Università degli Studi di Pisa
Dipartimento di Statistica e Matematica
Applicata all'Economia

Report n. 187

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Pisa, September 2000

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To what extent can inter-regional migration perturb local endemic patterns? Estimating numbers of measles cases in the Italian regions[1]

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Abstract

In order to evaluate levels of under-reporting of measles cases for the Italian regions, estimates of the total number of measles cases for the pre-vaccination period 1951-71 are provided by using the relationship between number of cases on one side and births and migrations on the other side.

During the decade 1951-61 for some typical "sending " regions such as Abruzzi, Basilicata and Calabria, the number of cases expected taking migrations into account is up to 7% less than it was expected by ignoring migrations. For typical "receiving" regions such as Piemonte and Liguria, the figures are even larger: the estimated number of cases exceeds the figures expected in absence of migration up to 10%.

1. Introduction

Vaccination against measles was introduced in Italy in October 1976. An important problem related with case-notification data for measles in Italy during the pre-vaccination era is the dramatic level of under-reporting (Edmunds et al. 2000, Williams and Manfredi 2000). A simple strategy for the estimation of under-reporting of measles cases in the pre-vaccination era may be based on the fact that, due to the epidemiological characteristics of measles, it is expected that nearly all individuals in the population would experience infection with measles at some time during their lives (Anderson and May 1991). Thus, ignoring migration, it would be expected that the mean number of measles cases over time should approximate the mean number of births. By systematically using such a relation between births and cases the authors have recently provided (Williams and Manfredi 2000) estimates of under-reporting of measles cases for the 20 Italian regions and also for some of those Italian provinces embedding large conurbation areas (Rome, Milan, Naples, Turin) for the pre-vaccination "window" 1949-

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[1] This paper was written within the research project Progetto Nazionale "Epidemiologia delle Vaccinazioni in Italia" (National Coordinator: Stefania Salmaso, Istituto Superiore di Sanità), funded by the Italian Ministery of Health within the 1% framework. We thank Stefania Salmaso, Marta Ciofi, Roberto Tozzi, Donatella Mandolini and Antonino Bella for their valuable comments and suggestions. Usual disclaimers apply.

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1976. The results are striking, suggesting not only dramatic levels of under-reporting, but also a strong variability on the spatial scale. In fact, the estimated fractions of notified cases ranged from around 20-25%, in the best situation (Emilia-Romagna), up to 1-3% in Campania (Naples region). These results offered the possibility to correct the national figures of case notifications data. This last fact appears of a certain interest in that high under-reporting at the regional level may be a responsible for a bias in the age distribution of cases at the national level, which in turn might lead to biased estimates of the key epidemiological parameters, such as the force of infection. More noticeable, this bias will arise even if under-reporting is constant over ages.

The aforementioned paper (Williams and Manfredi 2000) is based on standard epidemiological assumptions (Anderson and May 1991). In particular the Italian regions are treated as separate epidemiological units, i.e. as closed populations: migrations (i.e. permanent change of residence) are not taken into account. This assumption, though rarely met in reality, is usually sufficient for practical purposes, especially if one works on national data, and international migrations and commuting are negligible. At the regional level on the other side the relation between births and cases may be perturbed by inter-regional migrations. More precisely, in a sending region (i.e. a region which only exports population) to get the true number of cases one has to discount births in each cohort by the expected number of emigrations of susceptible individuals in the same cohort. Similarly in a receiving region the number of expected cases would, other things being equal, exceed the number of births by the number of entries of susceptible individuals.

In most cases the effect of migration is expected to be small. In fact, as what essentially matters for epidemiological purposes are migrations of susceptible individuals, and since in the pre-vaccination era everybody was getting measles at very young ages, massive migrations of very young individuals would be necessary in order to seriously affect the basic relation between cases and births. From this point of view the Italian case is potentially of interest, in that in the most recent part of its pre-vaccination era, namely the two decades between the censuses in 1951 and 1971, Italy has experienced a dramatic boom of inter-regional migration flows (Golini 1974, Bonaguidi 1985), which started to decline only at the beginning of the seventies. Up to now we do not know, perhaps also due to the paucity of age-structured migrations data in the pre-vaccination era, of any attempts to provide a quantitative assessment of the exact role played by migrations in influencing the local case-notification figures.

In this paper considerations from basic epidemiological models with (permanent) migrations are used jointly with estimates of the net migration flows by age for the 20 Italian regions in the pre-vaccination window 1951-1971 in order to estimate the order of magnitude of the true number of cases of measles occurred in Italy in the same period. More in detail, the basic relation between number of cases and births is now replaced by some broader relations, relating cases with births and migrations of susceptible individuals. These revised estimates are obtained by first estimating, for each region, the net migration flow by age in the two inter-census periods 1951-1961 and 1961-1971. Subsequently the net migration of susceptible individuals is estimated by adopting as a "background" force of infection, the EURO-FOI estimated by Edmunds et al. (2000).

