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Manchester triage system in paediatric emergency care: prospective observational study

M van Veen,[1] Ewout W Steyerberg,[2] Madelon Ruige,[3] Alfred H J van Meurs,[3] Jolt Roukema,[1] Johan van der Lei,[4] Henriette A Moll[1]

EDITORIAL by Maconochie and Dawood

[1]Department of Paediatrics, Erasmus Medical Centre, Sophia Children's Hospital, University Medical Centre Rotterdam, PO Box 2060, 3000 CB Rotterdam, Netherlands
[2]Centre for Medical Decision Making, Public Health, Erasmus Medical Centre, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, Netherlands
[3]Department of Paediatrics, Haga Hospital, Juliana Children's Hospital, PO Box 60605, 2506 LP, Hague, Netherlands
[4]Department of Medical Informatics, Erasmus MC, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, Netherlands
Correspondence to: H A Moll
h.a.moll@erasmusmc.nl

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ABSTRACT

Objective To validate use of the Manchester triage system in paediatric emergency care.

Design Prospective observational study.

Setting Emergency departments of a university hospital and a teaching hospital in the Netherlands, 2006-7.

Participants 17 600 children (aged <16) visiting an emergency department over 13 months (university hospital) and seven months (teaching hospital).

Intervention Nurses triaged 16 735/17 600 patients (95%) using a computerised Manchester triage system, which calculated urgency levels from the selection of discriminators embedded in flowcharts for presenting problems. Nurses over-ruled the urgency level in 1714 (10%) children who were excluded from analysis. Complete data for the reference standard were unavailable in 1467 (9%) children, leaving 13 554 patients for analysis.

Main outcome measures Urgency according to the Manchester triage system compared with a predefined and independently assessed reference standard for five urgency levels. This reference standard was based on a combination of vital signs at presentation, potentially life threatening conditions, diagnostic resources, therapeutic interventions, and follow-up. Sensitivity, specificity, and likelihood ratios for high urgency (immediate and very urgent) and 95% confidence intervals for subgroups based on age, use of flowcharts, and discriminators.

Results The Manchester urgency level agreed with the reference standard in 4582 of 13 554 (34%) children; 7311 (54%) were over-triaged and 1661 (12%) under-triaged. The likelihood ratio was 3.0 (95% confidence interval 2.8 to 3.2) for high urgency and 0.5 (0.4 to 0.5) for low urgency; though the likelihood ratios were lower for those presenting with a medical problem (2.3 (2.2 to 2.5) *v* 12.0 (7.8 to 18.0) for trauma) and in younger children (2.4 (1.9 to 2.9) at 0-2 months *v* 5.4 (4.5 to 6.5) at 8-16 years).

Conclusions The Manchester triage system has moderate validity in paediatric emergency care. It errs on the safe side, with much more over-triage than under-triage compared with an independent reference standard for urgency. Triage of patients with a medical problem or in younger children is particularly difficult.

INTRODUCTION

Emergency departments need systems to prioritise patients.[1] As "subjective" triage by nurses without using a system has low sensitivity and specificity, it is important to develop and evaluate triage systems.[2] The Manchester triage system is a five category triage system based on expert opinion.[3] The validity of this system has been studied in specific subgroups of adults and was shown to be sensitive in identifying seriously ill patients ("immediate" or "very urgent") and for the detection of high risk chest pain.[4 5] One small retrospective study validated the Manchester system in children.[6] We prospectively validated the Manchester triage system for children in paediatric emergency care.

METHODS

Study design—We measured validity by comparing the assigned urgency categories of the Manchester triage system with a predefined independent reference classification of urgency.

Study population—The study included children aged under 16 attending the emergency departments of two large inner city hospitals. At the emergency department of the Erasmus MC-Sophia Children's hospital (Rotterdam), the Manchester triage system has been in use since August 2005. We included in our study children who attended from January 2006 to January 2007. At the emergency department of the Haga Hospital-Juliana Children's Hospital (The Hague), the Manchester triage system was implemented in 2003 and we included children attending from January to July 2006.

Manchester triage system—Emergency department nurses performed a short assessment and triaged patients using the Manchester triage system. The system is an algorithm based on flowcharts and consists of 52 flowchart diagrams (49 suitable for children) that are specific for the patient's presenting problem. The flowcharts show six key discriminators (life threat, pain, haemorrhage, acuteness of onset, level of consciousness, and temperature) as well as specific discriminators relevant to the presenting problem (see bmj.com). If the nurse does not agree with the assigned urgency category, the system can be over-ruled. We used a computerised version that uses the official Dutch

translation of the flowcharts and discriminators of the first edition (1996).[3 7]

Data collection—Patients' characteristics, selected flowcharts, discriminators, and urgency category were recorded in the computerised triage system. Nurses or physicians recorded data concerning vital signs, diagnosis, diagnostic and therapeutic interventions, admission to hospital, and follow-up on structured electronic or paper emergency department forms. Trained medical students gathered and entered the data on a separate database, independent of the triage outcome.

Reference standard—Before the study we defined a reference standard based on literature and expert opinion.[6] It consists of a combination of vital signs, diagnosis, diagnostic and therapeutic interventions, and admission to hospital and follow-up. The reference standard classifies patients to one of five categories: immediate, very urgent, urgent, standard, and non-urgent (see bmj.com). We defined the reference standard for each patient independent of urgency according to the Manchester system and based on a computerised application of the classification matrix.

Data analysis—We validated the Manchester triage system by comparing the assigned urgency category with the category assigned with the reference standard. Patients categorised as immediate and very urgent were considered as high urgency and those classified as urgent, standard, or non-urgent as low urgency. Age was divided into subgroups (<3 months, 3-11 months, 1-3 years, 4-7 years, ≥8 years). The trauma flowcharts included limb problems, head injury, major trauma, falls, wounds, injury to the trunk, and assault; all other flowcharts were considered to be medical ones. We calculated the percentage over-triage and under-triage for patients triaged with commonly used discriminators (fever and recent problem). Secondly, we assessed validity for patients with fever divided into age groups.

RESULTS

Nurses applied the Manchester triage system in 16 735 of 17 600 children (95%) who attended the emergency department. Nurses over-ruled the urgency category in 1714 (10%); 735 of whom (43%) had originally been triaged with the Manchester triage system as very urgent compared with 21% of the patients triaged with the Manchester system overall. Of these children in whom the classification of very urgent was over-ruled, 720 (98%) were downgraded by at least one category.

