Prevalence of esophageal atresia among 18 international birth defects surveillance programs

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Running title: International prevalence of esophageal atresia

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Abstract

**Background:** The prevalence of esophageal atresia (EA) has been shown to vary across and within different geographical settings. Investigation of geographical differences may also provide an insight into the underlying aetiology of EA.

**Methods:** The study population comprised infants diagnosed with EA in 1998-2007 from 18 of the 46 birth defects surveillance programs, all of which are members of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR). Total prevalence per 10,000 births for EA was defined as the total number of cases in live births, stillbirths, and elective termination of pregnancy for fetal anomaly (ETOPFA) divided by the total number of all births in the population.

**Results:** Among the participating birth defects surveillance programs, a total of 2,943 cases of EA were diagnosed between 1998 and 2007 with an average prevalence of 2.44 (95% CI 2.35, 2.53) per 10,000 births, ranging between 1.77 and 3.68 per 10,000 births. Of all infants diagnosed with EA, there were 2,761 (93.8%) live births, 82 (2.8%) stillbirths, 89 (3.0%) ETOPFA, and 11 (0.4%) unknown outcomes. The majority of cases (2,020, 68.6%), had a reported esophageal atresia with fistula, 749 cases (25.5%) were without fistula, and 174 cases (5.9%) were registered with an unspecified code.

**Conclusions:** On average, EA affected 1 in 4,099 births (95% CI: 1 in 3,954-4,251 births) with the prevalence varying across and within different geographical settings, but relatively consistent over time and comparable between surveillance programs. Findings suggest differences in the prevalence observed between programs are likely to be attributable to variability in the ethnic composition or issues in reporting and/ or registration procedures of EA, rather than a real risk occurrence difference per se.

**Key words:** esophageal atresia, congenital anomalies, prevalence, epidemiology,
Introduction

Esophageal atresia (EA) is the most frequent anomaly of the esophagus and is characterised by the complete discontinuity of the esophagus with or without an abnormal connection between the esophagus and the trachea, tracheo-esophageal fistula (TEF). Infants are diagnosed either prenatally or, in most cases, at birth and require surgical repair in the first few days of life. Although the aetiology of EA is largely unknown (Felix et al., 2009) geographic, temporal and ethnic variations have been reported.

The prevalence of EA has been shown to vary across and within different geographical settings with a study from five regions in Britain reporting rates ranging between 0.7 and 3.2 per 10,000 births (Rankin et al., 2005) although EA cases in that study also included those with esophageal stenosis. Similarly, differences in rates among areas in the United States have been reported with a prevalence of 2.24 in Hawaii (Forrester and Merz, 2005), 2.33 in Texas (Ethen and Canfield, 2002) and 2.82 per 10,000 births in California (Torfs et al., 1995); among European countries, prevalence has been reported for Iceland (1.83 per 10,000) (Gunnarsdottir et al., 2004), France Strasbourg (2.96 per 10,000) (Stoll et al., 2009), and UK Northern Region (3.13 per 10,000 births) (Sparey et al., 2000). Given EA is a rare condition, small numbers may also have a potential impact on rates. Ethnic composition of a population may also influence EA prevalence with lower rates noted among Hispanic and African-American communities (Carmichael et al., 2004; Forrester and Merz, 2005).

International differences in the prevalence of EA across different geographical regions may also be attributable to differences in case identification methods, case definition, and case ascertainment. Best estimates of prevalence of major birth defects, based on international data, are important to serve as a reference point for the evaluation of individual, regional or national surveillance programs and to identify geographical regions of higher or lower than expected prevalence (Leoncini et al., 2008; Cocchi et al., 2010). Investigation of geographical differences may also provide an insight into the underlying aetiology of EA. The aim of this study was to investigate the international prevalence of EA among birth defects surveillance programs (BDSP) in North and South America, Europe and Australia and provide a worldwide collective estimate.
Materials and methods

Data for this study were sourced from 18 birth defects surveillance programs, all members of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR). Programs who agreed to participate provided relevant data on EA among live births, stillbirths and elective termination of pregnancy for fetal anomaly (ETOPFA), if permitted. All participating programs were also required to have a stable methodology of ascertainment and/or registration over the 10-year study period, 1998-2007. The following programs provided data for slightly different years: Slovak Republic 2001-2007, USA Texas 1997-2006, USA Utah 1999-2007.

