 in Italy, according to the Italian National
Institute of Statistics (Istat; www.demo.istat.it), there were 5014437 resident citizens with a foreign citizenship (8.2% of the overall resident population), 2372796 of them were men (8.0% of the men resident) and 2641614 (8.4%) women. The foreign population has grown at a staggering pace, its number has increased of about 1 million since 2012 (4052081 in 2012, 6.8% of the overall residents).

In Table 1 the ten most frequent countries for citizenship of immigrants in Italy are shown. About 1/4 of all the foreign citizens come from Romania (23.6%), and other four European countries rank in the first ten places (Albania, Ukraine, Republic of Moldova, and Poland); then there are three Asian countries: Republic of China, Philippines and India, and two countries from North Africa: Morocco and Tunisia.

Migration in Italy and cancer occurrence

We found out only a few papers which coped with the occurrence of cancer in migrants in Italy, which offer a scattered coverage of epidemiological indexes in local settings. Before describing such studies we have to underline that the migrant populations are usually young. In Figure 1 the Italian resident population is presented by citizenship (Italian and foreign) with their percentage distributions by 10-year age groups (Istat; www.demo.istat.it). It is evident that the foreign population is strikingly younger than the Italian one, not only for the greater amount of children but also for all the first five decades. Afterwards, the relevance of Italians increases and among the elderly there are just a few foreigners. Out of age, in comparing native and migrant populations, we have to take into account the "healthy migrant effect" which means that migration itself selects healthy people. This can contribute to the lower global migrant effect which means that migration itself selects populations, we have to take into account the "healthy migrants exists". Out of age, in comparing native and migrant populations, we have to take into account the "healthy migrant effect" which means that migration itself selects healthy people. This can contribute to the lower global occurrence of cancer in migrants in both sexes in comparison with Italian natives [3]. Some clues for the healthy migrant effect come also from the causes of hospitalization [4]: in fact, among acute care the most frequent causes for immigrants were traumatic accidents, which represented almost ¼ of all the hospitalizations, while they were 8.9% for Italians [5]. Moreover, the healthy migrant effect, but also the shorter length of residence, may contribute to explain the lower proportion of cancers diagnosed among immigrant (0.9%) than among Italian workers (2.2%) in the Lazio region (central Italy) in 2000-9 [6].

As regards skin cancers, 1474 patients coming from outside the European Community were compared with 2100 Italians, all referred at the Institute of Dermatology of the University of Rome during 1989-1994. These groups were of the same age (20-39 years) and sex. Skin cancer were uncommon in both groups; benign lesions (such as fibromas, nevi, cysts, etc.) were 15.8% among the Italians and less that the half, 6.7%, among the immigrants [6].

Migration in Italy and cancer risk factors

Cancer risk factors may be different in distinct populations, and studies carried out in migrant populations have greatly contributed to split the role of genetic and environmental factors in cancer development.

Although the term of migrant is used for very different people, at least for some of them, or more realistically for many, their condition corresponds to a low level of socioeconomic status. This is a well-documented risk factor for many cancers: lung, stomach, oral cavity, esophagus, cervix uteri. For some of those cancers the relationship is related to specific risk factors, as we later will show. The status of immigrant has been evaluated among other socioeconomic conditions in relationship to cancer but also to many other health and social states by Caiazzo et al. [7].

Xeroderma pigmentosus (XP) is an example of a genetic autosomal recessive disease caused by defects in the repair damaged DNA. An international study tested the frequency of XP and other similar diseases in 5 European countries, considering that its incidence is estimated to be 1 case every million in Europe, but more frequent in other countries (e.g. North Africa). In 1988-2004 in Italy, the incidence of XP was mainly evidenced in autochthonic patients, on the contrary in German, France, Netherlands and United Kingdom more than half of the patients belonged to immigrant populations; presumably because at that times the immigrants were less frequent in Italy than in the other countries [8].

Moreover, some cancer risk factors are related to a Western-type life. This, for example, could greatly contribute to explain the lower risk for female breast cancer in immigrants than in Italians (e.g. age at menarche, number of children, breast feeding, etc.) [2] and consequently, together with the younger age, could contribute to explain the lower rate of mastectomy identified in Italian hospital discharge codes, during 2006-8, between immigrants in comparison with Italians [9].