In 1467 (9%) children, complete data were unavailable for the reference standard, leaving 13 554 for analysis. Median age was 3.4 years (interquartile range 1.2-8.0) and 5740 (42%) were female.

Classification of urgency according to the Manchester triage system and the reference standard agreed in 4582 (34%) children. More children were classified as very urgent with the Manchester system than with the reference standard (2897 (21%) *v* 277 (2%)). Considerably fewer children were classified as non-urgent with the Manchester system than with the reference standard (112 (1%) *v* 2927 (22%)) (figure).

Manchester triage system	Reference standard					
	Immediate	Very urgent	Urgent	Standard	Non-urgent	Total
Immediate	70	22	80	26	7	205
Very urgent	233	119	1079	942	524	2897
Urgent	79	83	1729	2278	731	4900
Standard	48	53	1096	2621	1622	5440
Non-urgent	0	0	7	62	43	112
Total	430	277	3991	5929	2927	13 554

>1 category over-triaged; 1 category over-triaged; Correct triage; 1 category under-triaged; >1 category under-triaged

Manchester triage system compared with reference standard

Validity

The Manchester urgency level agreed with the reference standard in 34% (n=4582). Some 5001 (37%) children were over-triaged by one category and 2310 (17%) by more than one category. With the Manchester system 1474 (11%) were under-triaged by one category and 187 (1%) by more than one category. Agreement with the reference standard was particularly low for the very urgent category, with only 119 of 2897 (4%) classified correctly; 2545 (88%) were over-triaged and 233 (8%) patients were under-triaged (figure).

Overall, the Manchester system had a sensitivity of 63% (95% confidence interval 59% to 66%) and a specificity of 79% (79% to 80%) for identifying high urgency patients. The likelihood ratio was 3.0 (2.8 to 3.2) for a high urgency result and 0.5 (0.4 to 0.5) for a low urgency result. The Manchester system was less sensitive for very young patients (0-2 months) (sensitivity 50%) while specificity was better for older children (>4 years). The validity of the Manchester system was lower for children presenting with a medical problem, of whom 61% were over-triaged and 10% under-triaged compared with 32% and 19%, respectively, for patients presenting with trauma (table).

The validity of the Manchester system in children triaged with medical flowcharts differed considerably between the top 10 medical flowcharts, with poor validity for the worried parent flowchart (19% correct triage; likelihood ratio+ 0.9, likelihood ratio− 1.0) (see bmj.com for full results).

DISCUSSION

Principal findings and interpretation

The Manchester triage system has an overall moderate validity compared with an independent reference standard. The agreement with the reference standard was 34%, with over-triage in 54% and under-triage in 12% (mostly by one category). The sensitivity for high urgency was 63%, implying that 37% of the patients who actually needed to be seen within 10 minutes were not categorised as that urgent. The specificity was 79%, implying that 21% low urgency patients were categorised too high. In particular, patients in the very urgent category were over-triaged.

Sensitivity, specificity, and likelihood ratios with 95% confidence intervals for different subgroups on age, presenting problem, and medical Manchester triage system flowcharts

Subgroup	No of patients	High urgency %*		Sensitivity†	Specificity†	LR+	LR−
		Manchester	Reference				
Overall	13 554	23.0	5.2	63 (59 to 66)	79 (79 to 80)	3.0 (2.8 to 3.2)	0.47 (0.43 to 0.52)
Age:							
0-2 months	1033	25.0	14	50 (42 to 58)	79 (76 to 82)	2.4 (1.9 to 2.9)	0.63 (0.54 to 0.74)
3-11 months	1965	33.0	6.6	65 (56 to 73)	69 (67 to 72)	2.1 (1.9 to 2.5)	0.50 (0.39 to 0.63)
1-3 years	4427	27.0	5.7	67 (61 to 73)	75 (74 to 77)	2.7 (2.5 to 3.0)	0.43 (0.36 to 0.52)
4-7 years	2760	20.0	3.0	66 (55 to 76)	81 (80 to 83)	3.6 (3.0 to 4.2)	0.41 (0.31 to 0.56)
8-16 years	3369	13.0	2.8	64 (53 to 73)	88 (87 to 89)	5.4 (4.5 to 6.5)	0.41 (0.31 to 0.54)
Presenting problem‡:							
Medical	9774	30.0	7.0	64 (60 to 67)	72 (71 to 73)	2.3 (2.2 to 2.5)	0.50 (0.45 to 0.55)
Trauma	3332	4.9	0.6	55 (32 to 76)	95 (95 to 96)	12.0 (7.8 to 18.0)	0.47 (0.29 to 0.77)
Medical flowcharts‡:							
General	1703	34.0	7.9	63 (55 to 71)	68 (66 to 71)	2.0 (1.7 to 2.3)	0.53 (0.43 to 0.67)
Shortness of breath in children	1520	50.0	12	78 (72 to 84)	54 (51 to 56)	1.7 (1.5 to 1.9)	0.40 (0.30 to 0.53)
Worried parent	1457	45.0	6.0	42 (32 to 54)	55 (52 to 58)	0.9 (0.7 to 1.2)	1.0 (0.87 to 1.2)
Abdominal pain in children	839	5.6	0.6	40 (7 to 83)	95 (93 to 96)	7.4 (2.4 to 22)	0.63 (0.31 to 1.3)
Vomiting	808	4.2	5.2	14 (6 to 29)	96 (95 to 97)	3.9 (1.7 to 8.9)	0.89 (0.79 to 1.0)
Rashes	409	23.0	1.5	83 (36 to 99)	78 (74 to 82)	3.8 (2.6 to 5.7)	0.21 (0.036 to 1.3)
Diarrhoea	330	6.1	5.5	44 (22 to 69)	96 (93 to 98)	11.6 (5.4 to 25)	0.58 (0.38 to 0.87)
Fits	303	60.0	17	83 (70 to 91)	45 (39 to 51)	1.5 (1.3 to 1.8)	0.38 (0.21 to 0.69)
Ear problems	281	17.0	1.1	33 (2 to 87)	83 (78 to 87)	2.0 (0.4 to 10.0)	0.80 (0.36 to 1.8)
Urinary problems	237	28.0	2.1	80 (30 to 90)	73 (67 to 79)	3.0 (1.8 to 4.9)	0.27 (0.047 to 1.6)

LR+=likelihood ratio for high urgency triage test result, LR−=likelihood ratio for low urgency triage test result.
*Immediate and very urgent category.
†Sensitivity=high urgency (immediate or very urgent) according to Manchester system/high urgency according to reference standard. Specificity=low urgency (urgent, standard, or non-urgent) according to Manchester system/low urgency according to reference standard.
‡Flowcharts available for 13 106 (97%). Selection of the 10 most used medical flowcharts accounts for 80% (7887/9774) of patients' medical flowcharts.

