%、家庭での受動喫煙による人口寄与危険割合は15.6%と推計している[6]。本調査では、2003年から2006年の出生児に占める低出生体重の割合は8%前後と滝本らの報告と同程度であったが、妊娠中の喫煙の低出生体重発症に対する人口寄与危険割合は5.1%とこれまでの報告よりも若干低めに推計された。

妊娠は女性の喫煙者を禁煙に向ける最も大きな機会の一つであり、大井田らの報告によると、妊娠中は喫煙していないが妊娠前は喫煙していた妊婦の比率は平成18年度で25.7%と報告されている[9]。本調査では、同比率は28.6%であり、このうち喫煙を機に禁煙した妊婦は妊婦全体の16.2%にものぼり、妊娠前に禁煙していた妊婦の12.4%よりも多かった。妊娠を機に禁煙することで、LBWのリスクが下がることは数多く報告されており、本研究でも妊娠を機に禁煙した場合、妊娠中も喫煙した場合と比べての低出生体重や早産の発症割合が有意に低いことが確認された。また、妊娠中の飲酒と同居者の喫煙があると、妊娠を機に禁煙しにくく、これまでの研究報告を支持するものである。これらの結果は、妊婦の禁煙を推進するには家族の禁煙と妊婦の禁酒も同時に推進する必要性を示すものであり、今後の佐賀市の母子保健領域での喫煙対策の基礎資料として、啓発普及や禁煙支援において活用していく予定である。

本調査は既存データの照合による分析であるため、いくつかの限界がある。まず、照合できなかった約2000件についての詳細が得られていない。解析除外者の喫煙率は9.1%と解析対象者の6.3%に比べ有意に高く、除外者の中に低出生体重や早産が多い割合で含まれることが予想され、今回の結果は妊婦の喫煙や受動喫煙による低出生体重のリスクを控えめに評価していると考えられる。また、照合できなかった例は転出だけでなく流・死産が含まれている可能性もあり、喫煙の影響が関与する可能性も否定できない。また、妊娠届時点での喫煙状況を用いた解析を行っているので、調査後に禁煙をした場合や、禁煙者が再喫煙している場合が考えられる。しかし、いずれも喫煙の影響を過小評価する傾向に働くので、得られた結果はリスクを控えめに評価していると考えられる。また、低出生体重のリスク要因は、児、胎盤、母体における社会経済学的な要因、基礎疾患、妊娠前の体重、体重増加、栄養状態、感染症や疾病の罹患状況、喫煙、飲酒、カフェイン摂取、薬物使用、就業状態や精神的ストレスなど母体の環境や行動に関連する要因などが報告されている[1]が、今回は喫煙、家庭での受動喫煙、飲酒以外の情報については得られていない。また、これらの情報が自記式調査票への回答のみによっており、真の喫煙状況を反映していない可能性もある。今後低出生体重のリスク要因を詳細に検討するためには、呼気中ＣＯ濃度や尿中コチニン濃度など喫煙や受動喫煙のバイオマーカーの測定などを含めた研究が必要である。

D. 結論

妊娠初期の喫煙は低出生体重や早産の有意な危険因子であることが示された。また妊娠を契機とした禁煙を妨げる要因として家族の喫煙や妊婦自身の飲酒などが関連しており、妊婦とその家族も含めた禁煙支援、より早期からの喫煙開始防止のための啓発普及といったたばこ対策が重要である。

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E. 健康危機情報

なし

F. 研究発表

1. 論文発表　なし

2. 学会発表

G. 知的財産の出願・登録状況

該当せず

表1　妊娠届時の年齢、喫煙、受動喫煙、妊娠中の飲酒および出生体重、低出生体重の年次推移

	全体 (n=4391)	平成15年度 (n=1142)	平成16年度 (n=1106)	平成17年度 (n=1056)	平成18年度 (n=1033)	P値
年齢(%)						
20歳未満	81 (1.9)	25 (2.2)	19 (1.7)	16 (1.6)	21 (2.0)	0.03
20～29歳	2028 (46.7)	573 (50.9)	527 (45.8)	464 (44.9)	464 (44.9)	
30～39歳	2158 (49.7)	512 (45.5)	590 (51.3)	532 (51.5)	524 (50.7)	
40歳以上	74 (1.7)	15 (1.3)	14 (1.2)	21 (2.0)	24 (2.3)	
喫煙歴(%)						
非喫煙	2859 (65.1)	762 (66.7)	778 (67.1)	677 (64.1)	642 (62.2)	0.05
妊娠前に禁煙	543 (12.4)	125 (11.0)	127 (11.0)	142 (13.5)	149 (14.4)	
妊娠を機に禁煙	711 (16.2)	170 (14.9)	184 (15.9)	175 (16.6)	182 (17.6)	
妊娠中も喫煙	278 (6.3)	85 (7.4)	71 (6.1)	62 (5.9)	60 (5.8)	
家庭での受動喫煙(%)						
あり	2690 (61.3)	720 (63.1)	735 (63.4)	628 (59.5)	607 (58.8)	0.05
なし	1701 (38.7)	422 (36.9)	425 (36.6)	428 (40.5)	426 (41.2)	
妊娠中の飲酒(%)						
あり	304 (6.9)	78 (6.8)	94 (8.1)	70 (6.6)	62 (6.0)	0.26
なし	4087 (93.1)	1064 (93.2)	1066 (91.9)	986 (93.4)	971 (94.0)	
出生体重　平均(SD)	3011.0 (447.0)	3055.4 (414.5)	3020.4 (438.6)	3048.9 (446.4)	3034.1 (437.5)	0.16
出生体重(%)						
2500g未満	350 (8.0)	78 (6.8)	97 (8.4)	88 (8.3)	87 (8.4)	0.43
2500g以上	4041 (92.0)	1064 (93.2)	1063 (91.6)	968 (91.7)	946 (91.6)	
週数　平均(SD)	38.8 (1.9)	38.8 (416.8)	38.8 (1.7)	38.9 (1.7)	38.9 (1.8)	0.50
出生週数						
早産(%)	213 (4.9)	56 (4.9)	60 (5.2)	44 (4.2)	53 (5.1)	0.68
満期産(%)	4178 (95.1)	1086 (95.1)	1100 (94.8)	1012 (95.8)	980 (94.9)	