Among other well-known risk factors we underline...
that the prevalence of overweight and obesity, although not negligible in adults resident in North Africa, especially among women, increases after emigration to European countries [10]. The relationship between vitamin D and cancer is still under debate; however, it is worthwhile mentioning the deficiency of vitamin D identified in Piedmont among immigrants new-borns and in their mothers [11].

Among cancer risk factors those which have been more deeply evaluated in immigrant populations to Italy are infections. Infectious diseases were overall the most frequent cause of day care hospitalization for men illegal immigrants (42.7%), and also for legal ones they were more than for Italians (9.4% vs 3.0%). Among women the differences were still statistically significant but less striking (legal immigrants 3.4%, illegal 7.3, Italians 1.6, p < 0.0001) [4].

As regards HIV type-1 infection, the prevalence of genetic strains seems to have been strongly modified in the last 10-15 years, due to the flows of HIV non-B variants which are more common in the population of North Africa [12]. This situation is common to several European countries, including Italy, as an effect of migration of populations from Western and Northern Africa, where non-B sub-types and Circulating Reombinant Forms are prevalent. The changes in the genetic pattern of HIV have not just an epidemiological interest but also an impact on drug resistance and vaccine development [13].

The prevalence of hepatitis B virus (HBV) infections is strongly heterogeneous across countries and it might be particularly high in some of those countries from which the immigration to Italy is particularly common, e.g. Republic of China (HBV prevalence 10%), Philippines (8%), Tunisia (7%) [14].

Migration is sometimes associated with the fear for the introduction of new infectious in our country. A study, carried out in 2003-4, focused on Human T-lymphotropic virus type I (HTLV-1), an infection etiologically linked with adult T-cell leukemia. HTLV-1 is sporadic in Italy and it is restricted to immigrants arriving from Japan, the Caribbean, South America, Sub-Saharan Africa, Melanesia and the Middle East. The study enrolled 3408 HIV-1/2 negative immigrants from Africa who referred to the Sexually Transmitted Disease clinic and/or Oncologic department of the University of Bologna, and 534 blood donors. The study revealed 2 HTLV-1 infections in immigrants from Africa, corresponding to a very low prevalence, 0.058% [15].

Human Papilloma Virus (HPV) is the most documented infective exposure in immigrant female populations in Italy. In a sample of 45 women, mainly from Nigeria (84.4%) and with a high proportion with history of prostitution (44.4%), 42.2% of them were HPV positive. This proportion was higher, 57.1%, among those who were also HIV positive (31.1% HIV+, in comparison with those HIV negative, 35.5% [16]. In another group of 115 women immigrated in Sicily (south of Italy), enrolled among those who had attended in 2007-8 the main hospital of the city of Palermo for performing a gynecological examination, Pap smear and HPV testing, almost half of them (47.8%) were HPV+. The proportion of women with HVP+ was 45.0% among those from sub-Saharan Africa (27/60) and 51.0% among those from Eastern Europe (28/55). The most frequent HPV oncogenic types were 16 (7.8%), 18 and 51 (6%), 52 (5.2%), 31, 53, and 68 (4.3%) [17].

The pooled analysis of three large studies on HPV prevalence in cervical cancer in Italy included 526 cases from women born in Italy and 48 cases from women born abroad. In this study the distribution of HPV genotypes did not differ significantly between Italian and born abroad women, with the exception of an excess for HPV oncogenic types 33 in immigrants with borderline statistical significance (p = 0.076) [18]. The prevalence of HPV infection was evaluated in 233 migrants and compared to 98 native Italian women. The prevalence was 37.8% among the native Italians, 57.1% (32/56) among migrants from Africa, 59.7% (92/154) for those coming from Southern and Eastern Europe, 62.5% (5/8) for migrants from Southern and Central America and 73.3% for migrants from Southern Asia. 73.4% of all infections were due to carcinogenic HPV genotypes [19]. A higher proportion of HPV+ among immigrated than Italian native women has been observed also in Northern Italy, especially in women migrated from countries with high prevalence of HPV [20].