The main characteristics of the 18 participating programs in this study are reported in Table 1 with additional details available from the annual reports of the ICBDSR (www.icbdsr.org) (ICBDSR, 2008) and the National Birth Defects Prevention Network (www.nbdpn.org) (NBDPN, 2008), and from selected publications from individual programs (Mutchinick et al., 1988; Czeizel, 1997; Correa-Villasenor et al., 2003; Castilla and Orioli, 2004; De Vigan et al., 2005; Feldkamp et al., 2005; Bower et al., 2009; Lowry RB et al., 2009).

Classification of cases was undertaken by each individual program using either the British Paediatric Association International Classification of Diseases (ICD) coding system (ICD9-BPA) or ICD10. For this study, EA cases included all reported infants and fetuses diagnosed with an esophageal atresia with TEF (ICD9-BPA: 750.31, 750.33; ICD10: Q39.1) or without TEF (ICD9-BPA: 750.30; ICD10: Q39.0) or unspecified EA (750.3). Other types of EA including TEF without atresia (ICD9-BPA: 750.32; ICD10: Q39.2), esophageal stenosis or esophageal web (ICD9-BPA: 750.34, 750.35; ICD10: Q39.3, Q39.4) were considered separately.

Total prevalence per 10,000 births was defined as the total number of cases among live births, stillbirths, and ETOPFA divided by the total number of all births (livebirths and stillbirths) in the population. We used the term “total prevalence” instead of “prevalence” or “birth prevalence” to underline that ETOPFA were also included. To validate the total prevalence we undertook a sensitivity analysis by comparing overall total prevalence to estimated result for six programs previously shown to have good ascertainment of birth defects (Leoncini et al., 2010). Ninety-five percent confidence intervals for prevalence were calculated based on the Poisson distribution. Chi-square test for trend was used to evaluate homogeneity and time trend of the prevalence in the study period. Statistical analyses were performed using Stata 9.0 (Stata Corporation, College Station, TX, USA) and SAS 9.1 (SAS Institute Inc, Cary, NC), with P-values<0.05 considered statistically significant.
Results

Among the eighteen surveillance programs of the ICBDSR a total of 2,943 cases of EA were registered between 1998 and 2007 (Table 2). The majority of cases (2,020, 68.6%) had a reported esophageal atresia with fistula, 749 cases (25.5%) were without fistula and 174 cases (5.9%) were unspecified. The total prevalence of EA was 2.44 (95% CI 2.35-2.53) per 10,000 births; and on average, EA affected 1 in 4,099 births (95% CI: 1 in 3,954 - 4,251 births). The prevalence ranged from 1.77 (95% CI 1.52-2.06) per 10,000 births in Hungary and Atlanta to 3.68 (95% CI 3.41-3.97) in South America (Table 2). Sensitivity analysis utilising data from programs with optimal ascertainment of cases revealed total prevalence of EA was 2.47 per 10,000 births.

Overall, the average annual trend in EA remained fairly constant over the study period varying between 2.32 in 1998 to 2.60 per 10,000 births in 2007, and there was no evidence of a significant linear trend in EA among each of the programs (data not shown). However, there was a modest decline in the trend of EA in Alberta and Dublin; and a slight rise in cases in Western Australia, Mexico and Israel.

Of all infants diagnosed with EA, there were 2,761 (93.8%) live births, 82 (2.8%) stillbirths, 89 (3.0%) ETOPFA and 11 (0.4%) with unspecified outcome. Programs in Dublin and Alberta had a relatively higher proportion of stillbirths (14.0% and 11.4%, respectively) and in the case of ETOPFA, two programs (Central East, France and Wales) reported one in five cases that resulted in a termination of pregnancy (Figure 1). Excluding ETOPFA, the total prevalence of EA reduced slightly to 2.37 (95% CI 2.28-2.45) per 10,000 births.

