Identifying chromosomal anomalies using current health database: the Registry of Congenital Anomalies of Milan (Lombardy Region, Northern Italy)

Validazione di un nuovo algoritmo per identificare le anomalie cromosomiche utilizzando i flussi sanitari correnti: il Registro delle malformazioni congenite di Milano

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WHAT IS ALREADY KNOWN

- **Surveillance systems for malformations rely on active and passive population-based registries and it is complicated to detect anomalies associated with termination of pregnancy using healthcare databases.**
- **Data on chromosomal anomalies, in particular Down Syndrome, might be underestimated in passive population-based registries.**

WHAT THIS STUDY ADDS

- **Where no surveillance systems for malformations are available, existing healthcare databases can also be used to find anomalies associated with termination of pregnancy.**
- **Algorithms can be used to detect most chromosomal abnormalities, and Down Syndrome in particular.**

ABSTRACT

OBJECTIVES: to assess the potential of a new algorithm based on current healthcare databases to identify potential cases of malformation, particularly chromosomal anomalies associated with terminations of pregnancy.

DESIGN: retrospective observational study.

SETTING AND PARTICIPANTS: Registry of Congenital Anomalies of Milan, live births, still births, and termination of pregnancies for fetal anomalies from 2012 to 2016, detected by using current healthcare data.

MAIN OUTCOME MEASURES: prevalence between 2012 and 2016 of congenital malformations recorded by Milan's Registry of Congenital Anomalies, with particular regard to chromosomal anomaly trends. Variation in the percentage of malformations detected from terminations of pregnancy.

RESULTS: prevalence of malformations increased from 270 in 2012 to 283 per 10,000 in 2016; specifically, chromosomal abnormalities increased from 35 to 51 per 10,000 births. The algorithm detected a greater proportion of anomalies associated with therapeutic abortion, especially with respect to chromosomal anomalies, with an increase from 57.7% in 2012 to 75.8% in 2016 (test for trend p=0.002).

CONCLUSIONS: the proposed algorithm identified a greater number of chromosomal anomalies that caused termination of pregnancy and may be applied to existing Italian registries to evaluate the quality of healthcare services, in particular with regard to the effectiveness of prenatal trisomy screening policies. The algorithm may also be used where no active surveillance systems are present, as well as in epidemiological studies, to assess environmental impact on congenital anomalies.

Keywords: malformation registry, health administrative database, chromosomal anomalies

RIASSUNTO

OBIETTIVI: valutare la possibilità di implementare un nuovo algoritmo basato sui flussi sanitari correnti per identificare potenziali casi di malformazioni, in particolare per individuare le anomalie cromosomiche associate a interruzione di gravidanza.

DISEGNO: studio osservazionale retrospettivo.

SETTING E PARTECIPANTI: Registro delle malformazioni di Milano, nati e aborti volontari dal 2012 al 2016 individuati dai flussi sanitari correnti.

PRINCIPALI MISURE DI OUTCOME: prevalenza delle malformazioni congenite registrate dal 2012 al 2016dal Registro delle malformazioni di Milano; in particolare, valutazione dell'andamento delle anomalie cromosomiche. Variazione della percentuale di malformazioni individuate da interruzione di gravidanza.

RISULTATI: la prevalenza delle malformazioni è aumentata dal 270 per 10.000 del 2012 al 283 per 10.000 del 2016; in particolare, le anomalie cromosomiche sono aumentate da 35 a 51 per 10.000 nati. L'algoritmo ha individuato una proporzione maggiore di anomalie associate a interruzione terapeutica di gravidanza, soprattutto per le anomalie cromosomiche, aumentate dal 57,7% del 2012 al 75,8% del 2016 (*test for trend* p=0,002).

CONCLUSIONI: l'algoritmo proposto ha identificato un numero maggiore di anomalie cromosomiche causa di interruzione di gravidanza e potrebbe essere applicato dai registri già attivi a livello italiano per valutare la qualità dei servizi sanitari e, in particolare, l'efficacia delle politiche di screening prenatale sulle trisomie. Inoltre, l'algoritmo potrebbe essere utilizzato dove non sono presenti sistemi di sorveglianza attivi e nell'ambito di studi epidemiologici per valutare l'impatto ambientale sulle anomalie congenite.