One thousand recently migrated women (26-65 years) are one of the high risk groups involved in a cohort study planned in Lombardy region (northern Italy) for the evaluation and the monitoring of HPV infections and related cervical diseases in high risk women; this study is planned to provide results in 5-years [21].

Migration in Italy and cancer preventive activity

In Italy there are population-based public screening programs for female breast, colorectal and cervical cancers. The programs are based on active invitation addressed to all the target population (according to sex and age span), they include free screening testing, second level exams and treatment, and a comprehensive quality evaluation and monitoring of all the steps.

For the three mentioned cancers the risk for people immigrated from developed countries is similar to that of Italian natives. On the other hand, migrants from PFPM have generally a lower risk for breast and colorectal cancers. However, cervical cancer is much more frequent in PFPM than in Italian native citizens [2].

Moreover, in Italy since 2007 a HPV vaccination campaign addressed to all the girls 11-year old has been implemented. A survey carried out in Lombardy region among mothers showed that 55.3% of their daughters got the first dose of vaccine, 54% the second and 49.4% the third and last. Mothers coming from countries other than Italy were less informed about the pathogenesis of cervical cancer and about the efficacy of the vaccination, in comparison with Italian ones [22].

A recent survey was carried out on the Italian behavioral risk factors surveillance system (Progressi delle Aziende Sanitarie per la Salute in Italia, PASSI) based on information collected via telephone calls (during 2010-2013) on a random sample of the resident population in local health authorities. Among the other
In 2013, the National Centre for Screening Monitoring (Osservatorio Nazionale Screening, ONS) performed a survey on colorectal screening program, to which participated 85 of the 120 programs active. The aim was to compare natives in Italy with immigrants from low- or middle-income countries. Participation was lower for immigrants (34.3%) than for Italians (51.3%). Participation was higher among women (Italians and immigrants) than men, and among Italian-born women it increased with age while it decreased among migrants. The positivity to test standardized rate was higher for immigrants (Italians 4.4% vs Immigrants 4.8%, p < 0.05), while the participation rate to colposcopy was almost the same (81.8% vs 80.5%), as the detection rate for carcinoma and advanced adenoma at first (1.62‰ vs 1.34‰) and at repeated ones (9.25% vs 8.41%) [24]. On the contrary, in the Umbria region, where 12.2% of the resident female population come from PFPM, to be from PFPM in the cervical screening program was associated with a greater probability (in comparison with women from not PFPM, 97% from Italy and 3% from developed countries) to be referred for colposcopy (Odds Ratio (OR) adjusted for age, and for previous participation to cytology screening, 1.6, p = 0.002), to have a diagnosis of a cervical tumor (OR 4.2, p = 0.009), to have a diagnosis of squamous cell carcinoma (OR = 2.7, p = 0.1) and of a cervical adenocarcinoma (OR 11.6, p = 0.01) [25].

As regards cervical cancer screening, in Reggio Emilia (Northern Italy), the participation was higher for Italians (67%) in comparison with foreign women (54%), especially coming from countries with a prevalence of HPV above 12.6% (high human papillomavirus prevalence countries (HHPPC): Africa, except north Africa, Central and South America, and Eastern Europe) [20]. On the contrary the risk of a cervical cancer diagnosis was higher for foreign women both for invasive lesions (Standardized Incidence Ratios (SIR) 2.4, 95% Confidence Interval (CI)1.4-3.8) and for CIN3 (SIR = 1.2, 95% CI 1.9-1.4) [20]. All the tumor risk for foreign women was carried by those from HHPPC (SIR for invasive tumors 4.1, 95% CI 2.2-6 and for CIN3 SIR = 2.0, 95% CI 1.7-2.5). The ratio between pre-invasive (CIN3) and invasive cervical lesion was lower in foreign women (2.6 for those with HHPPC, and 3.6 for the others) in comparison with Italians (7.4). Pre-invasive lesions are asymptomatic and they can be detected only by Pap test; therefore, the low ratio is an index for low screening participation [20].