割合の検定は$\chi 2$検定

出生体重の平均値の検定はKruskal-Wallis検定

表2　妊娠届時の年齢階級別の喫煙歴および、喫煙状況別の受動喫煙、妊娠中の飲酒、出生体重

	非喫煙 (n=2859)	妊娠前に禁煙 (n=543)	妊娠を機に禁煙 (n=711)	妊娠中も喫煙 (n=278)	P値
年齢(%)*					
20歳未満	30 (37.0)	6 (7.4)	29 (35.8)	16 (19.8)	<0.0001
20～29歳	1169 (57.6)	273 (13.5)	421(20.8)	165 (8.1)	
30～39歳	1577 (73.1)	249 (11.5)	244 (11.3)	88 (4.1)	
40歳以上	56 (75.7)	9 (12.2)	4 (5.4)	5 (6.8)	
家庭での受動喫煙(%)					
あり	1516 (53.0)	337 (62.1)	593 (83.4)	244 (87.8)	<0.0001
なし	1343 (47.0)	206 (39.7)	118 (16.6)	34 (12.2)	
妊娠中の飲酒(%)					
あり	164 (5.7)	52 (9.6)	52 (7.3)	36 (13.0)	<0.0001
なし	2695 (94.3)	491 (90.4)	659 (92.7)	242 (87.1)	
出生体重　平均	3045.5	3060.6	3048.9	2914.2 **	<0.05
(SD)	(429.4)	(443.9)	(416.0)	(506.0)	
出生体重 (%)					
2500g未満	225 (7.9)	39 (7.2)	48 (6.8)	38 (13.7)	<0.01
2500g以上	2634 (92.1)	504 (92.8)	663 (93.3)	240 (86.3)	
週数　平均(SD)	38.9 (1.6)	38.9 (1.7)	38.9 (1.6)	38.5 (2.3) **	<0.05
出生週数					
早産(%)	134 (4.7)	25 (4.6)	33 (4.6)	21 (7.6)	0.19
満期産(%)	2725 (95.3)	518 (95.4)	678 (95.4)	257 (92.4)	

＊　年齢階級別の喫煙割合を表示、年齢階級が不明50

割合の検定は$\chi 2$検定

出生体重の平均値の検定はKruskal-Wallis検定

**　Tukeyのスチューデント化範囲検定にて、妊娠中も喫煙している妊婦の児の出生時体重および、週数は、他のいずれの群よりも有意に少ない(P<0.05)

表3 低出生体重(LBW)および早産に対する関連要因のオッズ比(OR)と95%信頼区間(95%CI)

	出生体重			出生週数		
	LBW	正常	粗OR (95%CI)	早産	満期産	粗OR (95%CI)
年齢						
20歳未満	8	73	1 (ref)	9	72	1 (ref)
20～29歳	152	1876	0.7 (0.4-1.3)	89	1939	0.6 (0.3-1.1)
30～39歳	172	1986	0.8 (0.4-1.4)	106	2052	0.6 (0.3-1.2)
40歳以上	13	61	1.9 (0.8-4.4)	8	66	1.5 (0.6-3.9)
		傾向性の検定	P<0.001		傾向性の検定	P<0.001
喫煙歴						
非喫煙	225	2634	1 (ref)	134	2725	1 (ref)
妊娠前に禁煙	39	504	0.9 (0.6-1.3)	25	518	1.0 (0.6-1.5)
妊娠を機に禁煙	48	663	0.8 (0.6-1.2)	33	678	1.0 (0.7-1.5)
妊娠中も喫煙	38	240	1.9 (1.3-2.7)	21	257	1.7 (1.0-2.7)
		傾向性の検定	P<0.001		傾向性の検定	P=0.19
妊娠届時の喫煙						
なし	312	3801	1 (ref)	192	3921	1 (ref)
あり	38	240	1.9 (1.3-2.8)	21	257	1.7 (1.1-2.7)
家庭での受動喫煙						
なし	135	1566	1 (ref)	72	1629	1 (ref)
あり	215	2475	1.0 (0.8-1.3)	141	2549	1.3 (0.9-1.7)
妊娠中の飲酒						
なし	323	3764	1 (ref)	197	3890	1 (ref)
あり	27	277	1.1 (0.8-1.7)	16	288	1.1 (0.7-1.9)
妊娠中の喫煙と受動喫煙の状況						
喫煙(-)受動喫煙(-)	131	1536	1 (ref)	68	1599	1 (ref)
喫煙(-)受動喫煙(+)	181	2265	0.9 (0.7-1.2)	124	2322	1.3 (0.9-1.7)
喫煙(+)受動喫煙(-)	4	30	1.6 (0.5-4.5)	4	30	3.2 (1.1-9.2)
喫煙(+)受動喫煙(+)	34	210	1.9 (1.3-2.8)	17	227	1.8 (1.1-3.1)
		傾向性の検定	P<0.05		傾向性の検定	P<0.05
妊娠中の喫煙と飲酒の状況						
喫煙(-)飲酒(-)	290	3555	1 (ref)	180	3665	1 (ref)
喫煙(-)飲酒(+)	22	246	1.1 (0.7-1.7)	12	256	1.0 (0.5-1.7)
喫煙(+)飲酒(-)	33	209	1.9 (1.3-2.8)	17	225	1.5 (0.9-2.6)
喫煙(+)飲酒(+)	5	31	2.0 (0.8-5.1)	4	32	2.5 (0.9-7.3)
		傾向性の検定	P<0.01		傾向性の検定	P<0.01