The validity was lower in children presenting with medical problems compared with those presenting with trauma. Any modifications should therefore be particularly targeted for medical problems. Specific discriminators can be considered for their role in the triage system. For example, children aged <3 months with fever are at greater risk for a serious bacterial infection, whereas children aged ≥3 months with fever might be allocated to a lower urgency category.[8] Such a modification was incorporated in the emergency severity index (ESI) (version 4), a commonly used triage system in Europe and the United States.[9] A modification of the paediatric CTAS, a Canadian triage system, in which febrile children aged 6-36 months with no signs of toxicity could be triaged to a lower urgency level (from level 3 to 4), has been shown to be safe.[10]

The validity of triage systems depends on the extent to which the system predicts urgency and on the accuracy of the nurse who applies the system (inter-rater agreement). We previously found a good inter-rater agreement of the Manchester system in children at our two emergency departments (M van Veen, personal communication). We can therefore assume that the validity of the Manchester system compared with the reference standard is mostly due to the predictive value of the system to assess urgency.

Limitations

The goal of seeing patients in the order of their category of urgency is to decrease morbidity and mortality.[11] Mortality, however, is rare in children presenting at the emergency department and thus cannot be evaluated. Also, differences in morbidity are hard to relate to shorter or longer waiting times.

Our reference standard was based on literature and expert opinion, which admittedly reflects a low grade of evidence.[12] Furthermore, the reference standard is based on a combination of patients' characteristics collected at the time of presentation and at the end of the consultation in the emergency department. Characteristics gathered at the end of the consultation might be less suitable to define urgency because of possible changes in the patient's condition over time. Another limitation is that nurses over-ruled the Manchester system urgency category in 10% of the patients. Inclusion of the 10% over-ruled patients would probably have lowered the validity of the Manchester system.

Comparison with other studies

Other triage systems studied in paediatric emergency care show a high validity (Soterion rapid triage system),[13] predicted admission (paediatric Canadian emergency department triage and acuity scale),[14] and predicted resource use and length of stay (emergency severity index).[15] Although all of these studies used outcome measures to correlate with urgency or to identify the high urgency patients (intensive care admission), they did not define a "reference standard" for urgency (see bmj.com).

The use of an independent reference standard for each patient will allow for further development and

WHAT IS ALREADY KNOWN ON THIS TOPIC

The consensus based five level Manchester triage system is sensitive in identifying seriously ill adults and those with high risk chest pain

Although the system is widely applied, a large prospective study to evaluate the validity on its use in children is lacking

WHAT THIS STUDY ADDS

In paediatric emergency care the Manchester triage system shows moderate validity but errs on the safe side as the proportion of over-triage is much larger than under-triage

Triage of children with a medical problem or young patients (aged <1 year) was particularly difficult and the system should be specifically modified to cope with such cases

evaluation of modifications to the Manchester triage system. When applying the Manchester triage system in paediatric emergency care, users should be aware of its moderate validity. We need to consider and study modifications for specific flowcharts, discriminators, and age groups for which the triage system has a low validity.

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Influence of general practice opening hours on delay in seeking medical attention after transient ischaemic attack (TIA) and minor stroke: prospective population based study

Daniel S Lasserson,[1] Arvind Chandratheva,[2] Matthew F Giles,[2] David Mant,[1] Peter M Rothwell[2]

EDITORIAL by Jiwa and Knight

[1]Department of Primary Health Care, University of Oxford, Headington, Oxford OX3 7LF
[2]Department of Clinical Neurology, Stroke Prevention Research Unit, University of Oxford, John Radcliffe Hospital, Headington, Oxford
Correspondence to: D Lasserson
daniel.lasserson@dphpc.ox.ac.uk

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ABSTRACT

Objective To assess the influence of general practice opening hours on healthcare seeking behaviour after transient ischaemic attack (TIA) and minor stroke and feasibility of clinical assessment within 24 hours of symptom onset.
Design Population based prospective incidence study (Oxford vascular study).
Setting Nine general practices in Oxfordshire.
Participants 91 000 patients followed from 1 April 2002 to 31 March 2006.
Main outcome measures Events that occurred overnight and at weekends (out of hours) and events that occurred during surgery hours.
Results Among 359 patients with TIA and 434 with minor stroke, the median (interquartile range) time to call a general practitioner after an event during surgery hours was 4.0 (1.0-45.5) hours, and 68% of patients with events during surgery hours called within 24 hours of onset of symptoms. Median (interquartile range) time to call a general practitioner after events out of hours was 24.8 (9.0-54.5) hours for patients who waited to contact their registered practice compared with 1.0 (0.3-2.6) hour in those who used an emergency general practitioner service (P<0.001). In patients with events out of hours who waited to see their own general practitioner, seeking attention within 24 hours was considerably less likely for events at weekends than weekdays (odds ratio 0.10, 95% confidence interval 0.05 to 0.21): 70% with events Monday to Friday, 33% on Sundays, and none on Saturdays. Thirteen patients who had events out of hours and did not seek emergency care had a recurrent stroke before they sought medical attention. A primary care centre open 8 am-8 pm seven days a week would have offered cover to 73 patients who waited until surgery hours to call their general practitioner, reducing median delay from 50.1 hours to 4.0 hours in that group and increasing those calling within 24 hours from 34% to 68%.
Conclusions General practitioners' opening hours influence patients' healthcare seeking behaviour after TIA and minor stroke. Current opening hours can increase delay in assessment. Improved access to primary care and

public education about the need for emergency care are required if the relevant targets in the national stroke strategy are to be met.

INTRODUCTION

Recent studies have shown that prompt assessment and treatment after TIA and minor stroke can substantially reduce the risk of early recurrent stroke.[1 2] The Department of Health's national stroke strategy[3] and guidance from the National Institute for Health and Clinical Excellence (NICE)[4] state that high risk patients must be seen within 24 hours after onset of symptoms.

A new general medical services (GMS) contract for primary care was introduced in April 2004, whereby responsibility for patients' care by general practitioners was reduced to office hours (8 am-6 30 pm, Monday to Friday). Recent proposed changes to the contract[5] could improve access to primary care, with general practices opening in the evenings and at weekends. Little research has been published on the association between general practitioners' opening hours and patients' healthcare seeking behaviour, particularly in emergencies. We examined the relation between practice opening hours and delay to access healthcare in a population based study of all TIA and minor strokes.