The total prevalence of TEF without atresia was 0.22 per 10,000 births (95%CI 0.19-0.24) (1 in every 46,398 births). Compared to EA, it was reported much less frequently (less than 0.5 per 10,000 births) by all members of ICBDSR except for Western Australia, where the prevalence was 1.3 per 10,000 births. Cases of esophageal stenosis or esophageal web (n=44) occurred rarely, 1 in every 274,170 births (0.04 per 10,000 births), but was more commonly diagnosed in Saxony–Anhalt, Germany (0.12 per 10,000 births) compared with all other surveillance programs.
Discussion

Esophageal atresia affects, on average, 1 in every 4,099 births, with a total prevalence of 2.44 (95%CI 2.35-2.53) per 10,000 births among 18 birth defects surveillance program members of the ICBDSR. The prevalence ranged between 1.77 and 3.68 per 10,000 births among members representing North and South America, Europe and Australia. However, sensitivity analysis limiting data to member programs with optimal case ascertainment revealed an almost identical total prevalence (2.47) and findings are also similar to an earlier study of EA among nine ICBDSR programs reporting a prevalence of 2.56 per 10,000 births from 1965 to 1989 (Robert et al., 1993).

Findings from other congenital anomaly surveillance programs such as EUROCAT, the European surveillance of congenital anomalies working group, reported a comparable prevalence of 2.46 per 10,000 births among 23 member registries for the years 1997-2006 (Pedersen et al., 2012). This analysis included five ICBDSR members from our present study; and when limiting our data to 10 European members of the ICBDSR, we also found the same result (2.44 per 10,000 births). The estimated national prevalence of EA reported by the US National Birth Defects Prevention Network was 2.12 per 10,000 births (adjusted for race/ethnicity) among 14 member programs for the period from 2004-2006. Slight differences in prevalence by case ascertainment methods were observed with results ranging from 2.17 among 10 programs using active birth defects surveillance to 2.36 among seven passive surveillance systems and 2.54 among five passive surveillance programs with a case confirmation component (Parker et al., 2010).

Despite the range of geographic locations and study periods, comparison of the total prevalence of EA by various international surveillance programs reveals relatively similar results with EA diagnosed among 1 in 4,099 to 4,608 infants. These findings highlight the relative stability of the prevalence of EA, internationally and over time. In our international study there was no consistent trend for neighbouring countries or states within continents, with small variability in prevalence potentially influenced by chance or differences in reporting or surveillance methods, study population, ethnic distribution, geographical or environmental factors. For example, the two programs reporting higher prevalence of EA may be explained by their hospital-based case ascertainment program with active notification by trained clinicians in each hospital. However, higher prevalence may also reflect a truly higher rate of EA and further investigation of these results is important. Conversely, slightly lower prevalence of EA reported from surveillance programs in USA Atlanta and USA Texas may be explained by the ethnic composition of the population in these two US states, with almost two-thirds of all infants born to African-American or Hispanic women, respectively (NBDPN, 2009). Studies of congenital malformations by ethnic groups in the US have
found that compared with non-Hispanic white women, Hispanic and African-American women had a reduced risk of EA without fistula (relative risk (RR) 0.75; 95% CI 0.62 – 0.90) and RR 0.59; 95% CI 0.62-0.90; respectively) (Carmichael et al., 2004; Forrester and Merz, 2005). In Hungary, a combination of incomplete registration of cases at birth and terminations of pregnancy, and a true lower prevalence may explain their lower rates.

Although there was some discrepancy among programs in the distribution of specific types of EA (with and without TEF), the overall proportions were similar to that reported in the literature (Clark, 1999; Shaw-Smith, 2006; Spitz, 2007). These differences may be due to variation in classification, identification or reporting practices across programs rather than reflect real differences (Shaw-Smith, 2006; Spitz, 2007). Higher prevalence of TEF without atresia in some settings may also be due to increased detection and sources of notification such as post-mortem evaluation (Bower et al., 2009). Several factors may also influence reporting and registration of EA including: screening policies and procedures, clinician skills, timing of aneuploidy and fetal anomaly screening, subsequent availability and timing of elective termination of pregnancy, and autopsy policies. Previous studies have shown that the rate of termination of pregnancy is higher for cases with chromosomal or additional congenital anomalies than for cases with an isolated anomaly (Haeusler et al., 2002; Garne et al., 2007). Chromosomal anomalies have been reported to occur in 6-10% of EA cases (Garne et al., 2007; Genevieve et al., 2007; Pedersen et al., 2012); while greater than 50% and up to two-thirds of infants with EA have additional anomalies (Genevieve et al., 2007; Spitz, 2007; de Jong et al., 2010a; Pedersen et al., 2012). Given EA is more likely to be diagnosed in conjunction with other syndromes (particularly VACTERL) or chromosomal anomalies that may result in termination of pregnancy, it is important to include terminated cases in ascertainment (Shaw-Smith, 2006; Felix et al., 2009). For some anomalies, availability and reporting of ETOPFA may increase ascertainment of cases. In this study, total prevalence of EA was only slightly attenuated to 2.37 per 10,000 births if terminations were excluded. This finding was confirmed by a study from Texas which found no impact on rates of EA when elective terminations before 20 weeks gestation were included in case ascertainment (Ethen and Canfield, 2002).