＊ 年齢、喫煙状況、受動喫煙の有無、飲酒の有無で調整、妊娠中の喫煙と受動喫煙の状況については年齢と飲酒、妊娠中の喫煙と飲酒の状況については年齢と受動喫煙の有無で調整しても同様の結果

表4　早産児および満期産における低出生体重(LBW)に対する関連要因のオッズ比(OR)と95%信頼区間(95%CI)

	早産			満期産		
	LBW	正常	粗OR (95%CI)	LBW	正常	粗OR (95%CI)
年齢						
20歳未満	5	4	1 (ref)	3	69	1 (ref)
20～29歳	57	32	1.2 (0.3-4.5)	95	1844	0.8 (0.4-1.9)
30～39歳	69	37	1.2 (0.3-4.7)	103	1949	0.9 (0.4-1.9)
40歳以上	6	2	2.0 (0.3-15.4)	7	59	1.9 (0.6-5.8)
		傾向性の検定	P=0.58		傾向性の検定	P=0.52
喫煙歴						
非喫煙	81	53	1 (ref)	144	2581	1 (ref)
妊娠前に禁煙	20	5	2.6 (0.9-7.4)	19	499	0.7 (0.4-1.1)
妊娠を機に禁煙	20	13	1.0 (0.5-2.2)	28	650	0.8 (0.5-1.2)
妊娠中も喫煙	17	4	2.8 (0.9-8.7)	21	236	1.6 (1.0-2.6)
		傾向性の検定	P=0.13		傾向性の検定	P=0.78
妊娠届時の喫煙						
なし	121	71	1 (ref)	191	3730	1 (ref)
あり	17	4	2.5 (0.9-7.7)	21	236	1.7 (1.1-2.8)
家庭での受動喫煙						
なし	48	24	1 (ref)	87	1542	1 (ref)
あり	90	51	0.9 (0.5-1.6)	125	2424	0.9 (0.7-1.2)
妊娠中の飲酒						
なし	128	69	1 (ref)	195	3695	1 (ref)
あり	10	6	0.9 (0.3-2.6)	17	271	1.2 (0.7-2.0)
妊娠中の喫煙と受動喫煙の状況						
喫煙(-)受動喫煙(-)	45	23	1 (ref)	86	1513	1 (ref)
喫煙(-)受動喫煙(+)	76	48	0.9 (0.4-1.5)	105	2217	0.8 (0.6-1.2)
喫煙(+)受動喫煙(-)	3	1	1.5 (0.2-15.6)	1	29	0.6 (0.1-4.5)
喫煙(+)受動喫煙(+)	14	3	2.4 (0.6-9.1)	20	207	1.7 (1.0-2.8)
		傾向性の検定	P=0.95		傾向性の検定	P=0.27
妊娠中の喫煙と飲酒の状況						
喫煙(-)飲酒(-)	113	67	1 (ref)	177	3488	1 (ref)
喫煙(-)飲酒(+)	8	4	1.2 (0.3-4.1)	14	242	1.1 (0.7-2.0)
喫煙(+)飲酒(-)	15	2	4.4 (1.0-20.0)	18	207	1.7 (1.0-2.8)
喫煙(+)飲酒(+)	2	2	0.6 (0.1-4.3)	3	29	2.0 (0.6-6.8)
		傾向性の検定	P=0.19		傾向性の検定	P=0.02

＊ 年齢、喫煙状況、受動喫煙の有無、飲酒の有無で調整、妊娠中の喫煙と受動喫煙の状況については年齢と飲酒、妊娠中の喫煙と飲酒の状況については年齢と受動喫煙の有無で調整しても同様の結果