METHODS

The Oxford vascular study (OXVASC) is a population based prospective study of all acute vascular events in 91 000 patients registered at nine general practices and is fully described elsewhere.[6] We included in this analysis all patients with a first incident or recurrent definite or probable TIA or minor stroke during the period 1 April 2002 to 31 March 2006. A study neurologist saw patients with TIA and stroke soon after the event, if possible within 24 hours. A consultant neurologist reviewed all cases. TIA was defined as a focal neurological deficit lasting <24 hours and minor stroke defined as persisting deficit with National Institute of Health (NIH) stroke scale[7] score <5 at the time of assessment.

We recorded the time of onset of the presenting event, time to calling healthcare services, and the choice of healthcare provider, along with clinical and sociodemographic data. In a minority of patients we derived timings from ambulance sheets, general practitioner referral letters, and consultation notes. If these data were uncertain and patients recalled the approximate time of day we imputed the modal call time for that part of the day.

We divided the week into surgery hours, defined as the times when contact can be made with a patient's registered general practice (Monday to Friday 8 am-6 30 pm) and out of hours (times outside this range). Before April 2004, Saturday morning (9 am to 12 noon) was also classified as during surgery hours.

We calculated median call times and analysed differences between groups. Scatter plots were drawn of delay in calling a general practitioner against time of event to show patterns of behaviour. We assessed the potential impact of increasing primary care opening hours to 8 am-8 pm daily on reducing delay and estimated the potential impact on stroke prevention.

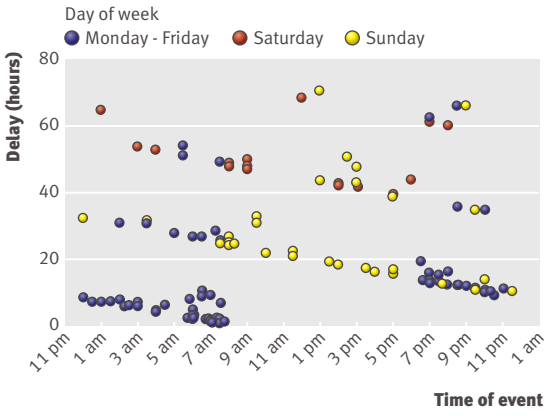

Fig 1 | Delay in calling regular general practitioner after TIA or minor stroke occurring out of hours

RESULTS

Of 359 patients with TIA and 434 with minor stroke, we excluded from the analysis 25 patients outside the study area at the time of their event. Mean (SD) age was 74.5 (11.8) years; 290 patients (38%) were aged ≥80; and 53% were women. Data on call delay were available in 721 patients (94%).

Most patients (73%) first sought attention from a general practitioner, with a small increase after introduction of the new GP contract in April 2004, in the numbers using accident and emergency departments (A&E) in patients with TIA (18% *v* 26%, P=0.055) but no change in those with minor stroke (23% *v* 24%, P=0.717). Some 387 patients had events during surgery hours, and 354 had events out of hours. For all patients in the out of hours setting, there was a non-significant increase in the proportion attending A&E after the introduction of the new contract (27% *v* 33%, P=0.216). Only 10 patients called NHS Direct, of whom seven were advised to be seen routinely in primary care and three to attend A&E.

The median (interquartile range) time to call a general practitioner was significantly greater in the out of hours setting compared with during surgery hours: 12.0 (2.1-43.0) *v* 4.0 (1.0-45.5) hours, P=0.006. Median (interquartile range) time to call for medical attention via A&E was not significantly different between events occurring out of hours and events during surgery hours: 0.91 (0.33-2.68) *v* 0.73 (0.38-2.01) hours, P=0.751.

Of 244 patients who had events out of hours and were seen first in primary care, 175 (72%) waited to call their registered practice, although after April 2004 there was a significant increase in the percentage of patients who used an on-call general practitioner service (20% *v* 32%, P=0.034). Median (interquartile range) time to call a general practitioner was significantly higher in those who did not, compared with those who did, use an on-call general practitioner service (24.8 (9.0-54.5) hours *v* 1.0 (0.3-2.6) hours, P<0.001).

Patients who correctly recognised the cause of their symptoms as TIA or stroke did not significantly differ in choice of provider or in median delay to call for

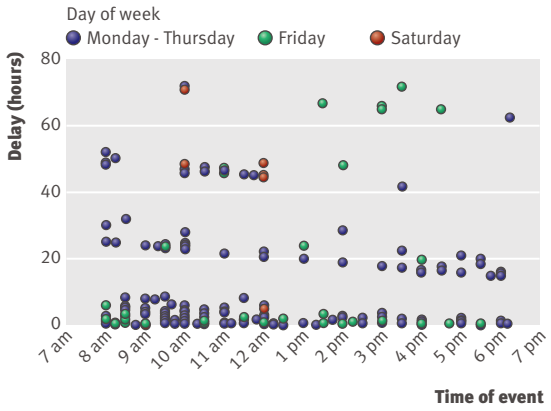

Fig 2 | **Delay in calling general practitioner after TIA or minor stroke occurring during surgery hours**

attention compared with patients who did not think they had stroke-like symptoms.

In patients with out of hours events, most (70%) of those who waited to call their GP did so within two hours of their registered practice opening. Figure 1 shows the delay to calling the registered practice after an out of hours event for the first 72 hours after events. In patients with events out of hours who waited until practice opening hours to call, 70% with events on Monday to Friday rang within 24 hours of symptom onset, but this proportion fell to 33% on Sundays and none on Saturdays. The odds ratio of calling within 24 hours after weekend events compared with weekday events was 0.10 (95% confidence interval 0.05 to 0.21).

The plot of delay against time of event for patients with events in hours (fig 2) also shows clustering of delay. Some patients with events during surgery opening hours also seek care in the days after the event, with gaps on the scatter plot corresponding with times when the practice is closed. Around two thirds (68%) of patients with events during surgery hours called within 24 hours.

We analysed the possible effects of extended opening hours—for example, from 8 am to 8 pm seven days a week. Seventy three patients who waited until office hours to call had events at times during the extra period of cover that such centres would offer. The median (IQR) delay to calling primary care in this subgroup was 50.1 (22.5-118.0) hours, and 34% called within 24 hours of symptoms. If these patients behaved like the patients with events during surgery hours then delay would be reduced to 4.0 (1.0-45.5) hours and the percentage calling within 24 hours would increase to 68%.

