Introduction

For a long time there has been considerable debate concerning the consequences of induced abortions for the outcome of subsequent pregnancies. Although legal induced abortion is considered safe, its potential impact on subsequent fertility, ectopic pregnancy and the length of gestation is a public health concern. A number of previous studies concluded that a history of one induced abortion is not a risk factor for preterm birth (Hogue et al., 1982; Atrash and Hogue, 1990; Berkowitz and Papiernik, 1993). More recent studies have shown that the risk of preterm birth is higher in women who have undergone induced abortion, and that the risk is related to the number of abortions (de Haas et al., 1991; Pickering and Deeks, 1991; Lang et al., 1996; Lumley, 1998; Martius et al., 1998; Zhou et al., 1999; Henriet and Kaminski, 2001). These results have several implications. First, as the frequency of induced abortion was high for many years in Eastern Europe (Anderson et al., 1994; World Health Organization, 1995), contributing to high rates of maternal mortality and morbidity with limited facilities for treatment of maternal complications (Tulchinski and Varavikova, 1996), the risk of subsequent preterm birth in these countries should differ from that in other countries with different abortion policies and practices (Hogue et al., 1982). Second, only limited information is available concerning the mechanisms determining the risk of preterm birth after induced abortion. The roles of cervical trauma, synechiae and infection following abortion have been discussed (Hogue et al., 1982). However, there is no strong evidence that prior induced abortion increases the risk of preterm birth due to specific complications of pregnancy. Third, Lumley (1998) showed that prior abortion was associated with a risk of preterm birth that was higher for gestations of <28 weeks than for gestation of 28 weeks or more. However, very few studies have examined the relationship between previous induced abortion and early and moderate preterm births.

In this study, we aimed to estimate the risk of preterm birth associated with a history of induced abortions in the first trimester of pregnancy from data collected in a large case–control survey in Europe, the EUROPOP study. This survey included detailed information on past obstetric history, making it possible to analyse the relationship between a history of
induced abortions and preterm birth in various European countries. Our hypothesis was that the risk of subsequent preterm birth was likely to be higher in Eastern European countries than in other countries. With the aim of increasing our understanding of the underlying mechanisms, we studied the effect of previous abortions on various preterm birth groups defined as a function of the complications of pregnancy leading to delivery. As induced abortion may affect the outcome of subsequent pregnancies via mechanical or infectious factors, we hypothesized that previous induced abortions would be associated with spontaneous deliveries and non-hypertensive pregnancy complications. Finally, we compared association of previous induced abortion with subsequent preterm birth for very and moderate preterm births. We expected the risk to be higher for birth at younger gestational ages.

Materials and methods

Study design and subject recruitment

Between 1994 and 1997, an unmatched case–control survey, the EUROPOP study, was conducted in 60 maternity units from 17 European countries, with the same protocol and questionnaire used in each country. The details of the survey have been published elsewhere (Saurel-Cubizolles et al., 1997). For each maternity unit, the cases comprised all consecutive single preterm births occurring between 22 and 36 completed weeks of amenorrhoea. The sample included stillborn as well as liveborn infants. Preterm births were identified on the basis of the best obstetric estimation of gestational age according to ultrasound examination, date of last menstrual period, and clinical neonatal estimation. The unmatched control group included every tenth consecutive term (≥37 weeks of amenorrhoea) single birth occurring during the recruitment period of cases. Data from Turkey were not used in the analysis because the control group was incomplete.

Data from Ireland were excluded because induced abortion was not legal in this country. Data from Spain and Poland were also excluded because very few previous induced abortions were declared. Finally, we excluded data from France and The Netherlands because no distinction was made between spontaneous and induced first trimester abortions in these countries. The analysis was carried out in the following ten countries, in which information about previous first trimester induced abortions was collected correctly: Germany, Finland, Scotland, Sweden, Italy, Czech Republic, Slovenia, Romania, Russia and Hungary. In these countries, data on previous induced abortions were missing for only 2.5% of controls (n = 120) and 4.1% of cases (n = 120). The analysis included 2938 cases of preterm birth and 4781 controls at term.