Some of the results are striking: during the decade 1951-61 for some typical "sending " regions such as Abruzzi, Basilicata and Calabria, the number of cases expected taking migrations into account is up to 7% less than it was expected by ignoring migrations, whereas for typical "receiving" regions such as Piemonte and Liguria, the number of cases expected exceeds the figures expected in absence of migration up to 10%. Remembering that under the action of the Euro FOI less than 35% of the children in each cohort are still susceptible by age five (at equilibrium) this is suggestive of the massive population flows occurred in the period considered.

On the other side the net impact of migrations on the estimated levels of under-reporting is quite limited: only in some case absolute variations in excess of 1% are observed: this confirms the usefulness of the approach in Williams and Manfredi (2000).

The present paper is organised as follows. Section two is theoretical and shows how the basic relation between births and cases at equilibrium modifies when migrations are explicitly introduced in the standard epidemiological model for childhood diseases. In section three the results on the estimates of net migration and number of cases for the Italian regions are reported. Concluding remarks and direction for future work follow.

2. Methods: epidemiological models with permanent migrations

In this section we use standard epidemiological models and equilibrium arguments. In a closed stationary population with B births per year and C cases of measles per year at equilibrium it holds, with an excellent approximation, the relation $C=B$.[3] This relation is of course perturbed by migrations. Inter-regional migrations are perturbation factors of population processes which may lead to biased estimates of the underlying parameters. The transmission dynamics of infectious diseases does not escape this rule. The estimation of basic epidemiological parameters, such as the force of infection (FOI) and the basic reproduction ratio, of childhood infectious diseases is usually based on data from the pre-vaccination era, under the assumption that the disease be in a state of equilibrium in its environment. The environment, i.e. the population in which the disease evolves, is in turn assumed to be stationary and closed to migrations. If the population is subjected to substantial migration flows the estimates of the FOI might be seriously biased, unless all migrations take place quite later in the life cycle, i.e. after the age at which "almost everybody has got measles". Generally speaking the estimation of the FOI in presence of migrations is a problem of estimation from censored data: emigration and/or immigration of susceptible individuals will change the susceptible pool which appears in the population at risk, i.e. the susceptible population, used in the computation of the FOI at each age. Similar problems occur in the estimation of the levels of under-reporting by using the relation between births and total cases, as used in Williams and Manfredi (2000). If the population rather than being closed, experiences substantial migration flows, as it happened in several Italian regions during 1950-70, the aforementioned relation between birth and cases has to be corrected. In this section we explicitly take migrations into account in the standard epidemiological model for childhood diseases (Anderson and May (1991). For simplicity we consider two basic cases, i.e. the case of a "purely sending" (or "source") region, and the case of a "purely receiving" ("sink") population. As we will see the old relation (holding at equilibrium) between the number of cases and the number of births is replaced by new relations between cases and size of the susceptible pool in the local population.

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[3] We are always considering a highly infectious disease, such as measles, during its pre-vaccination era. Moreover we assume that essentially everybody already experienced measles before mortality has started to remove a substantial part of the population.

2.1. The population is a source population

Let us consider first the case of a source population having positive emigration rates by age, but zero immigration.[4] In the extreme case in which all emigration in the population at risk of getting measles occur at age zero in a fraction *f* of total births, then it obviously holds *C/B=1-f*, which represents a lower bound in the ratio cases/births. Similarly, if all emigrations take place after the age "at which every one gets measles", then *C/B=1*, by recovering the basic relation. Outside the limit cases some of the outgoing individuals will experience the disease before they leave, so that the number of observed cases lies somewhere in between. To clarify the point, let us consider more in depth the role of emigration in the standard epidemiological model (Anderson and May 1991, pp. 58) by considering the following extended model:

$$\begin{array}{ll} \Delta X(a,t) = -(\mu(a)+\lambda(t)+q(a))X(a,t) & X(0,t)=B(t) \\ \Delta Y(a,t) = \lambda(t)X(a,t)-(\mu(a)+v+q(a))Y(a,t) & Y(0,t)=0 \qquad (1) \\ \Delta Z(a,t) = vY(a,t)-(\mu(a)+q(a))Z(a,t) & Z(0,t=0 \end{array}$$