表5 妊娠を機に禁煙した場合の低出生体重（LBW）、早産に対するオッズ比

	LBW	正常	粗OR (95%CI)	早産	満期産	粗OR (95%CI)
妊娠届時も喫煙継続	38	240	1 (ref)	21	257	1 (ref)
妊娠を機に禁煙	48	663	0.5 (0.3-0.7)	33	678	0.6 (0.3-1.0)

＊ 年齢、受動喫煙の有無、飲酒の有無で調整しても同様の結果

表6 妊娠を機に禁煙をすることに対する関連要因のオッズ比（OR）と95%信頼区間（95%CI）

	禁煙	喫煙	粗OR (95%CI)
年齢			
20歳未満	29	16	1 (ref)
20～29歳	421	165	1.2 (0.7-2.1)
30～39歳	244	88	1.3 (0.7-2.4)
40歳以上	4	5	0.4 (0.1-1.6)
	傾向性の検定	P=0.72	
家庭での受動喫煙			
なし	118	34	1 (ref)
あり	593	244	0.7 (0.5-1.1)
妊娠中の飲酒			
なし	659	242	1 (ref)
あり	52	36	0.5 (0.3-0.8)

＊ 年齢、受動喫煙の有無、飲酒の有無で調整しても同様の結果

厚生労働省科学研究費補助金（がん臨床研究事業）
分担研究報告書

母親の妊娠中の喫煙と児の思春期の肥満の関連性に関するメタアナリシス
A Meta-Analysis of Association between Maternal Smoking during Pregnancy and Offspring Obesity

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研究要旨
最近では欧米から母親の妊娠中における喫煙はその母親から生まれた児が成長した時に肥満になるとの報告が散見されている。すなわち、児の肥満は現在の受動喫煙の結果であるのか母親の妊娠中喫煙の影響であるのか不明点が多かった。そのため過去の論文を調査・収集し、母親の妊娠中喫煙と児の肥満について DerSimonian 法を用いてメタアナリシスを行なった。その結果、PubMed から 444 英文論文のうち 17 論文がこの趣旨に合致し、メタアナリシスの対象とされた。17 論文の全てにおいて母親の妊娠中喫煙と児の肥満の関係で正の相関が得られた。統合オッズ比は 1.64（95%C.I.=1.42-1.90）であった。公開バイアスで調整した結果、調整オッズ比は 1.52（95%C.I.=1.36-1.70）であった。これらの結果から母親の妊娠中喫煙はその母親から生まれた児が 3 歳～33 歳の間に約 1.5 倍肥満になる危険性が高いと結論できた。しかし、母親の妊娠中喫煙をしていたものは分娩後も喫煙を継続しているものが多く、児の肥満の危険因子として断定はできない。

A: 研究目的

As reported by the Centers for Disease Control (CDC) in the United State, obesity and smoking are two major causes of preventable death [1]. Childhood obesity is an increasing problem in Japan as well as the US [2-3]. Obese and overweight children often remain overweight in adulthood and therefore have an increased risk of metabolic syndrome. On the other hand, it is well known that maternal cigarette smoking during pregnancy can caused reduced birth weight and height [4-5]. Low-birth-weight infants often show greater 'catch-up growth' than normal-weight infants, and subsequently become obese in childhood. Recent review articles have suggested that maternal smoking is a significant risk factor for obesity in later life [6-7]. To our knowledge, only one meta-analysis regarding the association of maternal smoking and offspring obesity has been reported, by Oken and colleagues [8], although the results of our meta-analysis study have been reported in part in a Japanese review article as well [9]. In our study, the adjusted odds ratio of maternal smoking during pregnancy on childhood obesity was similar to that reported by Oken and colleagues. However, a further detailed evaluation of the association

between maternal smoking during pregnancy and offspring obesity in the future life should be performed.

We also conducted a meta-analysis that included few more papers reporting the association between maternal smoking during pregnancy and body weight in future offspring.

B: 研究方法

Data source and selection:

We searched the PubMed database for papers published from January 2000 to April 2008 that reported studies of the association between maternal smoking during pregnancy and obesity in offspring (http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed). Studies published before December 1999 were excluded owing to inappropriate study design or insufficient study population. We limited our search to studies published in the English language. Studies were included if they involved human participants with obesity or individuals at risk from obesity. The search strategy and terms that were used to identify studies on maternal smoking during pregnancy and obesity in later life were: "smoking", "pregnancy" and "obesity" (Fig. 1). The terms "childhood", "overweight" and "passive smoking" were subsequently also used to identify studies.

Data extraction and synthesis:

For each study, we collected detailed information on year and country of study, study design, study population, sample size, choice of controls, definition and measurement of tobacco smoking, confounders that were adjusted for, effect sizes and 95% confidence intervals (CIs). For each analysis in which we found no significant heterogeneity, effect estimates were given equal weight to the inverse variance of the study (fixed effects model). For the analyses for which we noted significant heterogeneity, we used a random effects model to assign the weight of each study according to the DerSimonian-Laird method. As above, pooled estimates were calculated using Excel software as described by Masui [10]. To assess the effect of the study quality on the reported effect estimates, we conducted a sensitivity analysis in which we compared pooled effect estimates for groups stratified according to quality-associated study characteristics such as study design (cohort, case-control or cross-sectional), type of control selection (population-based or other), adjustment for important potential confounders, and outcome classification.