Data collection

Information about previous induced abortion, social class, marital status, smoking habits, maternal age, and obstetric history was collected by interviewing women during their stay in the maternity unit. Women were assigned to one of the following three categories on the basis of self-reported history of first trimester induced abortion: no previous induced abortion, one previous induced abortion, or two or more previous induced abortions. The social class of the household was that corresponding to the occupation of the woman or the child’s father (whichever was higher), and was scored using the International Labour Office classification (ILO) (ISCO-88, 1991).

We defined various subgroups of preterm births on the basis of gestational age, pregnancy complications and medical delivery information collected from medical records. Delivery onset was defined as spontaneous or indicated. Spontaneous delivery included cases with spontaneous onset of labour or preterm premature rupture of membranes. Indicated deliveries included cases of induced onset of labour or elective Caesarean section, but excluded preterm premature rupture of membranes. We also classified preterm births according to the pregnancy complications leading to delivery. Women were assigned to five mutually exclusive groups: (1) preterm premature rupture of membranes, defined as spontaneous rupture of the fetal membranes before the onset of labour, without ante-partum haemorrhage and hypertension; (2) idiopathic preterm labour, defined as spontaneous onset of labour before membrane rupture, without ante-partum haemorrhage and hypertension; (3) maternal hypoten-

Statistical analysis

We defined three groups of countries according to the frequency of induced abortion, based on national statistics from 1995 (World Health Organization, 1995). The first group included countries with a high abortion rate: Romania and Russia. The second group included countries with intermediate rates: Hungary, Slovenia and the Czech Republic. The third group included the countries with the lowest rates: Sweden, Italy, Scotland, Finland and Germany. The characteristics of the women with and without a history of previous induced abortions were compared in the control groups of the three groups of countries, using the χ²-test. Multiple logistic regression was used to estimate the odds ratios (OR) of preterm birth, with 95% confidence intervals (95% CI), associated with previous induced abortions, after adjustment for confounding factors. The following factors were included in multivariate analyses because they are known risk factors for preterm delivery (Berkowitz and Papiernik, 1993): maternal age, marital status, social class of the household, smoking during pregnancy and parity. Because adjustment slightly modifies odds ratios, only adjusted associations are shown in the Results section. Preterm births are uncommon events, so odds ratios are good estimates of relative risks. The adjusted odds ratios were compared between groups of countries using the following statistic: I = wi(InORi − InOR)² + wi(InORi − InOR)² + wi(InORi − InOR)² + wi(InORi − InOR)², where InORi is estimated from the independent logistic regressions for group i (i = 1, 2, 3) of countries, wi is the inverse variance (1/variace), and InOR (adjusted parameter) is the mean of the parameters estimated for the three groups (Paul and Donner, 1989). Under the null hypothesis of no difference in odds ratios, this statistic will follow a χ² distribution.

In the second step of the analysis, data were grouped because no significant variation between groups of countries was observed for the relationships between previous induced abortion and preterm births. We first investigated the relationships between previous induced abortions and very and moderate preterm births. We then estimated the odds ratios for spontaneous and indicated preterm delivery associated with previous induced abortions. Finally, we investigated the relationships between previous induced abortions and the possible causes of preterm delivery (preterm premature rupture of membranes, idiopathic preterm labour, maternal hypertension, ante-partum haemorrhage, and other). In these analyses, odds ratios were estimated by polynomal logistic regression (Hosmer and Lemeshow, 1989), using all births at term as controls, and adjusting for confounding factors.
Factors. The analyses were performed with SAS software (SAS Institute, 1999).

Results

For deliveries at term (controls), 36% of women reported having previously undergone induced abortions in the countries of group 1, versus only 17 and 13% in groups 2 and 3, respectively (Table I). The proportion of women with two or more previous induced abortions was higher in group 1 of countries (16%) than in the countries of group 2 (4%) and group 3 (2%).

The women who had undergone previous induced abortions differed from the others in terms of various socio-demographic and behavioural factors (Table II). In all three groups of countries, women who reported previous induced abortions were significantly older and less likely to be married than those who did not report previous induced abortions; they were also less likely to be primiparous, but were not more likely to have a history of adverse pregnancy outcomes, except in group 3. Little variation was observed with respect to social status. In groups 2 and 3, women with a history of previous induced abortions were more likely to be living alone and to smoke.