where $\Delta=\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)$ is the population operator along characteristics, *X(a,t),Y(a,t),Z(a,t)* respectively denote the numbers of susceptible, infective and removed (with permanent immunity) individuals aged *a* at time *t*, *B(t)* denotes the yearly number of births, $\lambda(t)$ the force of infection (FOI), $\mu(a)$ the age-related mortality rate of the overall population, *q(a)* the emigration rate at age *a*, *v* the recovery rate. The total population X+Y+Z obeys:

$$\Delta n(a,t) = -(\mu(a)+q(a))n(a,t) \quad ; \quad n(0,t)=B(t) \qquad (2)$$

For simplicity we assume that the population is stationary, i.e. *B(t)=B*, and homogeneously mixing:

$$\lambda(t)=\beta Y(t)=\beta\int_0^\infty Y(a,t)da \quad (3)$$

Model (1) is formally identical to the standard model by Anderson and May (1991) when one defines the total exit rate from the population as $m(a)=\mu(a)+q(a)$. Let us consider the behaviour at equilibrium. The total population at age a is:

$$n(a)=B^{-\int_0^a(\mu(s)+q(s))ds}=Bp(a)Q(a) \qquad (4)$$

where $p(a)=\exp\left(-\int_0^a\mu(s)ds\right)$ is the usual survival (to mortality) function, $Q(a)=\exp\left(-\int_0^a q(s)ds\right)$ is the survival to emigration function (it is usually a defective survival function with $Q(\infty)=Q(L)<1$). Let moreover *G(a)=Q(a)q(a)*, be the relative improper emigration density satisfying: *Q'(a)=(-1)Q(a)q(a)=-G(a)*. The emigration flow per unit time at age *a* at equilibrium is *q(a)n(a)*, and the total emigration flow is $E=\int_0^\infty q(a)n(a)da$.

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[4] Here for migration we mean a permanent change of residence; commuting is neglected as not relevant for the purpose of this paper.

Intuitively we expect that the old relation *Nr.Cases=Nr.Births* is to be modified in a new relation of the type:

N. of cases≈Nr of births-Nr. of exits (emigrations) of susceptibles

Let us consider type 1 mortality, i.e. p(a)=1 for 0<a<L, the maximal age, and p(a)=0 elsewhere. The total number of cases is $C = \int_0^L \lambda X(a)da = \lambda X$ where $X(a) = Be^{-\lambda a}Q(a) = e^{-\lambda a}n(a)$. Therefore

$$C = \int_0^L \lambda e^{-\lambda a} n(a)da \qquad (5)$$

An integration by parts gives:

$$C = n(0) - n(L)e^{-\lambda L} + \int_0^L e^{-\lambda a}\frac{dn(a)}{da}da = n(0) - n(L)e^{-\lambda L} + \int_0^L e^{-\lambda a} B\frac{dQ(a)}{da}da$$

Now *n(0)=B* and *n(L)=BQ(L)*. Therefore

$$C = B\left(1 - Q(L)e^{-\lambda L}\right) - \int_0^L e^{-\lambda a} n(a)q(a)da$$

With an excellent approximation (we are considering developed countries in their pre-vaccination era) it therefore holds

$$C = B - \int_0^L E(a)e^{-\lambda a}da \qquad (6)$$

which is exactly the relation " N. of cases≈Nr of births - emigrations of susceptibles " introduced before in intuitive terms, and which reduces to the standard relation *Nr of cases=Nr. of births* when emigration is absent (q=E=0). In particular the ratio between cases and births is

$$\frac{C}{B} = 1 - \int_0^L e^{-\lambda a}Q(a)q(a)da \qquad (6')$$

The relations (6) or (6') provide a clue in order to evaluate under-reporting in presence of emigration, provided one dispose of a "sufficiently correct" estimate of the local FOI. Notice moreover that the relation is general and does not depend on the assumption of homogeneous mixing. In presence of a general age-dependent FOI $\lambda(a)$ we have:

$$C = \int_0^L \lambda(a)\Lambda(a)n(a)da \qquad (7)$$

where $\Lambda(a) = \exp\left\{-\int_0^a \lambda(u)du\right\}$ is the survival to infection function, and $\lambda(a)\Lambda(a)$ the corresponding density of infection. Hence an integration by parts gives the approximate relation (we recall that: $\lambda(a)=(-1)\Lambda'(a)/\Lambda(a)$)

$$C=(-1)[\Lambda(a)n(a)]_0^L-\int_0^L(-\Lambda(a))BQ'(a)da=\Lambda(0)n(0)-\Lambda(L)n(L)-\int_0^L(-\Lambda(a))BQ'(a)da=$$
$$=B-\int_0^L\Lambda(a)E(a)da$$

As $\Lambda(L)=0$ in the pre-vaccination era we simply get

$$C=B-\int_0^L\Lambda(a)E(a)da \qquad (8)$$

which generalises the previous findings.