We also tested for possible publication bias using Begg's and Egger's tests and by visually inspecting a plot of the natural logarithms of the effect estimates against their standard errors for asymmetry, according to method described by Begg [11]. To adjust for the publication bias, the Trim-Fill algorithm method was used [12]

C: 結果

Using the search terms listed above, we identified 444 papers by screening titles and abstracts. A total of 400 were excluded because after further screening they were judged not to be related to maternal smoking during pregnancy and childhood obesity. Of the remaining 44 articles, the full manuscripts were obtained for detail review. Of these, 9 papers were excluded because they were review

articles, and 18 were excluded owing to the effect size and because CIs of interest were not described or could not be estimated, or there were some flaws in study design. As a result, 17 papers were included in the final analysis [13)-29)].

Study Characteristics:

Table 1 shows the study characteristics reported in the 17 articles selected here (Table 1). The study design consisted of 10 cohort, 2 prospective, 2 cross sectional, 2 longitudinal and 1 retrospective studies. The studies were conducted in seven countries: USA, UK, Australia, Brazil, Germany, Japan and Norway. The year in which the articles were published ranged from 2002 to 2007. Although the timing of smoking during pregnancy (first, second or third trimester) in relation to the study varied, we did not differentiate between these reported exposures because the actual timing of smoking during pregnancy was unknown. The study populations ranged from 252 to 34866 individuals (total of 94997, with a mean of 5588 individuals) and the age at which body weight was assessed ranged from 3 to 33 years after birth. The prevalence of smoking during pregnancy in this population ranged from 7.5% to 51%.

In all 17 studies, possible confounding factors such as socio-economic status, breast feeding and mother's weight were evaluated, as shown in Table 2 (Table 2). Confounders identified as a positive effect in more than two-thirds of the studies included maternal obesity, maternal socio-economic status, whether the child was breast fed, and birth weight. The other possible confounders were not identified as having significant positive effects in all studies.

Result of analysis:

Figure 2 shows the risk of obesity in offspring of the mothers who smoked during pregnancy. Based on 17 studies in this meta-analysis, the children of mothers who smoked during pregnancy had an increased risk of obesity [pooled adjusted odds ratio (OR) 1.64, 95% CI: 1.42–1.90, P for heterogeneity <0.0001]] compared with children of mothers who did not smoke during pregnancy. In this analysis, two studies included individually assessed odds ratios for males and females. All studies found a positive association between maternal smoking during pregnancy and future offspring obesity. A recent study reported by Tomes FS and colleagues in Brazil has shown a weak positive correlation between childhood obesity and maternal smoking during pregnancy. This study did not show data supporting the association of maternal smoking during pregnancy and childhood obesity ≥95% BMI, but did show an association between maternal smoking during and obesity ≥85% BMI plus normal body weight child. Therefore, this paper was excluded from the final meta-analysis. Exclusion of an additional four studies that included fewer than 1000 individuals did not change the pooled estimate (OR: 1.63, 95% CI: 1.39–1.93, P for heterogeneity < 0.0001). Exclusion of three papers in which obesity was defined as more than 85% BMI resulted in a slight increase in the pooled odds ratio (OR: 1.65, 95% CI: 1.40–1.96, P for heterogeneity <0.0001).

Publication bias:

Plotting the natural logarithms of the effect estimates against their standard errors using the methods described by Begg showed

some asymmetry in the funnel plot of small studies, which is indicative of publication bias. The asymmetry of the effect estimates was adjusted using the Trim-Fill algorithm method. According to the Trim-Fill algorithm, seven "missing" studies were imputed to simulate a database without publication bias (Fig. 3). After the adjustment, we found no evidence for substantial publication bias. As a result, the adjusted pooled odds ratio for obesity was 1.52 (95% CI, 1.36–1.70, p< 0.0001).

D: 考察

This meta-analysis shows that maternal smoking during pregnancy is consistently associated with future offspring obesity and overweight. It has been well known that maternal smoking during pregnancy is an important risk factor for low birth weight, and is associated with an average reduction in birth weight of 150 to 300 g. According to Baker's hypothesis (FOAD hypothesis = fetal origin of adult disease hypothesis), adult diseases such as coronary artery disease, diabetes mellitus or hypertension may be due to an imbalance in metabolism or hormones due to fetal malnutrition [30)-31)]. A baby of low birth weight often experiences a rapid 'catch-up' growth phase during infancy and childhood, often then becoming obese or overweight [32)]. Fetal growth is considered to be controlled by the effects of environmental factors on the mother's body rather than through genetic factors [33)]. These environmental factors include the mother's body composition, her nutrient status, food intake during pregnancy, and the transport capacity of the placenta [34)]. However, it is unclear how these factors are affected by maternal smoking. In general, the body weight of an active smoker is less than that of a non-smoker, and often increases by an average of 2 to 3 kg after cessation of smoking [35)]. This phenomenon may involve a similar hormonal mechanism as that of the catch-up growth phase in babies of mothers who smoked during pregnancy.