After adjustment for potential confounders, the risk of preterm delivery was significantly higher in women with a history of previous induced abortions than in those without such a history in groups 1 and 2, and this relationship was close to the threshold of significance in group 3, with an adjusted odds ratio of 1.2 to 1.5 (Table III). The adjusted odds ratios were higher for women who reported two or more previous abortions than for women with only one previous abortion. No significant difference in odds ratio was observed between the three groups of countries ($P = 0.50$).

The association with a history of induced abortion was stronger for very preterm birth than for moderate preterm birth, with adjusted odds ratios of 1.5 and 1.2 respectively (Table IV). In both cases, odds ratios increased with the number of previous abortions. A history of previous induced abortions was significantly associated with spontaneous preterm birth with a dose–response relationship, but no such association was observed with indicated preterm birth (Table IV). However, a history of two or more previous abortions was significantly associated with indicated preterm birth, with an adjusted odds ratio of 1.6.

A history of previous induced abortions was significantly associated with preterm delivery following preterm premature rupture of membranes (odds ratio, OR = 1.4), idiopathic preterm labour (OR = 1.3), placenta praevia (OR = 2.3) and other types of ante-partum haemorrhage (OR = 1.7) (Table V). No relationship was observed between a history of induced abortion and preterm delivery following maternal hypertension or abruptio placenta.

Discussion

In the EUROPOP study, the participating maternity units were selected on a voluntary basis. Thus, the controls may not necessarily be representative of the general population. They may experience more pregnancy complications than expected from the general population if the maternity units tend to recruit women at risk. However, the frequencies of maternal hypertension (6%), placenta praevia (0.4%) and abruptio placenta (1.5%) in the control group were similar to those usually reported (Zhang et al., 1997; Demissie et al., 1999; Ananth et al., 2001). For the cases, the frequencies of most pregnancy complications (preterm premature rupture of membranes, idiopathic preterm labour, maternal hypertension, ante-partum haemorrhage) were similar to those previously reported for preterm and very preterm deliveries (French and McGregor, 1996; Hagan et al., 1996). Thus, there is no evidence of selection bias based on medical factors in this study.

We cannot exclude the possibility of underreporting of previous induced abortion. In previous studies, underreporting varies from 16 to 65% (Anderson et al., 1994; Fu et al., 1998). The validity of survey responses can be checked by comparing with external sources of information such as patient records.
(Anderson et al., 1994) or national counts (Fu et al., 1998), but the proportion of abortions reported probably depends on the characteristics of the women (Fu et al., 1998), the mode of data collection, the wording of the questions used (Houzard et al., 2000), and the broader context of public opinion on this topic. Underreporting may have been more frequent in Northern and Western Europe than in Eastern Europe, because abortion was legalized a long time ago in Eastern Europe and carries out a lower level of social stigma than in Western Europe. This could have led to a larger underestimation of the association between previous induced abortion and preterm birth in group 3 than in groups 1 and 2. However, differences in the reporting by women of previous abortions in the various countries (Table I) were similar to differences in the actual frequency of induced abortion based on national statistics (World Health Organization, 1995).

Another possible problem is that underreporting may differ between cases and controls. Although selective underreporting, by cases or controls, may have occurred, no data were available to check whether this bias resulted in the under- or over-estimation of odds ratios. In a Danish register-based study with <10% underreporting of previous induced abortion, the odds ratios for preterm birth were 1.9 for one previous induced abortion and >2.0 for at least two abortions (Zhou et al., 1999).

### Table II. Maternal characteristics according to previous induced abortions (‘No’/‘Yes’) in the controls of the three groups of countries

<table>
<thead>
<tr>
<th></th>
<th>Group 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 2&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 3&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 2&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 3&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried cohabiting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried living alone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social class of the household&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Service worker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Industrial worker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking during pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 cigarettes/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous 2nd trimester abortion or preterm birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers in parentheses.