2.2. *The population is a sink population*

Let us now consider the case of a "sink" population[5], denoted in the sequel as "population 1":

$$\begin{aligned}
&\Delta X_1(a,t)=I_X(a)-(\mu(a)+\lambda_1(a,t))X_1(a,t) && X_1(0,t)=B_1(t) \\
&\Delta Y_1(a,t)=\lambda_1(t)X_1(a,t)+I_Y(a)-(\mu(a)+v)Y_1(a,t) && Y_1(0,t)=0 \qquad (9) \\
&\Delta Z_1(a,t)=vY_1(a,t)+I_Z(a)-(\mu(a)+q(a))Z_1(a,t) && Z_1(0,t)=0
\end{aligned}$$

where $I_X(a)$,$I_Y(a)$,$I_Z(a)$ denote immigration flows in the three epidemiological classes, assumed constant over time, and $q(a)=0$. The FOI has been assumed age dependent. The total population satisfies:

$$\Delta n_1(a,t)=I(a)-\mu(a)n_1(a,t) \qquad n_1(0,t)=B_1(t) \quad (10)$$

Populations exposed to regular immigration inflows are not necessarily stationary (Cerone 1987). They become stationary in the long term when the number of births over time is constant (i.e. independent on the total population size), and also in the less trivial case in which the population has below replacement fertility. Otherwise a stationary population exposed to a constant immigration inflow will increase linearly in the long term. Here we assume for simplicity that the population is at its long-term equilibrium. At the long term equilibrium the total number of susceptible individuals aged *a* is:

$$X_1(a)=B_1p(a)\Lambda_1(a)+\int_0^a I_X(s)\frac{p(a)}{p(s)}\frac{\Lambda_1(a)}{\Lambda_1(s)}ds \qquad (11)$$

Let us assume, as usual, type 1 mortality. The total number of cases is the sum of cases in the native population plus those in the immigrated individuals:

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[5] The treatment of emigration is not difficult: one can again think of μ as the total exit rate

$$C_1 = B_1 \int_0^L \lambda_1(a)\Lambda_1(a)da + \int_0^L I_X(s)\left(\int_s^L \frac{\Lambda_1(a)}{\Lambda_1(s)}\lambda_1(a)da\right)ds \quad (12)$$

As in the pre-vaccination era "almost everybody gets measles at some stage", it holds with an excellent approximation

$$\int_0^L \lambda_1(a)\Lambda_1(a)da = 1 \quad ; \quad \int_s^L \frac{\Lambda_1(a)}{\Lambda_1(s)}\lambda_1(a)da = 1$$

(the second expression represents the conditional density of getting infection by age s). Therefore:

$$C_1 = B_1 + \int_0^L I_X(s)ds \quad (13)$$

which is the (equilibrium) extension of the basic relation Nr Cases≈Nr Births in closed populations. Formula (13) says exactly that, as expected, in a sink population (at equilibrium) the total number of cases in the pre-vaccination era is well approximated by the sum of the local births plus the total number of susceptible individuals which are expected to be present in the migrant pool on the basis of the FOI prevailing in regions of origin.

Let us now suppose that $I_X(a)$ is the outflow of susceptible material from a stationary source population as that described in the previous sub-section. Denote with sub-fix 2 such a source population. It holds

$$I_X(s) = q(s)X_2(s) = I(s)\Lambda_2(s) \quad (14)$$

where $\Lambda_2(s)$ is the "survival to infection" function in population 2. As a consequence (13) becomes:

$$C_1 = B_1 + \int_0^L I(s)\Lambda_2(s)ds \quad (15)$$

Formula (15) allows estimating the number of cases in the sink population provided one knows the FOI in the sending regions. Formula (15) is general. If there are *m* independent source regions sending susceptible materials to region 1, then (15) straightforwardly modifies as

$$C_1 = B_1 + \sum_{j=1}^{m}\int_0^L I_j(s)\Lambda_j(s)ds \quad (16)$$

Remark. The two limit cases considered in this section, namely the pure source and sink populations are simplistic: return migrations are necessarily excluded; moreover most populations are at the same time sending and receiving. Nonetheless, for practical purposes, they will represent excellent approximation of real populations, provided the age structure and FOI of exits and entries are not very different. Moreover, they are certainly useful for those situations in which the only "reconstructible" datum on age structured migrations are net migration, as was the case for Italy in the period 1950-1970. Though the previous results pertain to equilibrium regimes, one can reasonably trust that they approximately hold also in non stationary situations, provided one averages data over a sufficiently long time window. Discrete approximations of formulas (8) and (16) will be used in the next section in order to estimate the number of cases in the Italian regions in the pre-vaccination window 1950-70.

