Possible role of unmeasured confounding by smoking in the evaluation of environmental factors associated with preterm births

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Moniter Project

Multisite project on environmental monitoring and epidemiological investigation on area surrounding MSW incinerators in Emilia Romagna Region

- Cross-sectional study on relation between pollution due to incinerators and birth outcomes.

- Preterm birth: RR 1.75 [1,25-2,46] for subgroup at higher exposure to incinerators

Confounding by exposure to tobacco smoke??

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BEST PRACTICE GUIDELINE ARTICLE

Morphological and biological effects of maternal exposure to tobacco smoke on the feto-placental unit

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Table 1 Placental and fetal side-effects of maternal tobacco smoking in early and late pregnancy

Early pregnancy
Miscarriage
Ectopic pregnancy
Placenta previa and placenta previa-accreta
Fetal orofacial clefts
Late pregnancy
Fetal growth restriction
Placental insufficiency
Placental abruption
Premature rupture of the placental membranes and preterm delivery

Nicotine & Tobacco Research Volume 6, Supplement 2 (April 2004) S125–S140

Taylor & Francis Healthcare

Review

The epidemiology of smoking during pregnancy: Smoking prevalence, maternal characteristics, and pregnancy outcomes

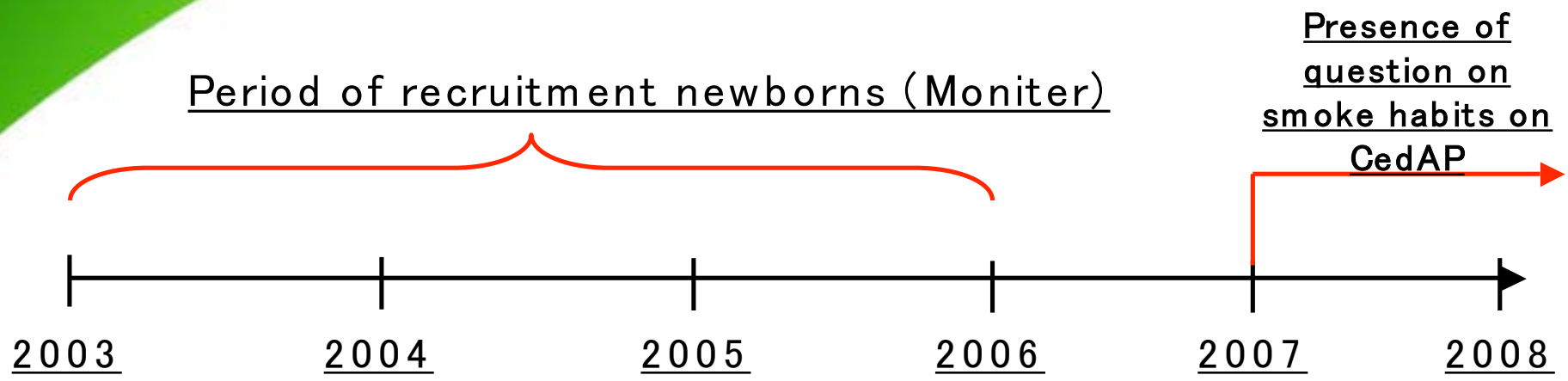
Sven Cnattingius

Table 1. Summary of smoking-related risks and pregnancy complications.

	Relative risk[a]	Dose response?	Consistency between findings?	Smoking cessation influences risk?
Infertility	1.2–3.6	?	Most studies	Yes
Ectopic pregnancy	1.5–2.5	?	Most studies	?
Spontaneous abortion	1.0–1.8	?	No	?
Placental abruption	1.4–2.4	Yes	Yes	Yes
Placenta previa	1.5–3.0	?	Yes	?
Preeclampsia	0.5–0.7	No	Most studies	?

[a]Smokers vs. nonsmokers.

Birth Certificate (CedAP): Question on smoke habits



Question: Tobacco smoke habit in the 5 years prior to pregnancy

1: no smoking habits since 5 years

2: She stopped smoking before pregnancy

3: She stopped smoking at the beginning of pregnancy

4: She continued smoking during pregnancy

CedAP 2007 and 2008

Loc. Health Authority	smoke (n° and %) 1	2	3	4	Missing	Total
Piacenza	1,819 84.37	94 4.36	89 4.13	154 7.14	0 0.00	2,156 100.00
Parma	1,036 77.14	98 7.30	109 8.12	95 7.07	5 0.37	1,343 100.00
Reggio E.	2,231 80.19	117 4.21	209 7.51	225 8.09	0 0.00	2,782 100.00
Imola	892 76.30	61 5.22	90 7.70	126 10.78	0 0.00	1,169 100.00
Ferrara	977 76.33	79 6.17	117 9.14	98 7.66	9 0.70	1,280 100.00
Ravenna	2,652 78.74	160 4.75	178 5.29	275 8.17	103 3.06	3,368 100.00
AOSPU PR	2,081 82.16	133 5.25	127 5.01	155 6.12	37 1.46	2,533 100.00
AOSP RE	2,150 86.52	51 2.05	126 5.07	158 6.36	0 0.00	2,485 100.00
AOSP MO	2,767 83.70	36 1.09	47 1.42	180 5.44	276 8.35	3,306 100.00
AOSPU BO	3,012 85.96	26 0.74	47 1.34	203 5.79	216 6.16	3,504 100.00