This meta-analysis shows an increased risk of obesity at a mean age of 9 years in children whose mothers smoked during gestation. Children of high birth weight were also found to be more obese than those of low birth weight [36)]. In all studies analyzed here, babies of mothers who smoked were lighter at birth than babies of non-smokers, which is in agreement with many previous studies. This may indicate that maternal smoking influences childhood obesity independently of its effects on fetal growth. Body size at birth seems to be associated with distribution of body fat rather than with total body mass [37)].

Two possible mechanisms may be considered to explain the development of obesity in offspring of mothers who smoked [38)]. One involves hypothalamic function and the second involves abnormalities in fat cells. Previous studies in rats have shown that gestational starvation of the mother is associated with offspring obesity [39)-40)]. A series of studies in rats found differences in effects of maternal starvation between male and female offspring, and larger retroperitoneal and parametrial fat pads in the offspring rather than increased total body weight. These findings indicate that obesity in the offspring of mothers who were starved during early gestation is due to altered hypothalamic

regulatory mechanisms of energy intake and expenditure rather than to abnormalities of the adipocytes. A similar mechanism may be involved in offspring of mothers who smoked during gestation because nicotine induces maternal starvation or reduced appetite owing to the effects of known chemical mediators in the brain [41]. In addition, fetal exposure to nicotine has been shown to cause abnormal cell proliferation, differentiation and synaptic activity in the brain and the peripheral autonomic pathways [42]. If these explanations regarding with two mechanisms are correct, fetal exposure to nicotine may lead to permanent changes in hypothalamic regulation of food intake and energy expenditure.

In such cohort and retrospective studies, potential confounders that could affect the results should be evaluated. From this meta-analysis, maternal obesity, social status, birth weight and breast-feeding seem to be risk factors for offspring obesity. These confounding factors were assessed in almost all of the 17 studies. Obesity of the parents, and social status were reported to be strong determinants of childhood obesity [43]. Paternal obesity is due to both genetic factors and lifestyle. In 11 of the 17 studies, maternal obesity was identified as a risk factor for later offspring obesity. Maternal age and socio-economic status also seemed to affect the later obesity of children.

Confounders factors affecting each individual child are also important. School type, gestational age, number of siblings, season of birth and year of birth were considered to be risk factors in a few studies. Toschke and Widerøe reported a positive association between watching television and playing video games with offspring obesity [15] [28]. In addition, mothers who are obese or of lower social class tend to have less success in breast-feeding [44]. Early bottle-feeding accelerates the 'catch-up' growth phase of lower birth weight infants during the first years of life, although the details of the mechanism by which this occurs remain unknown [45]. In addition to low birth weight, high birth weight is also a risk factor for obesity in later life. Even if all of these confounders are considered, it is clearly demonstrated that maternal smoking during pregnancy is an independent risk factor for childhood obesity.

On the other hand, it is not well known whether maternal smoking during pregnancy is associated with metabolic syndrome in the opffspring [46]. Obesity is an important component of metabolic syndrome and one of the main etiological factors for insulin resistance and glucose intolerance. In addition, maternal smoking during pregnancy is associated with increased blood pressure in the offspring [47] [48]. Previous studies have shown that adolescents with high levels of urinary cotinine are at increased risk of metabolic syndrome [49] [50]. Metabolic syndrome is more prevalent in active smokers than passive smoker in adolescence. These results indicate that both fetal and postnatal exposure of nicotine may be related to the onset of metabolic syndrome in later life.

E: 結論

Despite heterogeneity in design, measurement, and quantitative effects estimates in the studies included in this

meta-analysis, we found consistent evidence that maternal smoking during pregnancy increases the risk of obesity in offspring. These offspring may then be more likely to develop metabolic syndrome in later life. These long-term effects of maternal smoking provide further incentive not to smoke and additional evidence to discourage smoking in women of reproductive age.

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F: 健康危険情報

特になし。

G: 学会発表

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H：知的財産権の出願・登録状況

特になし

Table 1

No.	type of study	Journal	author	location	year	population	age	adjusted OR	95%CI	95%CI
1	cohort	Brz J Med Biol Res	Tome FS	Brazil	2007	2797	8~10	1.07	0.84	1.37
2	cohort	Obesity	Mizutani T	Japan	2007	1417	5	2.15	1.12	4.11
3	cohort	Int J Obes	Hauang RC	Australia	2007	406	8	1.82	1.05	3.2
4	longitudinal	In J Obes	Dubois L	UK	2006	1550	4.5	1.8	1.2	2.8
5	prospective	Int J Epidemiol	chen A	USA	2006	34866	7	M:1.21	0.96	1.51
								F:1.31	1.06	1.61
6	prosepective	Am J Epidemiol	AlMamun	Australia	2006	3253	14	1.4	1.01	1.94
7	cohort	BMJ	Reilly JJ	UK	2005	5493	7	1.76	1.21	2.52
8	longitudinal	Pediatrics	Salsbery PJ	USA	2005	3022	6~7	1.74	1.32	2.29
9	retorspective	Am L Clin Nutr	Adams AK	USA	2005	252	3	2.16	1.05	4.47
10	cohort	Obes Res	Oken E	USA	2005	746	3	2.2	1.2	3.9
11	cohort	Pediatrics	Whitaker RC	USA	2004	8494	4	1.21	1.01	1.45
12	cross-sect	Int J Obes Relat Metab Disord	Bergmann KE	Germany	2003	918	6	2.3	1.15	4.6
13	cohort	Am J Epidemiol	Toschke AM	Germany	2003	4974	5	2.22	1.33	3.69
14	cohort	Pediatr Perinat Epidemiol	Widerøe M	Norway	2003	5722	5	3.8	2	7.2
15	cohort	Am J Epidemiol	von Kries R	Germany	2002	6483	5-6.9	2.06	1.31	3.23
16	cohort	Int J Epidemiol	Power C	UK	2002	5839	33	M:1.55	1.19	2
								F:1.45	1.13	1.87
17	corss-sect	Eur J pediatr	Toschke AM	Germany	2002	8765	5-6.99	1.92	1.29	2.86