3. Estimation of number of cases in the Italian regions in the pre-vaccination era

In the period 1950-1970 for many Italian regions migrations represent the most relevant source of population growth or decay. For instance in Piemonte, a typical sink region, net migration significantly exceeds the yearly number of births for all the period. In particular in its capital Turin net migration systematically exceeds yearly birth by about a factor two (fig. 1) in the period 51-65. Similarly for many regions of the Southern part of the country, essentially acting as source regions, migrations are responsible for zero population growth or even slow decay, despite high fertility rates. Of course these figures do not yet imply anything in terms of number of cases, since, as already pointed out the relevant question essentially concerns the extent of the flows of susceptible individuals. To answer this question we need information on the age distribution of the flows. But available migration data in the involved period only concern total flows, whereas the use of the relations (8) and (16) needs at least data on net migrations by age. In Italy age structured data on migration flows are available only since 1970, i.e. quite close to the end of the pre-vaccination era. Moreover already since the end of the sixties the peace and direction of Italian inter-regional migrations patterns undergo substantial changes compared to the previous period (Golini 1974, Bonaguidi 1985, Bisogno 1997). Therefore in this preliminary work we decided to estimate net migrations by age for each region by relying on census data available in the years 1951, 1961, and 1971.[6] The following steps were performed: a) the "initial" age structure (5 years age groups) at 31/12/1951 for each region plus inter-census births were projected at 31/12/1961 by using as "average" life table for the period considered the national Italian life table observed in the period 1954-1957. The projection was performed separately for both sexes. b) the net migration in each cohort during the period was estimated by subtracting the projected figures at 1961 from the population observed at the corresponding census; c) net migration by age was then estimated from the corresponding cohort figure by using standard formulas. Steps a),b),c) were then repeated for the period 1961-1971, by using as "average" life table for the period considered the national Italian life table observed in the period 1964-1967. Finally: d) the number of total cases of measles expected under the equilibrium assumption was estimated by using a discrete version of formulas (8) and (16) by adopting the EURO FOI. From the computed number of cases average under-reporting coefficients were estimated for the period 1951-1971.

Fig. 1. Province of Turin. Births and net migrations during 1951-71.

3.1. Net migration by age in the Italian regions during 1951-61 and 1961-71

Table 1 reports net migration by age in each Italian region during the two inter-census periods 1951-61 and 61-71 for five years age groups in the "susceptibility age window" (SAW) here identified as the class 0-19 years (this being motivated by the fact that under the action of the EURO FOI above 99% of the susceptible pool would be depleted before age 20). These results, i.e. the extent of migrations in the susceptibility age window are striking. Table 2 and fig. 2 report, for both the decades 51-61 and 61-71 the ratios between the number of net exits or entries in each region in the SAW and the number of births in that region, which can be

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[6] This approach was used by Golini (1974) in order to evaluate net migration by age at the national level during the period 1951-61, but was not used up to now, as far as we know, to estimate net migration by age for all the Italian regions.

taken as an indicator of the impact of migration in the SAW. For some regions the impact of migrations is considerable. In the first decade (51-61) among the source regions in the Southern part of the country, Molise lost around 500 individuals below 20 years for every 1000 live births, followed by Abruzzi and Calabria (around 320 per 1000) and Basilicata (280 per 1000). In the subsequent decade Basilicata (413), Molise (380), Calabria (344) continue to have big losses with the addition of Sicily (275 per 1000). On the other side Piemonte is the leader among the sink regions in the North (an average of respectively 454 and 310 entries per 1000 births in the two decades), followed by Liguria (371 and 168) and Lombardia (228 and 203). Quite important is also the attracting role of Rome (180 and 130 entries per 1000 births in the two decades).

Table 1. Italian regions: net migration by age during 51-61 and 61-71. Absolute figures.

Table 2. Italian regions. Ratios between net migration in the age class (0,20) and total births.

Fig. 2. Ratios between net migration in the age class (0,20) and total births for the Italian regions

3.2. Estimated number of cases and related under-reporting coefficients

A critical point in the application of formulas (8) and (16) lies in the fact that they need some further assumptions on the structure of the local force of infection, for "source" regions, and of both the local FOI and the FOI's of the sending regions in the case of "sink" regions. In order to make a sufficiently neutral choice we assumed for simplicity that no regional heterogeneity in the FOI prevailed in Italy during the pre-vaccination era, and, moreover, we adopted as a common value for the FOI of both sending and receiving regions during the pre-vaccination era, the "EURO" FOI for measles recently estimated by Edmunds et al. (2000) for a wide range of European countries. Table 3 reports the values of the EURO FOI as estimated by Edmunds et al. (2000). Table 4 reports, for each of the 5-years age groups of the susceptibility age window, the corresponding values for the fractions of susceptible individuals, which are expected on the basis of the EURO FOI. These latter were computed by using formulas for the standard epidemiological model with piece-wise constant FOI (Anderson and May 1985, 1991).