Increasing opening hours could reduce recurrent stroke. Thirty seven patients had a recurrent stroke after an initial TIA or minor stroke for which they did not seek medical attention. Of these, 13 had an initial event out of hours and five had an event at times during the period of extra cover that a centre open 8 am to 8 pm daily would offer.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Urgent treatment after TIA and minor stroke can prevent recurrent disabling or fatal stroke

The Department of Health's national stroke strategy calls for investigation of high risk patients with TIA within 24 hours after onset of symptoms

Most patients with TIA or minor stroke seek health care via their general practice rather than via emergency services

WHAT THIS STUDY ADDS

After TIA or minor stroke, only 1% of patients contact NHS Direct for advice

Most patients with TIA and minor stroke out of hours delay seeking health care until their registered general practice is open, causing long delays, particularly at weekends

Patients with out of hours events are much less likely to call their GP within 24 hours after symptoms at weekends than overnight on weekdays

DISCUSSION

Most patients chose to seek help from their own practice after TIA or minor stroke. Reduction in general practice opening hours after April 2004 did not significantly increase the use of A&E outside office hours, but small improvements were seen in the use of emergency primary care services. The few patients who used NHS Direct had variable guidance, with most advised to attend primary care routinely. Among patients seen in primary care, considerable delays in calling for medical attention were seen after events out of hours compared with events during surgery hours, and striking patterns of delay (figs 2 and 3) resulted from patients waiting for the earliest opportunity to contact their registered practice. A small number of patients who had an event out of hours delayed seeking care and went on to have a recurrent stroke before their practice reopened.

Strength and weaknesses

We did not have exact data on timings of events and on delays to seeking medical attention in all patients because of factors such as dysphasia and cognitive impairment. Reliable data, however, were available in 94% of patients, of whom over 37% were aged ≥80, and so there is unlikely to have been substantial inclusion bias. TIAs and minor strokes before major disabling strokes might have been under-reported as some patients with major stroke are unable to give an account of previous TIA or minor stroke.

Recognition of stroke-like symptoms was not associated with shorter delays to call for medical attention or with use of emergency services. Similar findings in other studies[8-10] suggest a need for more public education, although awareness campaigns have not always had a predictable effect.[11]

Increasing access to primary care might have a variable impact on TIA and stroke outcomes. If general practitioners had access to urgent secondary care investigation and treatment with effects similar to those in the EXPRESS study,[1] our data suggest that one stroke per 91 000 population per year could be prevented (that is, over 500 strokes annually in England alone). However longer delays from onset of TIA or stroke symptom to emergency hospital admission have consistently been associated with involving primary care rather than simply calling for an ambulance.[12-15] Increased general practice opening hours requires secondary care capacity in terms of

access to investigations and specialist assessment if the full benefits of stroke prevention are to be seen.

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Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis

M Arbyn,[1,2] M Kyrgiou,[3] C Simoens,[1] A O Raifu,[1] G Koliopoulos,[4] P Martin-Hirsch,[3] W Prendiville,[5] E Paraskevaidis[4]

EDITORIAL by Jakobsson and Bruinsma
RESEARCH, p 803

[1]Scientific Institute of Public Health, Brussels, Belgium
[2]European Cooperation on Development and Implementation of Cancer Screening and Prevention Guidelines, IARC, Lyon, France
[3]Department of Obstetrics and Gynaecology, Central Lancashire Teaching Hospitals, Preston, Lancashire
[4]Department of Obstetrics and Gynaecology, University Hospital of Ioannina, Ioannina, Greece
[5]Department of Obstetrics and Gynaecology, Coombe Women's Hospital, Dublin, Ireland
Correspondence to: M Arbyn
Marc.Arbyn@iph.fgov.be

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ABSTRACT

Objective To assess the relative risk of perinatal mortality, severe preterm delivery, and low birth weight associated with previous treatment for precursors of cervical cancer.

Data sources Medline and Embase citation tracking from January 1960 to December 2007.

Selection criteria Eligible studies had data on severe pregnancy outcomes for women with and without previous treatment for cervical intraepithelial neoplasia. Considered outcomes were perinatal mortality, severe preterm delivery (‹32/34 weeks), extreme preterm delivery (‹28/30 weeks), and low birth weight (‹2000 g, ‹1500 g, and ‹1000 g). Excisional and ablative treatment procedures were distinguished.

Results One prospective cohort and 19 retrospective studies were retrieved. Cold knife conisation was associated with a significantly increased risk of perinatal mortality (relative risk 2.87, 95% confidence interval 1.42 to 5.81) and a significantly higher risk of severe preterm delivery (2.78, 1.72 to 4.51), extreme preterm delivery (5.33, 1.63 to 17.40), and low birth weight of ‹2000 g (2.86, 1.37 to 5.97). Laser conisation, described in only one study, was also followed by a significantly increased chance of low birth weight of ‹2000 g and ‹1500 g. Large loop excision of the transformation zone and ablative treatment with cryotherapy or laser were not associated with a significantly increased risk of serious adverse pregnancy outcomes. Ablation by radical diathermy was associated with a significantly higher frequency of perinatal mortality, severe and extreme preterm delivery, and low birth weight below 2000 g or 1500 g.

Conclusions In the treatment of cervical intraepithelial neoplasia, cold knife conisation and probably both laser conisation and radical diathermy are associated with an increased risk of subsequent perinatal mortality and other serious pregnancy outcomes, unlike laser ablation and cryotherapy. Large loop excision of the transformation zone cannot be considered as completely free of adverse outcomes.

INTRODUCTION

Adverse obstetric outcomes have been reported after cold knife conisation for treatment of cervical intraepithelial neoplasia.[1 2 w1-w3] Divergent conclusions have been drawn for other excisional treatment procedures,[3 4 w4-w7] whereas ablative methods such as laser ablation or cryotherapy, which destroy cervical tissue, are believed to be free of adverse obstetric risk.[5 w8 w9]