Parole chiave: registro malformazioni, flussi sanitari correnti, anomalie cromosomiche

INTRODUCTION

In several European countries, active and passive surveillance systems have been developed whose main objective is to monitor the trends of congenital malformations over time and by area. These surveillance systems essentially rely on population-based registries.[1] Chromosomal anomalies, defined as quantitative and qualitative alterations of one or more chromosomes, are among the most frequent types of congenital malformations, with a prevalence of over 48 cases per 10,000 births.[2] The prevalence of all malformations is 260 cases per 10,000 births and, conventionally, includes Terminations of Pregnancy for Fetal Anomaly (ToPFAs) in the numerator, but not in the denominator.[1,2] ToPFAs account for about 20% of total malformations and over two thirds of the cases are due to chromosomal abnormalities.[3,4] In particular, trisomy 21 and other aneuploidies, thanks to modern prenatal diagnostics, can be diagnosed early, allowing women to make an informed choice within the time limits established by Italian law.[5] Both trisomy 21 and other aneuploidies are associated with a greater probability of induced abortion.[6]

Data on the European prevalence of malformations are published periodically, showing that, in particular, values vary widely for chromosomal abnormalities, ranging from 18 per 10,000 in Portugal to 70 per 10,000 in the Basque Country.[7,2] In addition to national prenatal screening policies and laws regarding therapeutic abortion, this variability can also be ascribed to differences in the quality of surveillance systems. Active surveillance systems, i.e., systems that collect data from information sources with the aim of detecting cases, report higher prevalence data for chromosomal anomalies than passive surveillance systems, where cases are reported by the hospitals and clinics that provide data to the registry.[7] This phenomenon is particularly evident with respect to Down Syndrome.[2] It is essential, therefore, to analyse the completeness and accuracy of the collection of data, especially when its source is the integration of existing healthcare databases, whose original purpose was not epidemiological and – as in the case of data flows on induced abortions in Italy – which cannot be fully accessed due to privacy laws.

At an international level, since 1979, the European network of population-based registries for the epidemiological surveillance of congenital anomalies (EUROCAT) has promoted qualitative standards for the systematic collection of data on congenital malformations. It currently includes 39 European registries in 21 countries overall. According to the EUROCAT accreditation process, associate membership is granted when data on congenital malformations is sent in aggregate form, while full membership requires registries to send anonymized data on individual anomalies recorded in the area served by the registry. In 2016, the Health Protection Agency (*Agenzia per la Tutela della Salute*, ATS) of Milan set up a population-based Registry of Congenital Anomalies in the 193 towns that make up its population pool, and in 2019 the registry was accredited as "Full member" of EUROCAT.[8] The Registry of Congenital Anomalies of the ATS of Milan (RMC-ATS-MI) is based on the integration of various existing databases; as of now, data from 2012 to 2016 have been published.[2] Up until 2015, an algorithm based only on hospital discharge data (HDD) was used to identify malformations associated with termination of pregnancy. Starting in 2016, the algorithm was changed to include data from outpatient services. Aim of this work is to illustrate the effects of the application of new rules for the extraction of potential malformation cases in terms of data completeness and, in particular, the variations detected in the prevalence of chromosomal anomalies associated with ToPFA.

MATERIALS AND METHODS

POPULATION AND SETTING

The ATS of Milan was established in 2016, following Regional Law No. 23/2015, merging the Local Health Units (ASL) of the city of Milan with ASL Milano 1, Milano 2, and Lodi, thus serving an area comprising 193 towns and a population of 3.5 million people.[9] Every year, about 25,000 women give birth in one of the 19 birthing centres of the area, although about one quarter of the births take place in one of the two main maternity hospitals of Milan.[10] In 2019, 4,579 induced abortions were registered, of which only 1% had a malformation diagnostic code (International Classification of Diseases, 9th Revision, Clinical Modification, ICD-9-CM, codes 740 through 759) recorded in any of the six diagnosis fields of the hospital discharge database.