The participation of foreign women to cervical cancer screening has been also evaluated by Visioli et al. [26] who reviewed the cohort of invited women during three following screening rounds in Florence (Central Italy) during 2002-2008. The attendance at the first round was 33.9% for Italians, 29.6% for women from developed countries and 21.6% for those from PFPM. Although in all the three groups the participation had increased in the second and third round, the gap among groups did not change (in the third round Italians 57.4%, developed countries 50.2% and PFPM 45.4%). The risk ratio of participating to the cervical cancer screening was lower for foreign women (developed countries 0.88 at 1st round and 0.89 at 2nd or 3rd, and for PFPM women 0.65 at 1st and 0.80 at 2nd or 3rd round) than for Italian (reference = 1). The odds ratio of developing a high grade squamous intraepithelial cytology or worse was twice higher for immigrants from PFPM (OR = 2.09) or from developed countries (2.22) that for Italians [26].

The participation of immigrant women to cervical screening has been widely investigated in a survey recently carried out by the Italian Group for Cervical Cancer Screening (GISCi) in a study to which participated 48 out of the 120 active programs. In 2009-2011, among women aged 25-64 years, the participation was 45.4% for Italians and 39.9% for foreigners. The age-adjusted relative risk (RR) of Atypical Squamous Cells of Undetermined Significance + (ASC-US+) was higher for immigrated (RR = 1.25, 95% CI 1.24-1.27), including High-grade Squamous Intraepithelial Lesion (HSIL) (RR = 1.78, 95% CI 1.71-1.86) and cancer (RR = 3.33, 95% CI 2.57-4.31). The compliance to colposcopy was almost the same (90.3% vs 89.7%). It must be mentioned that the proportion of undelivered letters was 0.9 for those addressed to Italian women and 4.3% to immigrants [27].

Almost the same results were confirmed in a survey including those Italian pilot screening programs HPV DNA-based. Resident women born outside Italy had a RR of 0.84 (95% CI 0.82-0.85) to participate; participation: 52.2% for those born in Italy vs 43.6 born outside. To this difference could have played also the higher proportion (0.9% vs 5.2%) of undelivered letter of invitation. Italian women born outside had a higher positivity to HPV (7.8% vs 6.1%) and a higher proportion of CIN3 (56.7% vs 44.7%) and of invasive cancers (17.2% vs 5.6%) in comparison with those born in Italy [28].

In Veneto Region, the detection rate for cervical intraepithelial neoplasia grade 2 or more (CIN2+) at first exam was higher for foreign women than for Italian ones (5.1 per 1000 for Italians vs 10.1 per 1000 for immigrants); it was slightly higher also at subsequent tests (2.2 per 1000 for Italians vs 3.1 per 1000 for immigrants) [29].
Migration in Italy and cancer care

As regards the utilization of hospital services for cancer care in Italy, an evaluation of hospital discharge data collected by the Lazio Region (central Italy) for the year 2005 compared migrants and Italians [4]. In this study only people with a citizenship from less developed countries were considered immigrant and among them to have or not a regular stay permitted to split them into legal and illegal immigrants. The proportion of hospital discharges for neoplasms was lower among immigrants than Italians adults, presumably also for the younger mean age. In particular, in acute care the proportion of discharges for men was 5.2% of the total discharges among legal immigrant, 2.9% for illegal and 12.1% for immigrants from countries economically and culturally very different (p < 0.0001) and for females: 4.6%, 4.7% and 2.7%, respectively (p < 0.0001) [6].

For children is relevant also the so called health-migration, that is migration aimed at seeking a better medical care. In fact, the number of children with cancer coming from foreign countries is growing in specialized Italian centers. For example, the Gaslini Children’s Research Hospital documented an increasing number of immigrant patients from 2000 to 2008. This type of patients represents growing challenge which implies clinical, financial, administrative, logistical, psychological difficulties [30]; moreover, there are the problems of communication with children and their families [31]. In this difficult process of communication foreign children replace the unknown word with drawings as a mean of self-expression, expressing their willingness to go back home [32].