abbreviation: OR=odds ratio, CI= confidence interval, M=male,F=female

Table 2.

No.	author	maternal			child		other main positive factors	
		obesity	age	s.e status	breast feeding	birth weight	maternal	child
1	Tome FS	-	-	-	-	+		shool type
2	Mizutani T	-	-	-	-	-	sleep duration, breakfast	
3	Hauang RC	-	-	-	+	+		
4	Dubois L	+	-	+	-	+	paternal overweight	gestational age
5	chen A	+	-	+	+	+		
6	AlMamun	+	+	+	+	+	diet	
7	Reilly JJ	+	+	+	+	+	parity	sex, number of siblings, season at birth
8	Salsbery PJ	+	+	+	+	+	parity, race	sex, age, birth year, height
9	Adams AK	+	+	+	+	+		
10	Oken E	+	-	-	-	+		
11	Whitaker RC	+	+	+	-	-	race, pregnancy weight	fetal growth, sex, year of birth
12	Bergmann KE	-	-	+	+	-		
13	Toschke AM	+	-	+	+	-	paternal weight	TV/video game, activity, infant weigt gain
14	Widerøe M	-	-	-	-	+		TV/video game, diet in front of TV
15	von Kries R	+	-	+	+	+		physical activity, diet, education
16	Power C	+	-	-	+	+		social class
17	Toschke AM	-	-	+	+	+		

s.e=socio-economic (including education, income and marital status)