The underlying aetiology of EA has been described as multifactorial and is likely to differ across settings (Robert et al., 1993; Felix et al., 2009; de Jong et al., 2010b). In addition to maternal ethnicity and geographic location, previous studies have reported EA to be associated with maternal age (Harris, 1995 #8; Leck, 1968 #25), multiple gestation (Harris, 1995 #8; Riley, 1998 #24), infant sex (Robert, 1993 #13) and use of assisted reproductive technology (Reefhuis, 2009 #23). In a recent study of EA in the US, women using assisted reproductive technology had a 4.5-fold
increased risk of having an infant diagnosed with EA (Reefhuis et al., 2009). Prevalence of EA has also been found to be higher among multiple births compared with singletons (Harris et al., 1995; Riley et al., 1998), and increased risk was reported with increasing maternal age (Leck et al., 1968; Harris et al., 1995). In contrast, a protective effect was found among women who have had three or more births (OR 0.50, 95% CI 0.36-0.71) (Harris et al., 1995; Carmichael et al., 2004). However, given the low frequency of occurrence of most of these factors in the general population, the population attributable risk is likely to be minimal. Variations in ethnicity as detailed above may also be surrogates for a number of different exposures, including socioeconomic status, nutrition, stress and access to services. Differences in lifestyle factors, such as smoking or dietary habits within countries or regional variation may also impact rates. However, lack of temporal trends among the included programs suggests environmental factors, which change over time, are less likely to play a role in development of EA (Robert et al., 1993; Canfield et al., 2006; Garne et al., 2007). Underlying genetic susceptibility, biological or physical differences may also modify risk of exposures. Although a number of genetic abnormalities have been associated with EA, to date, no specific gene has been implicated (Felix et al., 2009). Further studies with more detailed information to assess risk factors and underlying characteristics of cases with EA are required.

One of the limitations of the study is that it did not collect information on maternal risk factors that might help elucidate the aetiology of EA or explain differences in the prevalence across settings. Further, we did not collect information to differentiate between isolated cases and those with associated (multiple) or chromosomal anomalies due to difficulties in standardizing the definition of associated anomalies across programs. Despite these limitations, one of the strengths of the study is that case identification is likely to be complete as EA is diagnosable either antenatally or at the time of birth and require surgical attention. Recent studies from the Netherlands and Oxford, UK, reported about one third of infants were diagnosed with EA prenatally (38%) (Choudhry et al., 2007; Garne et al., 2007; de Jong et al., 2010a; Pedersen et al., 2012). Postnataally, EA are suspected and diagnosed by respiratory or feeding difficulties and inability to pass a nasogastric tube and confirmed on chest x-ray with surgical correction within 24-48 hours (Spitz, 2007).

In conclusion, EA affects, on average 1 in every 4,099 births worldwide and has remained surprisingly stable over time. Although there was some variation in the reported prevalence between and within countries, overall EA was also relatively consistent across European and American surveillance programs. Findings suggest differences in the prevalence observed between programs are likely to be attributable to local phenomena affecting reporting and/or case registration of EA or ethnic composition, rather than a real difference in risk occurrence per se. Future epidemiological
studies taking into account ethnic distribution, maternal characteristics, genetic factors and associated anomalies may provide important information regarding underlying epidemiology of EA.