REGISTRY OF CONGENITAL ANOMALIES OF MILAN'S ATS

■ Definition of potential malformation cases from existing healthcare databases

The Registry of Congenital Anomalies of Milan's ATS is an active population-based registry which integrates hospital discharge data (HDD), maternity discharge papers (*Certificati di Dimissione al Parto*, CEDAP), outpatient service data, and mortality data. Two algorithms are used to create a list of potential cases of malformation: one algorithm searches for malformations in live births and still births, while the other searches among terminated pregnancies. Since EUROCAT requires coding according to the 10th revision of the British Paediatric Association Classification of Diseases (ICD-10-BPA), while HDDs use ICD-9-CM, a set of tables were drafted to transform

the ICD-9 codes into the corresponding ICD-10-BPA codes required by EUROCAT.

The algorithm selecting potential cases of malformation in births carries out a search – among all 6 fields of diagnosis of hospital discharge data – for the ICD-9-CM codes that identify congenital anomalies. Additionally, a number of specific codes are selected, as shown in Table 1. Subsequently, cases that only have codes of potential malformations listed as minor by EUROCAT are excluded.[11] The specific codes are reported in Table S1 (see online Supplementary Materials). Record linkage procedures using the child's tax ID number are employed to select from the maternity discharge data flow most of the variables required for full member EUROCAT accreditation.[11]

The algorithm for the selection of potential cases of malformation in pregnancy terminations carries out a search – among all 6 fields of diagnosis of hospital discharge data – for ICD-9-CM codes that start with 635, i.e., legally induced abortion. The version of the algorithm used until 2015 also sought for the simultaneous presence of codes that identify congenital anomalies. Starting in 2016, all hospital admissions for legally induced abortion preceded by genetic testing were added as potential cases, after having been identified through the databases of outpatient services, regardless of whether malformation codes were present. In practice, using record linkage to the women's tax ID code all hospital admissions for induced abortion were selected that had appeared in the preceding six months in the outpatient service database with a procedure code referable to genetic testing (Figure 1).

The cohorts of potential cases of malformations in births and terminations of pregnancy are searched, respectively, for newborns or women who at the time of birth or abortion were living in the 193 towns served by the Milan ATS.

After running the algorithms, a final list of hospital admissions for possible malformations is produced and, in compliance with Italian privacy laws and the Prime Minister's Decree dating 3rd March 2017, 'Surveillance systems and registries for all-cause mortality, cancer, and other diseases',[12] each hospital is asked for the relevant clinical documentation.

ICD-9-CM CODE	DESCRIPTION
215.6	Other benign neoplasm
279.11	Digeorge's syndrome
228.1	Lymphangioma, any site
771.0	Congenital rubella syndrome (billable)
771.1	Congenital cytomegalovirus infection
771.2	Other congenital infections specific to the perinatal period
524.06	Major anomalies of jaw size, microgenia
762.3	Placental transfusion syndromes affecting foetus or newborn
066.3	Other mosquito-borne fever
760.7	Noxious influences affecting foetus or newborn via placenta or breast milk

Table 1. Additional ICD-9-CM codes selected from hospital discharge databases to create a cohort of potential cases of congenital anomalies.
Tabella 1. Codici aggiuntivi ICD-9-CM selezionati dal flusso dei ricoveri ospedalieri per la creazione della coorte di potenziali casi di anomalie congenite.