As regards children and adolescents cured in one of the Italian Association of Pediatric hematology and Oncology centers (AIEOP) from 1999 to 2008, 4.1% (608) of them were born and living abroad and 3.7% (538) were born abroad and living in Italy. The number of foreign children patients has increased over time from 2.5% of the total case-series in 1999 to 8.1% in 2009 [33]. The proportion of leukemia and lymphomas among immigrants, 59% (95% CI 56-62), was higher than among patients born in Italy, 48% (95% CI 47-49). Survival for acute lymphatic leukemia was lower for immigrants (10-year observed survival = 71.0%) than for Italians (80.7%) [33].

DISCUSSION

This review underlined the shortage of information on cancer incidence in immigrants in Italy, with only scattered and local studies available [2-7]. Therefore, the lack of a comprehensive picture addressing different epidemiological measures and outcomes in a national scenario should be bridged.

In Italy, immigrants are becoming a growing component of the population. Immigrants are sensibly younger than Italians and generally the migration selects the healthier among them as those more capable to stand the difficulties of migration. Therefore, cancer among immigrants is not overall a hot topic. However, since immigrants represent a melting pot of people they might hide specific needs for cancer prevention and care.

From this literature review we evidenced that immigrant is a rough definition. In fact, in the analyzed papers several different classifications have been used [34]: based on citizenship, on nationality (country of birth), on different grouping of countries (according to similarity to Italy, to the level of migration pressure or to the prevalence of HPV). Moreover, only some of the studies included also data and results for not legal immigrants, which presumably represent a not negligible and highly selected sample of people. Therefore, the first and unresolved problem in comparing results of studies on immigrants carried out in Italy is to find out if we are comparing the same people from one study to another one.

As regards cancers, immigrants, at least those coming from countries economically and culturally very differe-
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The results for this difference are complex because many factors could act simultaneously, including the different life experience at birth, the role of competitive causes of diseases and death, the possible different in intensity and typology exposure to carcinogens, up to the reliability of information related to the lower availability of cancer registration in such countries.

However, the role of infections cannot be minimized. In Italy, on average 8.5% of all the new cancers are due to infections [35]. Also among immigrants one of the main key targets is the HPV for its causative role in cervical cancer. Some of the countries from which the immigrants come have a high prevalence of HPV, moreover, the immigrant population has a relevant proportion of women and they are not aware about or used to undergo preventive tests. The variables that may enhance the risk for cervical cancer in the migrant female population are many and may depend on: a) social integration in the host-country: communication and racial difficulties, utilization of preventive care, discrimination, type of employment; b) personal-life: sexual behavior, number of partners, smoking and dietary habits, etc.; c) personal life conditions: homeless, refugee, legal status (irregular), temporary or permanent mobile status, victim of prostitution with the possible major risk under such sexual conditions.

Moreover, most of the immigrant women are not aware of cancer screening or facilities available, and the knowledge of cancer related problems is also very limited [36].

In Italy, cervical cancer is preventable either with vaccination of young girls and with regular screening of women 25-64 years old, both free of charge. Therefore, it is necessary to improve the knowledge of families on the benefits of HPV prevention of their daughters, and to support the participation of women to all public cancer screenings, especially cervical one. The target of prevention would decrease the requests to all public cancer screenings, especially cervical one. Moreover, cultural mediators and religious referees should be involved for achieving the best relationship with the patients and their families [30].

Screening is also invaluable for reducing the inequalities [38], particularly important for the population of immigrants which has less economic resources for accessing the private health system. A lot of work is still necessary; in fact, although participation of immigrants to screening has increased over time the gap between Italians is still as wide as in the past [26].

We used information about screening tests from two sources: ONS and PASSI [23, 24], which complemented each other. In fact, the different design of their surveys (observed data from organized programs vs self-reported testing in a sample of the population) provides a comprehensive picture of the overall “coverage”. On the other hand, it may also justify discrepancies in the proportions of tested people (within and/or outside screening programme).

Some points belong directly to the organization of the screening programs, for example reducing the proportion of undelivered letters increases the change for someone to have access to a service which otherwise would be unaffordable.

CONCLUSIONS

Prevention is the most effective weapon against cancer. Italy offers freely cancer prevention to all the resident target population; immigrants should be in the bull’s eye. HPV vaccination and cervical cancer screening should be exploited on risk migrant populations coping which those barriers which still hamper their comprehensive participation.

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