<sup>a</sup>Group 1: Romania and Russia; Group 2: Hungary, Slovenia and Czech Republic; Group 3: Germany, Finland, Scotland, Italy and Sweden.

<sup>b</sup>Professional = ILO code 1–2 for the child’s father or 1–3 for the woman; intermediate = ILO code 3 for the child’s father or 4 for the woman; service worker = ILO code 4–5 for the child’s father or 5 for the woman; industrial worker = ILO code 6–9 for the child’s father or the woman; unemployed = woman and her partner have no job.

NS = non significant.

### Table III. Preterm birth and previous induced abortions in Europe: adjusted values

<table>
<thead>
<tr>
<th>No. previous induced abortions</th>
<th>Group 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 2&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 3&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>95% CI</td>
<td>OR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>95% CI</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>1.52</td>
<td>1.09–2.12</td>
<td>1.26</td>
<td>1.03–1.55</td>
</tr>
<tr>
<td>1</td>
<td>1.33</td>
<td>0.89–2.00</td>
<td>1.22</td>
<td>0.97–1.54</td>
</tr>
<tr>
<td>≥2</td>
<td>1.76</td>
<td>1.15–2.70</td>
<td>1.38</td>
<td>0.97–1.97</td>
</tr>
</tbody>
</table>

<sup>a</sup>Group 1: Romania and Russia; Group 2: Hungary, Slovenia and Czech Republic; Group 3: Germany, Finland, Scotland, Italy and Sweden.

<sup>b</sup>OR = odds ratio; 95% CI = 95% confidence interval; adjusted for maternal age, marital status, social class of the household, smoking during pregnancy, parity and country.
In an Australian population-based study, relative risks of preterm delivery were from 1.5 to >4.0, depending on the number of previous induced abortions (Lumley, 1998). This suggests possible slight underestimation of the associations in our study.

Our results are consistent with other studies reporting a significant increase in the risk of preterm birth with the number of previous induced abortions (de Haas et al., 1991; Kristensen et al., 1995; Lang et al., 1996). In our study, a history of prior induced abortion seemed to be strongly associated with spontaneous preterm delivery. Unlike Henriet and Kaminski (2001), we found a significant association between a history of at least two previous abortions and indicated preterm birth. Spontaneous and indicated preterm births may not be aetiologically different entities. For example, in our study, delivery was induced in 60% of women with placenta praevia and in 30% of women with other types of ante-partum haemorrhage. This suggests that the classification of preterm birth according to the type of onset of labour may be insufficient to identify underlying pregnancy complications responsible for preterm delivery.

It has been suggested that infectious diseases following abortion may account for the relationship with subsequent preterm delivery (Stürchler et al., 1986). Women with a history of induced abortion have an increased risk of intra-amniotic infection (Krohn et al., 1998), intra-partum infection (Stürchler et al., 1986; Mühlemann et al., 1996) and of infection of their newborn children (Germain et al., 1995). Intra-amniotic infection is a known risk factor for idiopathic preterm labour and preterm premature rupture of membranes (Gomez et al., 1997; Romero et al., 2001). To our knowledge, no data are available concerning the risk of preterm birth according to the pregnancy complications that led to delivery. Thus, identifying subgroups of preterm births on the basis of pregnancy complications may help to increase our understanding of the mechanisms underlying the effect of previous induced abortion on subsequent pregnancy outcomes. Our results, showing a significant association between previous induced abortion and both idiopathic preterm labour and preterm premature rupture of membranes, are consistent with infectious processes. Although the association between prior abortion and intra-amniotic infection may result from latent upper genital tract infection, preceding or beginning at the time of abortion (Stürchler et al., 1986), other mechanisms should be considered. Cervical trauma from mechanical dilatation (Hakim-Elahi et al., 1990), by increasing the risk of cervical incompetence (Molin, 1993) and facilitating upper genital tract infection, may account for intra-amniotic infection.
following abortion. Consistent with previous studies (Ananth et al., 1997; Seidman et al., 1998), we also found a strong relationship between previous abortion and preterm birth after placenta praevia and other types of maternal haemorrhage. It has been suggested that surgical procedures, by damaging the endometrium, may increase faulty placentation in subsequent pregnancies.