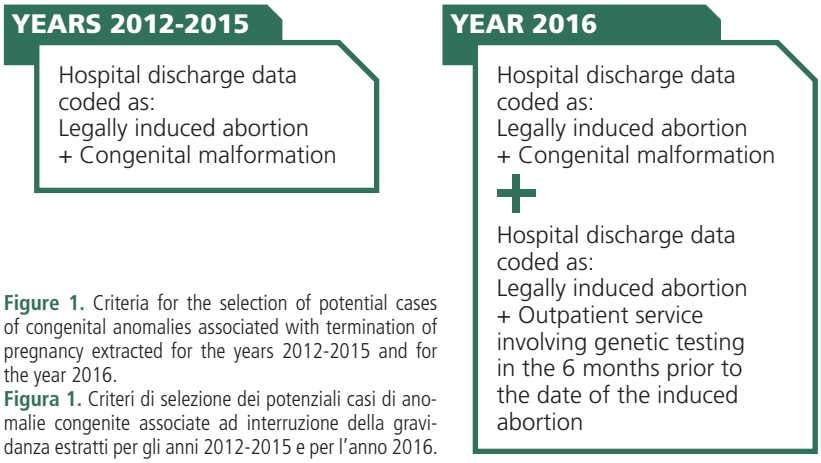

Figure 1. Criteria for the selection of potential cases of congenital anomalies associated with termination of pregnancy extracted for the years 2012-2015 and for the year 2016.
Figura 1. Criteri di selezione dei potenziali casi di anomalie congenite associate ad interruzione della gravidanza estratti per gli anni 2012-2015 e per l'anno 2016.

Consultation of clinical documentation and case validation

Registry clerks, who are adequately trained and periodically attend refresher courses on coding rules and laws regarding personal data processing, are involved both in requesting the clinical documentation from hospitals, as well as in analysing each case. For the years 2012 through 2016, 70 hospitals were contacted, which shared over 6,500 clinical records with ATS Milan using secure data-sharing computing environments. The custom-made malformation registry software creates a computer worksheet containing all 95 variables required by EUROCAT for full member accreditation and makes it possible, by linking records using tax ID codes, to see the information extracted from databases on maternity discharge records, outpatient services, drug prescriptions, pathology reports, and mortality. Registry clerks study the clinical documentation and conclude the procedure by confirming the malformation and filling in the worksheet or, in case of doubt, requesting assessment by the epidemiologist in charge of the registry. Each case of congenital abnormality can therefore be assigned to a (live or still) birth or a termination of pregnancy. By convention with EUROCAT, despite the fact that the selection of potential malformations is carried out on the basis of induced abortions, the cases assigned to this group are defined as malformations associated with ToPFA.

STATISTICAL ANALYSIS

The annual prevalence of malformations was calculated as indicated in the EUROCAT handbook,[11] i.e., as the sum of cases of anomalies identified from live births, still births, and ToPFAs out of the total number of births in the reference year extracted from the ISTAT demographic website.[13] The confidence interval of prevalence was calculated with Poisson's distribution according to the Begaud et al. method used by EUROCAT.[14]

The Cochrane-Armitage test for trend was used to test the significance of the variation over time of prevalence of anomalies identified through ToPFA, as well as chromosomal anomalies.[15]

All analyses were performed using SAS 9.4 software.

RESULTS

To create the cohort of potential cases with malformations from 2012 to 2016, 6,568 clinical records were selected, which led to the identification of 4,107 validated cases in the Milan Registry. Figure 2 shows the flow chart.

The prevalence of malformations over the entire period is 274.82 per 10,000 cases, with values ranging from 270.12 per 10,000 in 2012 to 283.76 per 10,000 in 2016. Analysis by body system showed the most frequent anomalies to be malformations of the cardiovascular system (101.77 per 10,000), followed by chromosomal abnormalities (38.83 per 10,000). Table 2 shows the values of individual malformations by year of birth/termination of pregnancy, which confirm the data reported in the analyses for the entire period (not shown); the table also shows an increase in the prevalence of limb malformations (from 37.03 in 2012 to 40.09 per 10,000 in 2016), mainly represented by foot abnormalities (talipes equinovarus) and polysyndactyly. Analysis of the mothers' age at delivery/abortion showed no changes over the years: mothers aged 35-40 were 24% in 2012 and 27% in 2016 and the percentage of mothers aged >40 remained stable at 9% (9.3% in 2012 and 9.8% in 2016).

Analysis of how the malformation was detected (birth vs. ToPFA) by reference year, both for anomalies as a whole and for chromosomal anomalies in particular (Table 3), reflects the application of the new algorithm and shows the increase in total malformations (from 13.2% in 2012 to 20.8% in 2016, test for trend p=0.001) and chromosomal abnormalities (from 57.7% in 2012 to 75.8% in 2016, test for trend p=0.002) associated with ToPFA.

Analysis of specific chromosomal abnormalities (Figure 3) showed an increase in the number of cases detected for every anomaly, but especially Down Syndrome, which increased from 2012 to 2016 from 23.50 to 33.18 per 10,000 (test for trend p=0.003). Analysis by detection method showed that in 2012 the proportion of trisomy 21 cases identified using pregnancy termination data was 50%, whereas it was 75% in 2016 (test for trend p=0.0004).