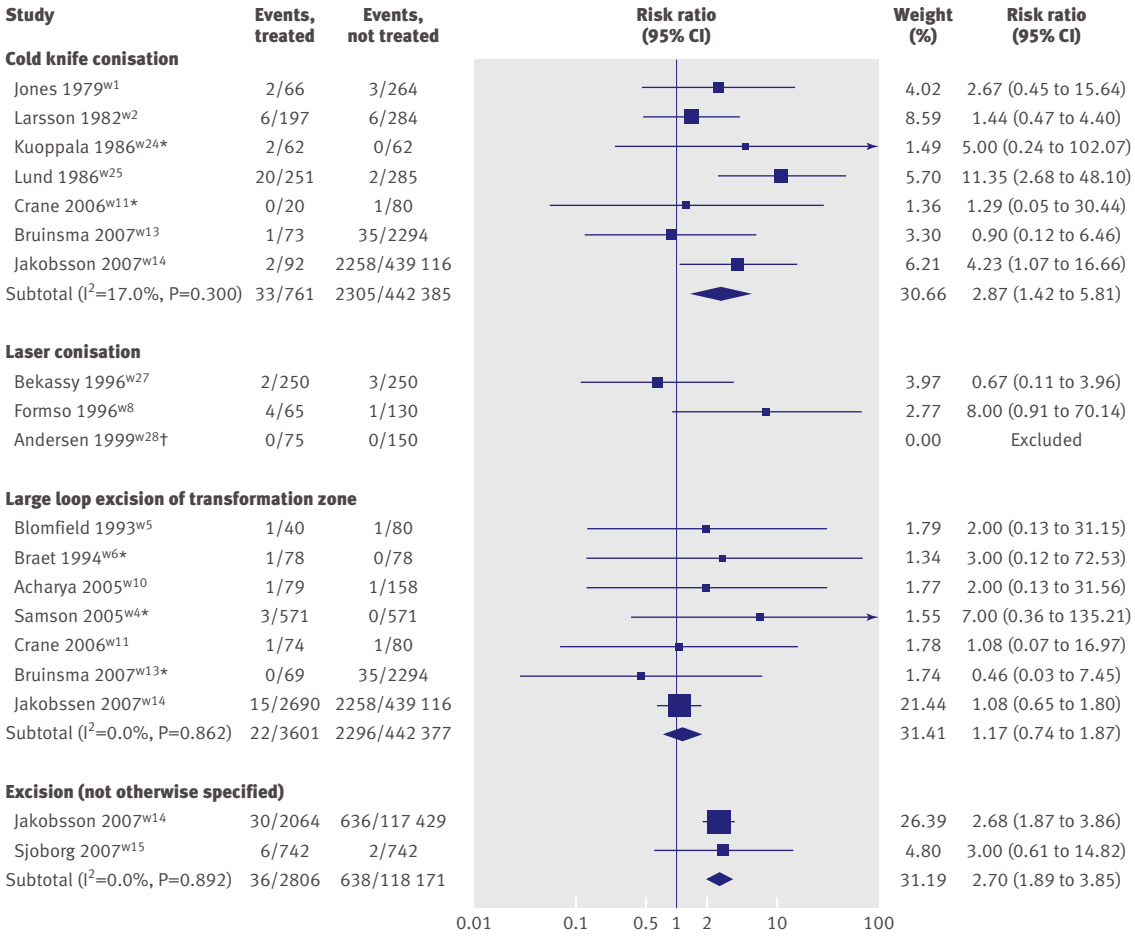
In a meta-analysis, Kyrgiou et al evaluated pregnancy outcomes in women previously treated for cervical intraepithelial neoplasia.[6] They found an increased risk for preterm delivery among women treated with large loop excision of the transformation zone or cold knife conisation compared with untreated women. A significantly increased risk was also noted for low birth weight after both these procedures, for premature rupture of membranes after large loop excision, and for caesarean delivery after cold knife conisation. Preterm delivery, low birth weight, and premature rupture were more common after laser conisation but the differences were insignificant. Laser ablation was not associated with adverse obstetric outcomes.

The publication of Kyrgiou et al's meta-analysis has been followed by two small studies[w10 w11] and four involving large populations.[w12-w15] This new information, together with data received directly from authors, now allows a new more comprehensive systematic review and meta-analysis with a focus on more serious outcomes.

METHODS

Studies and interventions, inclusion and exclusion criteria

We included studies with data on severe obstetric or neonatal outcomes in women treated for cervical intraepithelial neoplasia and in a control group of untreated women. Two types of treatment were considered: excisional procedures (cold knife conisation, large loop excision of the transformation zone, and laser conisation) and ablative procedures (laser ablation, cryotherapy, and diathermy).



Meta-analysis of relative risk of perinatal mortality associated with excisional treatment for cervical intraepithelial neoplasia. *0.5 added to each cell of 2×2 contingency table because no cases were found in one of comparison groups. †Excluded because no events in both groups. In subtotals relative risks are pooled by treatment procedure (only computed in absence of significant heterogeneity between studies)

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Outcome measures

The severe adverse obstetric or neonatal events were perinatal mortality, severe (at less than 32/34 weeks' gestation) and extreme (<28/30 weeks) preterm delivery, and severe low birth weight (<2000 g, <1500 g, and <1000 g).

Retrieval of studies and data extraction

Eligible studies published between 1960 and November 2007 were retrieved through a PubMed-Medline and Embase search. We hand searched references of retrieved articles and proceedings of relevant conferences to identify any more articles. There was no language restriction. Three authors verified inclusion and exclusion criteria independently and reached consensus in case of discordance. We contacted authors to obtain data where necessary.

Table 1 | Meta-analysis of studies comparing outcome of severe preterm delivery (<32/34 weeks) according to treatment for cervical intraepithelial neoplasia