Loc. Health Authority	smoke (n° and %) 1	2	3	4	Missing	Total
Piacenza	1,885 85.22	109 4.93	69 3.12	149 6.74	0 0.00	2,212 100.00
Parma	1,074 79.79	102 7.58	80 5.94	90 6.69	0 0.00	1,346 100.00
Reggio E.	2,273 81.29	95 3.40	204 7.30	220 7.87	4 0.14	2,796 100.00
Imola	948 80.34	45 3.81	72 6.10	115 9.75	0 0.00	1,180 100.00
Ferrara	1,042 75.62	104 7.55	126 9.14	100 7.26	6 0.44	1,378 100.00
Ravenna	2,827 79.17	225 6.30	205 5.74	260 7.28	54 1.51	3,571 100.00
Forli	1,240 75.84	132 8.07	121 7.40	142 8.69	0 0.00	1,635 100.00
Cesena	1,745 80.16	130 5.97	150 6.89	152 6.98	0 0.00	2,177 100.00
AOSP RE	2,205 89.05	42 1.70	114 4.60	115 4.64	0 0.00	2,476 100.00
AOSP MO	3,016 86.89	37 1.07	48 1.38	170 4.90	200 5.76	3,471 100.00
AOSPU BO	3,394 92.35	13 0.35	30 0.82	171 4.65	67 1.82	3,675 100.00
AOSPU FE	1,435 93.12	9 0.58	15 0.97	74 4.80	8 0.52	1,541 100.00

Smokers during pregnancy

- 2007:
  - Total: 23926; Answer 4: 1669
    - % of smokers during pregnancy: 6.98
- 2008:
  - Total: 27458; Answer 4: 1758
    - % of smokers during pregnancy: 6.40

% of smokers during pregnancy in 2007-8: 6.67

Indirect estimation

- Situation:
  - –absence of data on the % of smokers in different subgroups of population (divided by incinerator exposure);
  - –Known risk of preterm delivery in women highly exposed to the incinerator
  - –Knowledge of % of smokers during pregnancy in population
  - –Known risk (by literature) of preterm delivery due exposure to smoke during pregnancy

Objective: to estimate the percentage of smokers required in the group with higher exposure to incinerator so that the risk identified is attributable to exposure to tobacco smoke during pregnancy.

Axelson O, Steenland K. Indirect methods of assessing the effects of tobacco use in occupational studies. Am J Ind Med. 1988;13(1):105-18.

Forastiere F, Perucci CA, Arcà M, Axelson O. Indirect estimates of lung cancer death rates in Italy not attributable to active smoking. Epidemiology. 1993 Nov;4(6):502-10.

Worst scenario

- Risk of preterm (Moniter): 1.75 (highest vs. lowest exp.)
- % of smokers in population: 6.67
- Risk of preterm due to smoke: 2.7 (right highest value of all CIs)*

$$1.75 = \frac{I_{\exp}}{I_{un\exp}}$$

$I_{\exp}$ = Incidence in exposed to smoke

$I_{un\exp}$ = Incidence in not-exposed to smoke

** Suzuki K et al. Is maternal smoking during early pregnancy a risk factor for all low birth weight infants? J Epidemiol 2008; 18: 89-96)*

Incidence formula in population

$$I = I_0 + I_0 * (RR - 1) * P_{\exp}$$

I = incidence of disease

I_0 =background incidence

RR-1 = excess risk due to factor we are analyzing

P_{exp}= proportion of exposed to risk factor

$$1.75 = \frac{I_{\exp}}{I_{un\exp}} = \frac{(I_0 + I_0 * (2.7 - 1) * P_{\exp 2})}{(I_0 + I_0 * (2.7 - 1) * 0.0667)}$$

***Pexp2*=0.52, about 8 times more than general population**

Scenario simulation

- Hypothesis: % of smokers in population exposed to the incinerator is double than in general population (13%)

$$\frac{(1+1.7*0.13)}{(1+1.7*0.0667)} = 1.09$$

1.09 = risk of preterm in highest population due to smoke

More realistic scenario (1.5 risk for tobacco): ->1.03

Conclusion

- We apply an indirect methods to estimate the percentage of smokers required in the higher exposed group to totally explain the risk founded
- This approach applies to similar situations of unmeasured possible risk factors

- Conditions: it works perfectly if estimation of prevalence in population are possible and reliable.
- Limit: it does not depend upon age

(*)

(*) Richardson DB. Epidemiology, 21, 2010