DISCUSSION

In the period examined, the study found prevalence of congenital malformations to be over 270 cases per 10,000, with an absolute increase of about 10 points from 2012 to 2016, which can be attributed to the greater number of ToPFA cases identified by the new algorithm. The prevalence of chromosomal abnormalities was 38.3 per 10,000 and increased in the five-year study period from 35.7 to 51.7 per 10,000. In particular, the values recorded for Down Syndrome went from 23.50 in 2012 to 33.18 per 10,000 in 2016, and were identified in 75% of cases from pregnancy termination data. The data reported by EUROCAT for the same period indicate an overall prevalence of 256 per 10,000 for all types of malformation and 44 per 10,000 for chromosomal anomalies; the data derive from the 34 registries accredited as full members.[2] These registries use different data collection methods, and one of EUROCAT's activities is the assessment of the disparity between estimates, to determine whether the trends observed by individual registries may reflect different levels of technological development applied to the broad, multifaceted European setting.[16] An example is the introduction of ever more advanced foetal

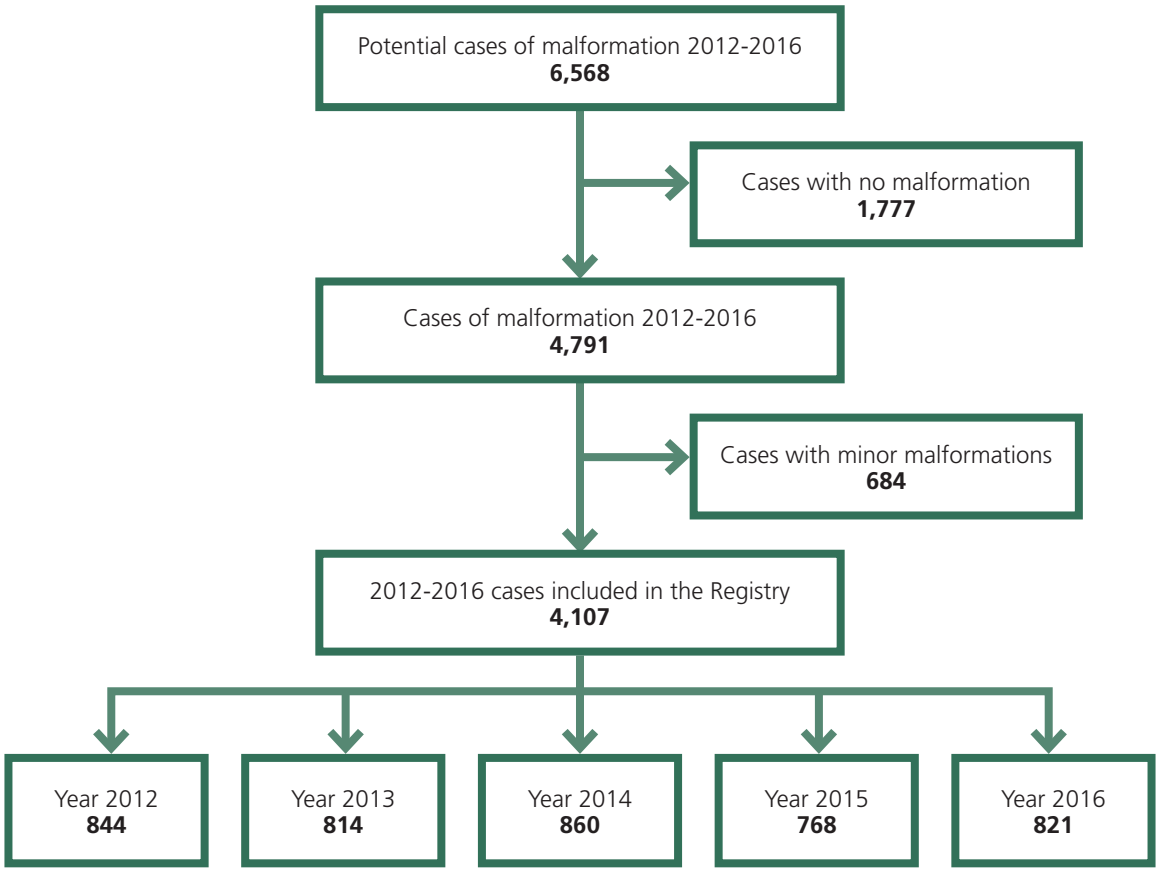

Figure 2. Definition of the cohorts of cases with congenital anomalies based on application of the criteria adopted by the Milan Registry for the selection of potential cases using existing healthcare databases.
Figura 2. Definizione delle corti di casi con anomalie congenite a partire dall'applicazione dei criteri adottati dal Registro di Milano per la sezione dei potenziali casi a partire dai flussi sanitari correnti.