**Contributors’ statement**

Pierpaolo Mastroiacovo developed the concept and design of the study. Emanuele Leoncini conducted the analysis and drafted the methods. Natasha Nassar was responsible for the drafting of the manuscript. All authors provided data for the study and contributed to the interpretation of data and had final approval of the manuscript to be published.

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References


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Table 1: Characteristics of eighteen surveillance programs of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) reporting on esophageal atresia

<table>
<thead>
<tr>
<th>Surveillance Programs</th>
<th>Coverage</th>
<th>ETOPFA</th>
<th>Maximum age or source of ascertainment or registration</th>
<th>Source of ascertainment of live births, stillbirths and ETOPFA</th>
<th>Criteria defining stillbirths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia Western Australia</td>
<td>PP1</td>
<td>P, R</td>
<td>6 years</td>
<td>M</td>
<td>20 wks or 400 g</td>
</tr>
<tr>
<td>Canada Alberta</td>
<td>RP</td>
<td>P, R</td>
<td>1 year</td>
<td>M</td>
<td>20 wks or 500 g</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>RP</td>
<td>P, R</td>
<td>15 years</td>
<td>M</td>
<td>28 wks or 1,000 g</td>
</tr>
<tr>
<td>France Paris</td>
<td>PP1</td>
<td>P, R</td>
<td>Hospital Discharge</td>
<td>M</td>
<td>22 wks</td>
</tr>
<tr>
<td>France Central East</td>
<td>RP</td>
<td>P, R</td>
<td>18 months</td>
<td>M</td>
<td>22 wks</td>
</tr>
<tr>
<td>Germany Saxony–Anhalt</td>
<td>PP2</td>
<td>P, R</td>
<td>1 year</td>
<td>M</td>
<td>500 g</td>
</tr>
<tr>
<td>Hungary</td>
<td>RP</td>
<td>P, R</td>
<td>1 year</td>
<td>M</td>
<td>24 wks or 500 g</td>
</tr>
<tr>
<td>Ireland Dublin</td>
<td>RP</td>
<td>NP</td>
<td>5 years</td>
<td>M</td>
<td>24 wks or 500 g</td>
</tr>
<tr>
<td>Israel</td>
<td>H</td>
<td>P, R</td>
<td>3-7 days</td>
<td>S</td>
<td>20 wks or 500 g</td>
</tr>
<tr>
<td>Italy Emilia Romagna</td>
<td>PP1</td>
<td>P, R</td>
<td>1 week</td>
<td>S</td>
<td>180 days</td>
</tr>
<tr>
<td>Mexico</td>
<td>H</td>
<td>NP</td>
<td>Hospital Discharge</td>
<td>S</td>
<td>20 wks or 500 g</td>
</tr>
<tr>
<td>Northern Netherlands</td>
<td>RP</td>
<td>P, R</td>
<td>15 years</td>
<td>M</td>
<td>24 wks</td>
</tr>
<tr>
<td>Slovak Republic</td>
<td>PP1</td>
<td>P, R</td>
<td>1 year</td>
<td>S</td>
<td>28 wks or 1,000 g</td>
</tr>
<tr>
<td>South America</td>
<td>H</td>
<td>NP</td>
<td>Hospital Discharge</td>
<td>S</td>
<td>500 g</td>
</tr>
<tr>
<td>USA Atlanta</td>
<td>RP</td>
<td>P, R</td>
<td>6 years</td>
<td>M</td>
<td>20 wks</td>
</tr>
<tr>
<td>USA Texas</td>
<td>RP</td>
<td>P, R</td>
<td>1 year</td>
<td>M</td>
<td>20 wks (*)</td>
</tr>
<tr>
<td>USA Utah</td>
<td>RP</td>
<td>P, R</td>
<td>5 years</td>
<td>M</td>
<td>20 wks</td>
</tr>
<tr>
<td>Wales</td>
<td>RP</td>
<td>P, R</td>
<td>1 year</td>
<td>M</td>
<td>24 wks</td>
</tr>
</tbody>
</table>

Coverage: RP=resident population (includes only cases born to mothers residing in the area covered by the registry during pregnancy, despite where the delivery took place, and excluding all cases born to non-resident mothers that delivered in the area covered by the registry). PP1=present population (includes all cases born to mothers that delivered in the area covered by the registry, regardless of where they were residing during pregnancy. The registry does not cover cases born outside the area, even if the mother is resident in the area). PP2=present population (excludes subjects born to mothers that delivered in the area covered by the registry but were residing out of the area. The registry does not cover cases born outside the area even if the mother is residing in the area. H=hospital-based (includes only a proportion - even near to 99% - of all subjects delivered in the area covered by the registry).