Age groups (years)	[0,2)	[2,5)	[5,11)	[11,18)	[18,75)
Force of infection	0,120	0,28	0,40	0,20	0,10

Table 3. Values of the "EURO" force of infection (Edmunds et al. 2000)

Age groups (years)	[0,5)	[5,10)	[10,15)	[15,20)
Fraction who is susceptible	0,6749	0,1468	0,0245	0,009

Table 4. Susceptible fractions in various age classes under the "EURO" FOI

The susceptible fractions of Table 4 were finally applied to the net migration figures estimated in the previous section in order to estimate migrating flows of susceptible materials, which are necessary in order to apply formulas (8) and (16). In table 5 the numbers of susceptibles expected in the migrant pool for each region are displayed. Table 6 reports, for the two decades 51-61 and 61-71 the total number of cases expected in each Italian region on the basis of formulas (8) and (16), and the number of cases that would be expected, on the same periods, by the simplified relation "Total number of cases=total births". The corresponding percent change is also added. In some cases the impact is remarkable, especially during the first decade. For source regions such as Abruzzi, Basilicata and Calabria, the number of cases expected taking migrations into account is up to 7% less than it was expected by ignoring migrations, whereas for sink regions such as Piemonte and Liguria it exceeds the figures expected in absence of migration up to 10%.

Table 5. Italian regions. Numbers of susceptibles (to measles) expected in the (net) migrant pool under the EURO force of infection during 51-61 and 61-71.

Table 6. Italian regions. Expected number of measles cases during 51-61 and 61-71.

The figures of the number of cases corrected by taking regional migration into account may be used to obtain corrected estimates of under-reporting of measles cases at the regional level. In a recent paper Williams and Manfredi (2000) provided estimates of under-reporting for the Italian regions by systematically using the identification between cases and births (and ignoring migration). Table 7 reports the ratios between cases and births (in absence of migration) and the ratios between cases and births plus net migration of susceptibles for the 20 Italian regions. Clearly, given the structure of the reporting ratios (less than 20%) observed in Italy during the pre-vaccination era, the variations are quite limited: for only two regions, Piemonte and Liguria, the corrected ratios exhibit variations, in absolute terms, bigger than 1% (during 51-61). In all the other cases the changes are much smaller. Table 7 confirms the goodness of the results provided in Williams and Manfredi (2000), and shows how limited could be, in the pre-vaccination era, the impact of migrations of susceptible material, despite the massive flows observed in the overall and also in the young population.

Table 7. Italian regions. Estimated coefficients of measles under-reporting during 51-61 and 61-71.

4. Conclusive remarks

The demographic interference of permanent inter-regional migrations on observed cases of measles during the pre-vaccination era is studied with reference to the 20 Italian regions.

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LIA-ROI	FRIULI-VG	LAZIO	LIGURIA	LOMBARDIA	MARCHE	MOLISE	PIEMONTE	PUGLIA	SARDEGNA	SICILIA	TOSCANA	TRENTINO-AI	UMBRIA	VALLE D'A	VENETO
1339	-4156	31643	18093	51252	-9757	-9906	49409	-63215	-15349	-67896	8626	-1776	-6211	717	-35946
1355	-2672	28167	15105	50655	-6835	-7869	43494	-36038	-7665	-36785	7824	-681	-3524	378	-32503
31	-2620	28217	15736	61115	-8939	-8233	47809	-34009	-6744	-36535	6205	-323	-4431	239	-39784
-1046	-4139	30385	18866	74955	-12853	-10842	55564	-42539	-11779	-47791	5346	44	-6562	305	-50501
1678	-13588	118412	67798	237977	-38384	-36849	196275	-175801	-43537	-189007	28001	-2736	-20727	1638	-158734
10032	1719	32459	10076	62678	1021	-4066	38037	-47677	-9824	-76922	12544	-98	-1404	383	8275
8251	1737	26845	9219	58419	-653	-4164	40916	-31516	-9082	-55814	10193	-169	-1930	402	3478
7198	919	23258	9702	70625	-4122	-5790	50474	-40142	-15143	-65074	8486	-459	-4004	430	-3973
6408	-685	23820	11174	90422	-8167	-8138	63291	-55737	-23161	-78044	8675	-1569	-6578	655	-11687
31890	3689	106382	40170	282144	-11922	-22157	192717	-175072	-57210	-275854	39898	-2294	-13916	1869	-3906