and postnatal ultrasound technology, which has resulted in an increase in the diagnosis of urogenital anomalies, or the increasing trend of gastroschisis at the end of the past century, which was probably due to environmental factors, regardless of maternal age.[17,18] With respect to chromosomal abnormalities, there is widespread evidence that – despite its extensively proven association with advanced maternal age at the time of delivery – the broad variability recorded in Europe also depends on national policies regarding prenatal screening and,[19,20] as reported in a recent paper by Lanzoni et al.,[21] the increase in the prevalence of chromosomal anomalies should be attributed to the greater number of prenatal diagnoses of Down Syndrome which were followed by ToPFA. Maternal age cannot be considered the only element to be taken into account in the analysis of chromosomal abnormalities, since, considering the five-year period 2012-2016, countries like France, where the mean age at delivery is under 30, report values exceeding 73 per 10,000,[2] whereas in Italy, where the mean age at delivery is 34,[22] the prevalence of chromosomal anomalies recorded is around 40 per 10,000.[2] Furthermore, in nations where prenatal diagnosis has been promoted, a progressive increase has been observed in Down Syndrome, associated in over 70% of cases with ToPFA,[21] confirming the data recorded by the Registry of Congenital Anomalies of the ATS of Milan. Another important aspect of the study is the method used to identify malformations by integrating existing healthcare data flows. Despite widespread experience in the exclusive use of healthcare databases for the creation of registries for cancer and cardiovascular diseases,[23,24] data in the literature are discordant with regards to congenital abnormalities. A study carried out in Florida on over 8,400 births reported that hospital discharge data flows are over 93% accurate in the identification of major congenital malformations; the percentage, however, varies depending on the site of the anomaly.[25] The same research group more recently showed that applying different algorithms to healthcare databases has an impact on the percentage of false negatives, reducing the probability of identifying mal-