Figure 1

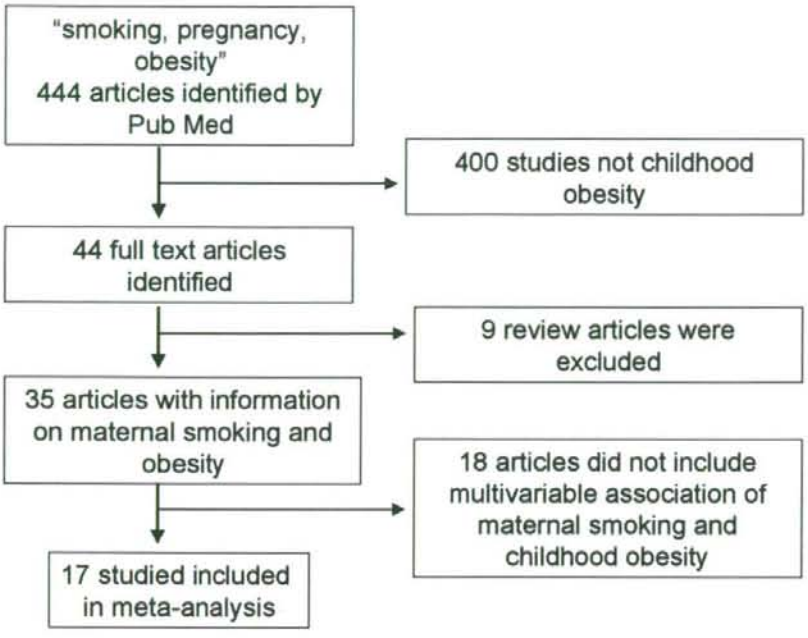

Fig.2

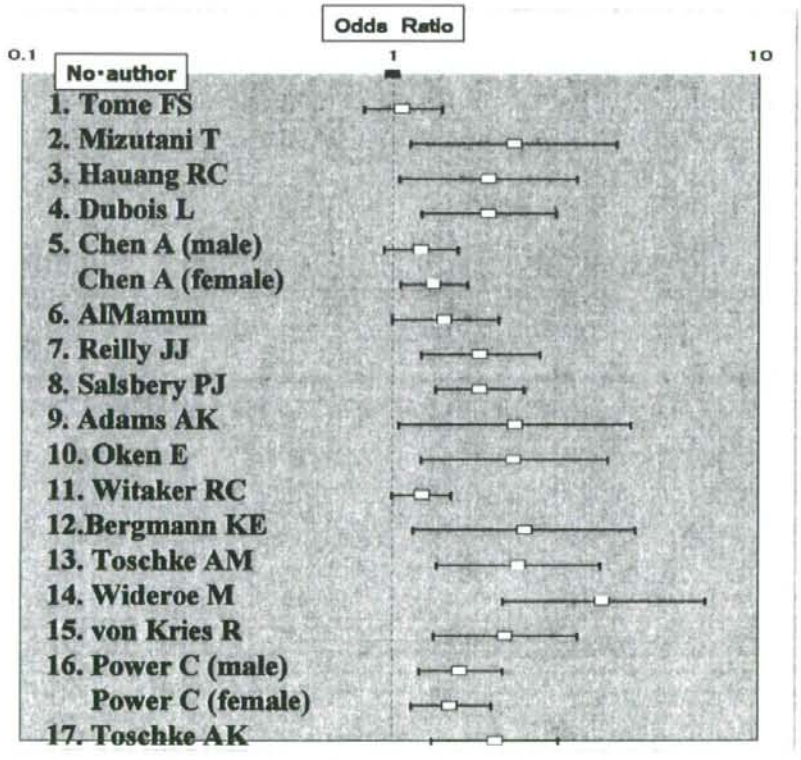

Fig.3

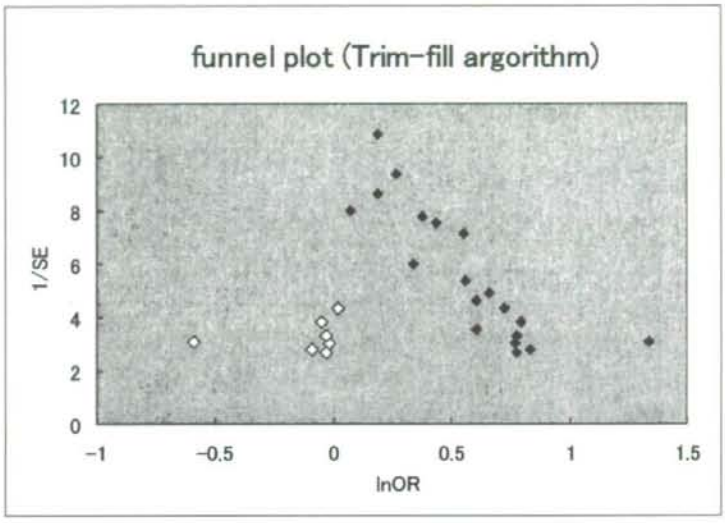

Figure Legend

Fig.1: Chart of data source and selection
Seventeen studies were selected for meta-analysis from 444 papers identified by Pub Med search.

Fig.2: Odds ratio in meta-analysis of association between maternal smoking during pregnancy and childhood obesity.
The open square boxes show odd ratios with 95 % CIs indicated by lines in an individual study.

Fig.3: Funnel plot by Trim-fill argorithm method
Open squares indicate simulated data, closed squares indicate observed date in this study.

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分担研究報告書

未成年者等を対象とした効果的な禁煙支援、受動喫煙防止対策の確立に関する研究
「未成年者・妊産婦への禁煙支援に関するガイドライン作成」

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研究要旨

わが国の未成年喫煙者、妊産婦喫煙者に対する禁煙治療・禁煙支援のガイドラインを作成するために、平成19年度までに喫煙の疫学関連情報、禁煙治療関連、未成年、妊産婦、胎児、周産期をキーワードとして、Medline およびCochrane Central データベースより1995年から2007年の論文3308件を、医学中央雑誌より1991年から2007年の論文710件を検索し、合計4018件の医学論文を抽出し、研究分担者および研究協力者42人がペアを作り選択文献の一次チェックを行い、440件の論文を選択した。平成20年度は、3組の臨床医、疫学者ペアよる二次チェックで151の論文が採択され、三次チェックを経て124件の論文を選択した。この124編の論文に関して構造化抄録を作成し総論的なまとめを作成した。

A．研究目的

わが国の未成年者の喫煙率は、昨今やや低下傾向にあるものの、依然として高値で推移している。たとえば高校3年生の男子では、喫煙経験のある者が37.0%、毎日喫煙する者が11.7%にのぼり、高校3年生の女子では、それぞれ23.4%、3.9%となっている（2005年度厚生労働省研究班調査）。

未成年者は一旦喫煙を始めると、成人に比べて短期間でニコチン依存状態になりやすいため、叱責や謹慎処分等によって禁煙させることは困難なことが多い。そのため、ニコチン代替療法をはじめとする禁煙治療が必要とされることが多いが、わが国においては、未成年者への禁煙治療に関するエビデンスやガイドラインがまだないのが現状である。

また、妊産婦の喫煙は胎児、新生児への悪影響が大きいため、その防止対策が重要であるが、妊婦、授乳婦にはニコチン製剤の使用が認められていないため、禁煙支援が困難なことが多い。

そこで、未成年者や妊産婦への禁煙治療・禁煙支援に関する世界各国の報告からエビデンスを集め、わが国の未成年者、妊産婦に対する禁煙治療・禁煙支援のガイドラインを作成することを目的とする。

B．研究方法

平成19年度までに、未成年（小・中・高・女子・その他など）や、周産期（妊婦・授乳婦・その家族）などごとに、禁煙支援・禁煙治療の具体的な方法と、短期および長期禁煙率についてのエビデンスとその質に関する評価が必要であるというリサーチクエスチョンのもと、Analytic Framework (AF)を作成した（図）。喫煙の疫学関連情報、禁煙治療関連、未成年、妊産婦、胎児、周産期をキ