The stronger association with very preterm birth than with moderate preterm birth is consistent with results from Australia (Lumley, 1998). It suggests that the underlying mechanisms involved in the adverse effect of previous induced abortion (e.g. infection and haemorrhage) are similar to the major causes of very preterm delivery (preterm premature rupture of membranes, idiopathic preterm labour, infection, ante-partum haemorrhage, and cervico-uterine abnormalities) (Hillier et al., 1988; Hagan et al., 1996).

Like any surgical procedure, dilatation–curettage and dilatation–suction procedures present a number of risks of early complications. Such complications, including pelvic infection, fever, tissue retention, bleeding and cervical trauma, are recorded for ~5% of women (Zhou et al., 1999). The procedures used may also have an effect on subsequent pregnancies. The risk of preterm birth has been shown to be related to (i) the technique used for induced abortion, with higher figures for dilatation and curettage than for aspiration (Zhou et al., 1999) and (ii) the timing of the abortion, with a higher risk for abortions after 8 weeks (Zhou et al., 1999). In Europe, between 1980 and 1995, >90% of abortions were carried out by surgical procedures (Abortion Statistics, 1995; Le Corre and Thomson, 2000; Zhou et al., 2002), suggesting that most of the abortions reported by the women included in our survey were carried out by such procedures.

Further studies are required because abortion procedures and their potential side-effects have changed. Drug-based abortion has been available since the early 1990s. The antiprogestogen mifepristone, in combination with a prostaglandin analogue, provides a suitable non-surgical method for early pregnancy termination (Ashok et al., 2002). The frequency of use of this method increased from 14% (1990) to 20% (1997) in France (Le Corre and Thomson, 2000), and from 9% (1995) to 20% (2001) in England and Wales (Abortion Statistics, 1995, 2001). Ashok et al. (2002) reported that women given such drug treatments had complete abortions in 98% of cases, with only 2% requiring surgical intervention. Thus, changes in the management of induced abortion may affect the relationship between previous induced abortion and subsequent pregnancy outcomes.

In conclusion, our results provide evidence that history of induced abortion is a risk factor for preterm delivery. Although the relationship between induced abortion and preterm birth was similar in all countries studied, public health consequences, depending on the frequency of prior induced abortion, varied considerably between countries. With a mean odds ratio for preterm birth of 1.6 associated with at least two previous abortions, assuming that this relationship is causal, and using the proportion of women who had undergone induced abortion in each of the three control groups, the attributable risk fractions are 4 and 2% in groups 2 and 3, and 12% in group 1. We were also able to show differences according to the cause of delivery, with an increased risk of preterm birth following preterm labour, preterm premature rupture of membranes and ante-partum haemorrhage. Although these complications of pregnancy result from cervico-uterine abnormalities, the precise underlying mechanisms, whether post-traumatic or post-infectious, remain unknown (Zhou and Olsen, 2003). As the techniques used for induced abortion have changed during the last decade, it would be useful to examine the long-term consequences of induced abortion with respect to new medical procedures.

Acknowledgements
We would like to thank the members of the EUROPOP group (see Appendix), the interviewers for data collection, and the technical teams for computerized data handling in all countries. This study was funded by the European Union (contract BMH1-CT94-1041).

Appendix: composition of the EUROPOP group

Members of the steering committee
Project leader: Di Renzo GC, Perugia, Italy. Bréart G, MD and Papiernik E, MD, Paris, France; Patel N, MD, Dundee, UK; Saurel-Cubizolles MJ, PhD, Villejuif, France; Taylor D, MD, Leicester, UK; Todini S, MsC, Perugia, Italy.

Members of the national staffs

Members of the epidemiological analysis staff
Ancel Pierre-Yves, MD, Bréart Gérard, MD, Lelong Nathalie, MsC, Saurel-Cubizolles Marie-Josèphe, PhD, France.

References
Abortion Statistics (2001) Legal abortions carried out under the 1967 Abortion


Submitted on May 21, 2003; resubmitted on September 26, 2003; accepted on October 29, 2003.