	YEAR				
	2012 (31,060)	2013 (30,258)	2014 (29,948)	2015 (29,233)	2016 (28,933)
TOTAL MALFORMATIONS					
Total	844	814	860	768	821
Prevalence	270.12	268.03	286.16	262.37	283.76
95%CI	(252.16-289.03)	(249.91-287.12)	(267.33-305.97)	(244.14 -281.61)	(264.69 – 303.84)
NERVOUS SYSTEM					
Total	64	68	62	50	48
Prevalence	20.61	22.47	20.70	17.10	16.59
95%CI	(20.44-20.87)	(22.3-22.76)	(20.54-20.97)	(16.97-17.33)	(16.46-16.81)
EARS, FACE, NECK					
Total	7	4	7	7	4
Prevalence	2.25	1.32	2.34	2.39	1.38
95%CI	(2.24-2.3)	(1.32-1.36)	(2.33-2.39)	(2.38-2.44)	(1.38-1.42)
CARDIOVASCULAR SYSTEM					
Total	311	329	315	273	293
Prevalence	100.13	108.73	105.18	93.39	101.27
95%CI	(99.23-101.25)	(107.76-109.94)	(104.24-106.36)	(92.56-94.44)	(100.36-102.4)
RESPIRATORY SYSTEM					
Total	16	15	17	6	11
Prevalence	5.15	4.96	5.68	2.05	3.80
95%CI	(5.12-5.23)	(4.93-5.04)	(5.64-5.77)	(2.04-2.1)	(3.78-3.87)
MOUTH					
Total	43	39	41	41	36
Prevalence	13.84	12.89	13.69	14.03	12.44
95%CI	(13.74-14.03)	(12.79-13.07)	(13.59-13.88)	(13.92-14.22)	(12.35-12.61)
DIGESTIVE SYSTEM					
Total	74	67	87	72	78
Prevalence	23.82	22.14	29.05	24.63	26.96
95%CI	(23.64-24.12)	(21.97-22.42)	(28.81-29.41)	(24.43-24.94)	(26.74-27.3)
URINARY SYSTEM					
Total	93	108	106	98	101
Prevalence	29.94	35.69	35.39	33.52	34.91
95%CI	(29.7-30.31)	(35.4-36.12)	(35.1-35.82)	(33.25-33.93)	(34.62-35.33)
GENITAL SYSTEM					
Total	100	71	85	89	76
Prevalence	32.20	23.46	28.38	30.45	26.27
95%CI	(31.93-32.59)	(23.28-23.76)	(28.15-28.73)	(30.2-30.82)	(26.06-26.6)
LIMBS					
Total	115	108	116	117	116
Prevalence	37.03	35.69	38.73	40.02	40.09
95%CI	(36.72-37.47)	(35.4-36.12)	(38.41-39.2)	(39.69-40.5)	(39.76-40.57)
GENETIC SYNDROMES					
Total	18	13	14	19	10
Prevalence	5.80	4.30	4.67	6.50	3.46
95%CI	(5.76-5.89)	(4.27-4.37)	(4.65-4.75)	(6.46-6.6)	(3.44-3.52)
CHROMOSOMIC SYNDROMES					
Total	111	94	113	107	149
Prevalence	35.74	31.07	37.73	36.60	51.50
95%CI	(35.44-36.17)	(30.81-31.45)	(37.42-38.19)	(36.3-37.04)	(51.06-52.1)

Table 2. Total malformations and anomalies grouped by the categories defined by EUROCAT, in absolute number, prevalence (number of cases per 10,000 births), and corresponding 95% confidence interval (95%CI).
Tabella 2. Malformazioni totali e raggruppate per le macrocategorie definite da EUROCAT espresse come numero assoluto, prevalenza (numero di casi per 10.000 nati) e relativo intervallo di confidenza al 95% (IC95%).

YEAR	TOTAL MALFORMATIONS					CHROMOSOMIC MALFORMATIONS				
	NEWBORNS		ToPFA		TEST FOR TREND	NEWBORNS		ToPFA		TEST FOR TREND
	No.	%	No.	%		No.	%	No.	%	
2012	733	86.8	111	13.2		47	42.3	64	57.7	
2013	707	86.9	107	13.1		39	41.5	55	58.5	
2014	739	85.9	121	14.1	<0.001	39	34.5	74	65.5	0.002
2015	665	86.6	103	13.4		45	42.1	62	57.9	
2016	650	79.2	171	20.8		36	24.2	113	75.8	

Table 3. Tipologia di individuazione (nati o ToPFA) per le malformazioni totali e il sottogruppo delle anomalie cromosomiche.
Tabella 3. Type of detection (birth or ToPFA) for total malformations and the subgroup of chromosomal anomalies