	No (%) of women		
	Treated	Not treated	Relative risk (95% CI)
Excisional treatment			
Cold knife conisation			
Ludviksson, 1982[w3]* (<34 weeks)	3/83 (3.6)	0/79 (0.0)	6.67 (0.35 to 127.03)
Crane, 2006[w11]* (<34 weeks)	0/21 (0.0)	1/81 (1.2)	1.24 (0.05 to 29.46)
Klaritsch, 2006[w12] (<34 weeks)	7/76 (9.2)	871/29 686 (2.9)	3.14 (1.55 to 6.38)
Bruinsma, 2007[w13] (<32 weeks)	4/71 (5.6)	43/2181 (2.0)	2.86 (1.05 to 7.74)
Jakobsson, 2007[w14] (<32 weeks)	4/92 (4.3)	9542/469 713 (2.0)	2.14 (0.82 to 5.58)
Pooled	18/343 (4.6)	10 457/501 740 (1.6)	2.78 (1.72 to 4.51), P=0.911 (I^2=0.0%)
Laser conisation			
Sagot, 1995[w29]* (<32 weeks)	1/53 (1.9)	0/59 (0.0)	3.33 (0.73 to 16.77)
Large loop excision of transformation zone			
Samson, 2005[w4] (<34 weeks)	7/558 (1.3)	2/558 (0.4)	3.50 (0.73 to 16.77)
Crane, 2006[w11] (<34 weeks)	3/75 (4.0)	1/81 (1.2)	3.24 (0.34 to 30.47)
Bruinsma, 2007[w13] (<32 weeks)	1/69 (1.4)	43/2181 (2.0)	0.74 (0.10 to 5.26)
Jakobsson, 2007[w14] (<32 weeks)	40/2690 (1.5)	9542/469 713 (2.0)	0.73 (0.54 to 1.00)
Pooled	51/3392 (2.0)	9588/472 533 (1.4)	1.20 (0.50 to 2.89), P=0.156 (I^2=42.7%)
Excision (not otherwise specified)			
El-Bastawissi, 1999[w30] (<34 weeks)	44/974 (4.5)	169/7975 (2.1)	2.13 (1.54 to 2.95)
Sjoborg, 2007[w15] (<32 weeks)	25/742 (3.4)	6/742 (0.8)	4.17 (1.72 to 10.10)
Pooled	69/1716 (4.0)	175/8717 (1.5)	2.63 (1.41 to 4.89), P=0.154 (I^2=50.7%)
Ablative treatment			
Cryotherapy			
Crane, 2006[w11] (<34 weeks)	1/36 (2.8)	1/81 (1.2)	2.25 (0.14 to 34.98)
Jakobsson, 2007[w14] (<32 weeks)	11/644 (1.7)	9542/469 713 (2.0)	0.84 (0.47 to 1.51)
Pooled	12/680 (2.2)	9543/469 794 (1.6)	0.88 (0.49 to 1.56), P=0.492 (I^2=0.0%)
Diathermy			
Bruinsma, 2007[w13] (<32 weeks)	38/760 (5.0)	43/2181 (2.0)	2.54 (1.65 to 3.89)
Laser ablation			
Bruinsma, 2007[w13] (<32 weeks)	23/1005 (2.3)	43/2181 (2.0)	1.16 (0.70 to 1.92)
Jakobsson, 2007[w14] (<32 weeks)	8/1349 (0.6)	9542/469 713 (2.0)	0.29 (0.15 to 0.58)

*Studies with continuity correction *k*=0.05.

Statistical analysis

We calculated the relative risks for each adverse pregnancy outcome in the treated versus untreated women. We used a random effects model to pool relative risks. We assessed heterogeneity between studies and evaluated the percentage of total variation across studies caused by heterogeneity. The relative risks for severe adverse pregnancy outcomes were not pooled when there was evidence of significant heterogeneity between studies (P<0.10).

As severe obstetric outcomes are rare the pooled relative risks can be unstable and influenced by the chosen continuity correction and pooling method. To test robustness, we applied several alternative methods for pooling.

Finally, we pooled the absolute frequency of adverse outcomes after treatment and in the cumulated control populations and derived the number needed to treat to harm (NNTH) as the reciprocal of the risk difference. This reflects the number of women who need to undergo treatment to result in one adverse obstetric event because of the treatment.

RESULTS

Inclusion of studies—We identified 15 studies that fulfilled the eligibility criteria and provided data on perinatal mortality.[w1 w2 w4-w6 w8 w10 w11 w13-w15 w24-w28] The number of studies that evaluated the other severe pregnancy outcomes was smaller: 11 studies reported on preterm delivery before 34 weeks of gestation[w13 w4 w7 w11-w15 w25 w29 w30] and five studies on birth weight of <2000 g.[w8 w9 w13 w15 w25] Two studies involved only women treated for carcinoma in situ,[w25 w30] while the rest included varying degrees of cervical intraepithelial neoplasia. We found eight new studies that were not included in the meta-analysis of Kyrgiou et al.[6 w10-w15 w25 w28]

Study characteristics—A total of 21 studies were included. See bmj.com for table of study characteristics. Women were treated by cold knife conisation in nine studies,[w1-w3 w11-w14 w24 w25] large loop excision of the transformation zone in eight studies,[w4-w7 w10 w11 w13 w14] and laser conisation in four studies.[w8 w27-w29] In three studies, women were treated with excision biopsies without further clarification of the specific treatment.[w14 w15 w30] Pregnancy outcomes after ablative treatment were less often described.

Perinatal mortality—The figure shows the variation in relative risk for perinatal mortality associated with excision of cervical intraepithelial neoplasia. The risk of perinatal mortality was significantly increased in women treated with cold knife conisation. The risk associated with laser conisation was heterogeneous and therefore not pooled. One study in which mini-conisation was used showed no increase[w27] and another showed a substantial increase but did not reach significance.[w8] Women treated with large loop excision of the transformation zone had a pooled relative risk of perinatal mortality of 1.17 (0.74 to 1.87). Women whose cervical intraepithelial neoplasia was treated by excision without specification of the procedure showed

a significantly increased risk of perinatal mortality. Although the risk associated with ablative treatment was not increased, there was a tendency for increased perinatal mortality in women treated with diathermy (1.54, 0.84 to 2.82). See bmj.com.

Severe and extreme preterm delivery—Severe preterm delivery (gestation <32/34 weeks) was significantly more common after cold knife conisation (table 1). One case of preterm delivery was observed in women who became pregnant after treatment with laser conisation, whereas none was observed in pregnancies before treatment.[w29] Treatment with large loop excision of the transformation zone was not associated with an increased risk of severe preterm delivery and showed heterogeneous results regarding extreme preterm delivery. In two studies that used cold knife conisation or another excisional procedure without distinction by procedure, relative risks for severe[w15 w30] and extreme preterm delivery[w15] were significantly increased. See table on bmj.com for results of extreme preterm delivery (<28/30 weeks). Laser ablation or cryotherapy was not associated with higher rates of severe or extreme preterm delivery. In one study diathermy resulted in significantly increased rates of both severe (2.54, 1.65 to 3.89) and extreme (2.15, 1.11 to 4.18) preterm delivery.[w13]

Severe and extreme low birth weight—Three studies that evaluated cold knife conisation, laser conisation, or excision with laser conisation/large loop excision showed a significantly increased risk for birth weights of <1500 g.[w8 w13 w15] In two Norwegian studies cold knife conisation and excisional treatment (with laser conisation/large loop excision) were associated with extreme low birth weight (<1000 g).[w15 w25] Laser ablation was not associated with increased risks for very low birth weight, while a significantly higher rate of birth weights of <2000 g and <1500 g was observed in women treated with diathermy.[w13]

Robustness of pooled relative risks—All models and continuity corrections resulted in similar pooled

Table 2 | Meta-analysis of adverse obstetric outcomes in treated women (by procedure) and in non-treated control populations, with pooled frequency of obstetric events and number needed to treat to observe harm (NNTH)