ETOPFA (= elective terminations of pregnancy for a fetal anomaly): P=permitted by country’s legislation; NP=not permitted; R=reported; NR=not reported

Source of ascertainment: S=Single source; M=Multiple sources

Stillbirths: wks=weeks; (*) Before 2001: 20 weeks. Since 2001: All stillbirths with documented birth defects included
Table 2: Prevalence of esophageal atresia among eighteen surveillance programs of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), 1998-2007, ordered by increasing prevalence

<table>
<thead>
<tr>
<th>Surveillance Program</th>
<th>Total Births</th>
<th>EA with TEF</th>
<th>EA without TEF</th>
<th>Unspecified atresia, fistula or stenosis</th>
<th>Total cases</th>
<th>Prevalence (per 10,000 births)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hungary</td>
<td>970,828</td>
<td>25</td>
<td>147</td>
<td>0</td>
<td>172</td>
<td>1.77</td>
<td>1.52</td>
</tr>
<tr>
<td>USA Atlanta</td>
<td>513,272</td>
<td>71</td>
<td>20</td>
<td>0</td>
<td>91</td>
<td>1.77</td>
<td>1.43</td>
</tr>
<tr>
<td>USA Texas *</td>
<td>3,305,512</td>
<td>495</td>
<td>102</td>
<td>0</td>
<td>597</td>
<td>1.81</td>
<td>1.66</td>
</tr>
<tr>
<td>Canada Alberta</td>
<td>404,595</td>
<td>66</td>
<td>13</td>
<td>0</td>
<td>79</td>
<td>1.95</td>
<td>1.55</td>
</tr>
<tr>
<td>Slovak Republic †</td>
<td>371,644</td>
<td>45</td>
<td>35</td>
<td>0</td>
<td>80</td>
<td>2.15</td>
<td>1.71</td>
</tr>
<tr>
<td>France Paris</td>
<td>363,914</td>
<td>72</td>
<td>8</td>
<td>0</td>
<td>80</td>
<td>2.20</td>
<td>1.74</td>
</tr>
<tr>
<td>Germany Saxony–Anhalt</td>
<td>162,723</td>
<td>24</td>
<td>14</td>
<td>0</td>
<td>38</td>
<td>2.34</td>
<td>1.65</td>
</tr>
<tr>
<td>USA Utah ‡</td>
<td>453,129</td>
<td>100</td>
<td>11</td>
<td>0</td>
<td>111</td>
<td>2.45</td>
<td>2.02</td>
</tr>
<tr>
<td>Ireland Dublin</td>
<td>227,586</td>
<td>55</td>
<td>2</td>
<td>0</td>
<td>57</td>
<td>2.50</td>
<td>1.90</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>969,144</td>
<td>169</td>
<td>82</td>
<td>0</td>
<td>251</td>
<td>2.59</td>
<td>2.28</td>
</tr>
<tr>
<td>Australia Western</td>
<td>262,338</td>
<td>65</td>
<td>4</td>
<td>0</td>
<td>69</td>
<td>2.63</td>
<td>2.05</td>
</tr>
<tr>
<td>Mexico</td>
<td>264,415</td>
<td>31</td>
<td>41</td>
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EA = Esophageal atresia; TEF = tracheo-esophageal fistula
EA with TEF (ICD9-BPA: 750.31, 750.33; ICD10: Q39.1); EA without TEF (ICD9-BPA: 750.30; ICD10: Q39.0); unspecified atresia, fistula or stenosis (ICD9-BPA: 750.3; no corresponding ICD10 codes).
* Includes a few cases of possible/probable diagnosed cases
Figure 1: Proportion of esophageal atresia among eighteen surveillance programs members of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), by pregnancy outcome, 1998-2007

ETOPFA = elective termination of pregnancy for fetal anomaly