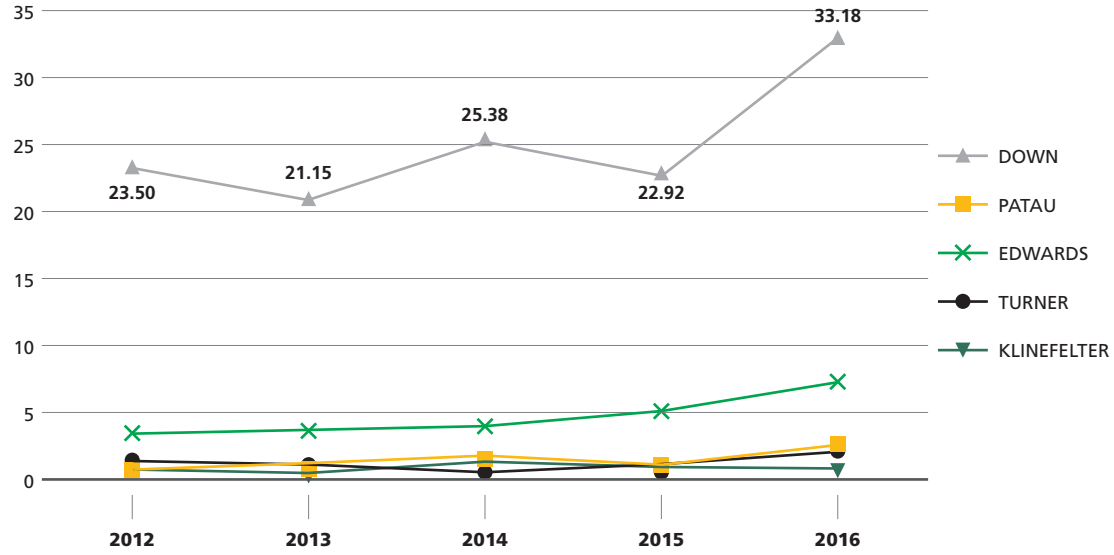

Figure 3. Chromosomal abnormality trend by year, classified by syndrome as established by EUROCAT.
Figura 3. Andamento per anno delle anomalie cromosomiche suddivise per le sindromi previste da EUROCAT.

formations associated with less severe clinical pictures, such as limb malformations or hypospadias.[26] Similar experiences have been reported in Italy, as well, with 90% sensitivity rates and a 93% negative predictive value (NPV), but, as in other countries, these tools are not sufficient to identify and collect all the variables that are needed to study congenital malformations, and, moreover, are only applicable to the cohort of births, excluding anomalies that were the cause of induced abortions.[27] Both in Italy and internationally, malformation registries are based on the integration of active and passive surveillance systems and there are no reports in the literature on the exclusive use of existing healthcare databases to identify abnormalities causing ToPFA.[25-28] In Italy, this topic is of particular interest because the epidemiologic system of surveillance for induced abortions of the Italian National Statistic Program[29] collects data in anonymized form, as its aim is to analyse the phenomenon in order to improve the services involved in abortion procedures, and not to implement population-based registries. In fact, both ISTAT form D12, which was used up until 2017, and the web platform set up by the Italian National Institute of Health (*Istituto Superiore di Sanità*) in 2018, only require that the presence or absence of foetal malformations be indicated, without specifying their type. This work, therefore, focuses on the development of a tool that can be applied to data flows other than the induced abortion database, such as the data flow of outpatient services, and the proposed algorithm enabled the detection of a proportion of malformations associated with ToPFA of about 7%. Furthermore, case validation by operators who are skilled in malformation coding makes it possible to achieve the highest levels of sensitivity. Among the study's main limits are the reproducibility of methods and the fact that it is impossible to identify privately provided outpatient services. The former limit is due to the magnitude of locally employed resources,

which are not equally available in most Italian settings, especially as regards to the investment in training and availability of operators specifically devoted to this task. Furthermore, this organizational structure can only be considered for low-prevalence conditions such as congenital malformations. Consequently, public healthcare services should carefully assess the decision to promote agencies or workgroups specifically designated with this purpose. The latter limit concerns the evolution in prenatal screening tests, especially since 2012, when foetal DNA testing was introduced as a non-invasive test to detect the most frequent aneuploidies (chromosomes 21, 13, 18, Y, and X).[30] Although these tests are not 100% accurate, and diagnostic testing is still needed for a definite diagnosis,[31] an ever greater number of women seeks out private labs whose records are not present in existing healthcare databases.[32] This behaviour, furthermore, could lead to an underestimation of cases of termination of pregnancy associated with chromosomal/genetic abnormalities. In conclusion, the algorithm proposed by our study used hospital discharge and outpatient data flows and detected a greater number of chromosomal abnormalities associated with ToPFA, in particular Down Syndrome. The model used by the ATS of Milan to validate cases requires the investment of considerable resources, but makes it possible to obtain high quality levels, and may be applied to already existing Italian registries to assess the quality of healthcare services, particularly with respect to prenatal trisomy screening policies. The algorithm may also be used where no active surveillance systems are present, as well as in epidemiological studies, to assess environmental impact on congenital anomalies.

Conflicts of interest: none declared.

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