ILIA-ROI	FRIULI-VEN	LAZIO	LIGURIA	LOMBARDIA	MARCHE	MOLISE	PIEMONTE	PUGLIA	SARDEGNA	SICILIA	TOSCANA	TRENTINO-AI	UMBRIA	VALLE D'A	VENETO
126945	-85,44731	179,92369	371,3766	228,1422844	-175,78194	-487,7742	454,1054825	-213,3991	-130,5055666	-179,56	66,9336981	-19,1769869	-170,5822	121,6592	-228,314
,311275	21,263093	129,21437	168,2597	203,9121566	-57,443511	-382,1397	310,7149629	-212,2728	-178,5632874	-275,674	83,647742	-14,2945788	-122,7644	115,1171	-5,29444

er the EURO FOI during 51-61 and 61-71.

ILIA-ROI	FRIULI-VEN	LAZIO	LIGURIA	LOMBARDIA	MARCHE	MOLISE	PIEMONTE	PUGLIA	SARDEGNA	SICILIA	TOSCANA	TRENTINO-AI	UMBRIA	VALLE D'A	VENETO
904	-2805	21357	12211	34591	-6585	-6686	33347	-42666	-10359	-45825	5822	-1199	-4192	484	-24261
199	-392	4135	2218	7437	-1003	-1155	6386	-5291	-1125	-5401	1149	-100	-517	55	-4772
1	-64	692	386	1500	-219	-202	1173	-835	-215	-897	152	-8	-109	6	-976
-9	-37	273	170	675	-116	-98	500	-383	-106	-430	48	0	-59	3	-455
1094	-3299	26458	14985	44203	-7924	-8141	41406	-49174	-11805	-52553	7171	-1306	-4877	548	-30464
6771	1160	21908	6800	42303	689	-2744	25672	-32179	-6631	-51917	8466	-66	-948	259	5585
1211	255	3941	1354	8577	-96	-611	6007	-4627	-1333	-8195	1496	-25	-283	59	511
177	23	571	238	1733	-101	-142	1239	-985	-372	-1597	208	-11	-98	11	-97
58	-6	214	101	814	-74	-73	570	-502	-206	-702	78	-14	-59	6	-105
8217	1431	26634	8493	53427	418	-3571	33488	-38292	-8544	-62411	10249	-116	-1388	334	5893

ILIA R_	FRIULI V_G	LAZIO	LIGURIA	LOMBARDIA	MARCHE	MOLISE	PIEMONTE	PUGLIA	SARDEGNA	SICILIA	TOSCANA	TRENTINO A_	UMBRIA	VALLE D'A	VENETO
492244	159497	660594	163384	1046529	218100	75282	434195	823894	333670	1053229	418949	142988	121332	13466	695408
93337,8	156198,06	687052,23	198368,7	1090731,716	210176,28	67141,08	475601,3651	774719,7	321864,6442	1000676	426120,336	141681,6753	116455	14013,77	664944
2222067	-2,068341	4,0052176	8,17124	4,223744984	-3,6330691	-10,8139	9,536352359	-5,968527	-3,53803332	-4,98966	1,71174448	-0,91359045	-4,019516	4,067814	-4,38074
537641	173532	824458	239200	1386933	207094	57609	623209	823405	319627	997867	477451	160359	113088	16265	737248
5857,63	174963,26	851092,03	247692,5	1440360,061	207512,26	54038,4	656696,5421	785112,5	311082,9516	935456	487699,93	160242,968	111699,5	16599,08	743141,2
,528274	0,8247808	3,2304895	3,550387	3,852173197	0,2019684	-6,197996	5,37340476	-4,650506	-2,673130986	-6,25444	2,14659301	-0,07235765	-1,227787	2,053984	0,799353

ILIA R_	FRIULI V_G	LAZIO	LIGURIA	LOMBARDIA	MARCHE	MOLISE	PIEMONTE	PUGLIA	SARDEGNA	SICILIA	TOSCANA	TRENTINO A_	UMBRIA	VALLE D'A	VENETO
111371	31432	61758	29530	116609	28617	6480	56204	24964	22676	33233	51017	11527	18895	2273	56974
2262516	0,1970695	0,0934886	0,161028	0,111424528	0,1312105	0,086076	0,129444144	0,0303	0,067959361	0,031553	0,12177377	0,080615157	0,15573	0,168795	0,081929
0,22575	0,2012317	0,0898884	0,148864	0,106908966	0,1361571	0,096513	0,118174598	0,032223	0,070451975	0,033211	0,1197244	0,081358439	0,162251	0,162198	0,085682
0501632	-0,416216	0,3600225	1,216405	0,451556209	-0,4946683	-1,043684	1,126954604	-0,192325	-0,249261436	-0,16571	0,20493757	-0,07432829	-0,652172	0,65979	-0,37535
117292	31227	60521	28067	112108	23473	7001	47025	25867	14658	29960	61177	11758	15820	1135	56993
2181604	0,1799495	0,073407	0,117337	0,08083159	0,1133447	0,121526	0,075456227	0,031415	0,045859705	0,030024	0,12813252	0,073322982	0,139891	0,069782	0,077305
2148765	0,1784775	0,0711098	0,113314	0,077833316	0,1131162	0,129556	0,071608417	0,032947	0,047119265	0,032027	0,12543984	0,073376075	0,14163	0,068377	0,076692
3283902	0,1472048	0,2297195	0,402308	0,299827414	0,0228459	-0,802988	0,38478101	-0,15322	-0,125955967	-0,20031	0,26926828	-0,00530932	-0,173891	0,140446	0,061304

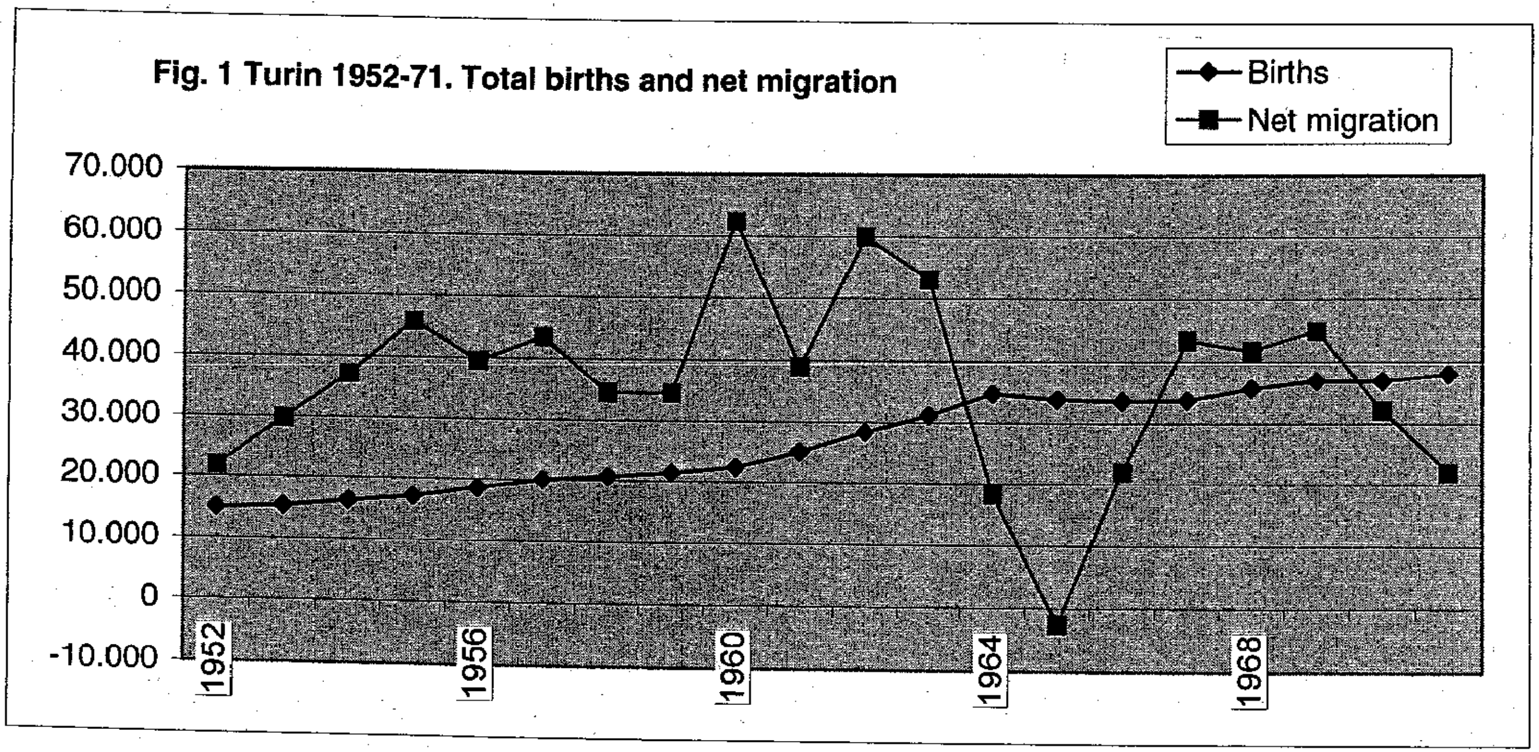

Fig. 1 Turin 1952-71. Total births and net migration