Outcome and procedure	No of studies	No of events	No (%, 95% CI)	NNTH
Perinatal mortality				
Cold knife conisation	6	13	510 (2.2, 1.5 to 2.9)	71
Laser conisation	3	6	390 (2.3, 0.8 to 3.9)	67
Large loop excision	7	22	3601 (1.0, 1.0 to 1.1)	500
Radical diathermy	1	18	773 (2.3, 2.3 to 2.3)	67
Control	14	6325	1 055 673 (0.8, 0.6 to 1.0)	—
Preterm delivery <32/34 weeks				
Cold knife conisation	5	18	343 (4.6, 3.0 to 6.1)	30
Laser conisation	1	1	53 (1.9, 1.8 to 2.0)	167
Large loop excision	4	51	3392 (2.0, 1.8 to 2.2)	143
Radical diathermy	1	38	760 (5.0, 5.0 to 5.0)	27
Control	9	10 634	500 440 (1.3, 0.9 to 1.7)	—
Preterm delivery <28/30 weeks				
Cold knife conisation	3	6	246 (2.5, 1.3 to 3.7)	53
Large loop excision	3	14	2908 (1.0, 0.0 to 2.7)	250
Radical diathermy	1	15	760 (2.0, 2.0 to 2.0)	71
Control	5	3962	473 013 (0.6, 0.1 to 1.0)	—
Low birth weight <2000 g				
Cold knife conisation	1	7	73 (9.6, 2.8 to 16.3)	16
Laser conisation	1	7	65 (10.8, 3.2 to 18.3)	14
Large loop excision	1	3	69 (4.3, <0.0 to 9.2)	106
Radical diathermy	1	53	773 (6.9, 5.1 to 8.6)	29
Control	4	96	2939 (3.4, 3.0 to 3.8)	—
Low birth weight <1500 g				
Cold knife conisation	1	3	73 (4.1, <0.0 to 8.7)	36
Laser conisation	1	5	65 (7.7, 1.2 to 14.2)	16
Large loop excision	1	1	69 (1.4, <0.0 to 4.3)	670
Radical diathermy	1	35	773 (4.5, 3.1 to 6.0)	31
Control	4	47	3209 (1.3, 0.5 to 2.2)	—
Low birth weight <1000 g				
Cold knife conisation	1	2	73 (2.7, <0.0 to 6.5)	54
Large loop excision	1	0	69 (0.0, 0.0 to 0.0)	—
Radical diathermy	1	11	773 (1.4, 0.6 to 2.3)	191
Control	2	42	3035 (0.9, <0.0 to 2.6)	—

estimates and showed a non-significant increased risk of perinatal mortality for large loop excision, underlying the robustness of the meta-analysis (see bmj.com). Similar pooled relative risks for perinatal mortality were also obtained for the other excisional methods.

Obstetric harm after treatment—We pooled the absolute frequency of adverse obstetric outcomes after treatment and in the cumulated control populations and derived the number needed to treat to observe obstetric harm in one treated woman (NNTH) (table 2).

DISCUSSION

The current meta-analysis shows that, among all the excisional methods used in the treatment of cervical intraepithelial neoplasia, cold knife conisation is consistently associated with serious adverse pregnancy outcomes. The earlier meta-analysis of Kyrgiou et al revealed an increased risk for preterm delivery and low birth weight associated with large loop excision.[6] Our meta-analysis now includes several new studies and reviews. We found that large loop excision did not significantly affect the more serious adverse obstetric events. Both meta-analyses corroborate the conclusion that ablation with laser has no effects on obstetric outcomes. The recent study by Jakobsson et al reported similar findings for cryotherapy.[w14] We found that laser conisation increased the risk of perinatal mortality and very low birthweight infants—when we excluded from the analysis one study that modified the technique and excised a substantially smaller amount of tissue.[w27] Bruinsma et al reported that radical diathermy was associated with perinatal mortality, extreme preterm delivery, and severe low birth weight, which was of the same order of magnitude as seen with treatment with cold knife conisation.[w13]

Biological mechanisms

Removal or destruction of part of the cervix might compromise its function, leading to lack of mechanical support in a future pregnancy and subsequent premature rupture of membranes and preterm delivery. The proportion of the total cervical volume or endocervical canal removed might be more important than the actual depth of excision. On average the knife excises more tissue than the loop, while loop excisions might vary considerably from superficial and low volume to deep and large volume cones. The studies included in this meta-analysis presented wide variations in the loop sizes used and consequently the cone volume removed, which probably explains the non-significant pooled effect of loop excision on perinatal mortality. Tissue is destroyed by laser ablation and cryotherapy at a rather steady depth which might explain the lack of any adverse effects. In loop excision the excision is usually deeper at the centre than at the edges. Mechanisms might also be mediated by the different quality of collagen in the regenerated cervix[7] or other immunological factors, such as impairment of the defence mechanisms and alteration of the cervicovaginal flora.[8]

Alternative explanations

As comparison groups were non-randomised, effects and effect sizes cannot be attributed with certainty to the treatment.[9] Women with cervical intraepithelial neoplasia are known to have demographic, behavioural, and sexual characteristics that increase their risk of adverse obstetric outcomes. See bmj.com for further discussion of the potential inflation of the relative risks due to the choice of a reference group.

Women who require treatment for cervical intraepithelial neoplasia are selected for one treatment or another on the basis of several characteristics that are likely to affect the chance of subsequent morphological damage to the cervix. So there is already an inherent bias towards removal of larger areas of the cervix with excisional treatments, which one would expect to be associated with a worse obstetric outcome in the future.

Implications for practice

Recent studies have shown that treated women are still at higher risk than the general population for developing subsequent invasive cervical cancer, even many years after treatment,[10-12] and some gynaecologists warn that less aggressive treatments might increase this risk.[13] Testing for human papillomavirus can help with the follow-up of women after treatment for cervical intraepithelial neoplasia.

Conclusions

All excisional procedures used to treat cervical intraepithelial neoplasia seem to be associated with adverse obstetric morbidity, but among these, only cold knife conisation is associated with a significantly increased rate of severe outcomes. The risk of serious obstetric morbidity associated with large loop excision of the transformation zone was not significantly different from unity, though we cannot excluded the possibility of any increased risk. Loop excisions that remove large amounts of cervical tissue probably have the same effect as knife cone biopsies. Gynaecologists should tailor the management of young woman to minimise possible adverse obstetric outcomes at the same time as minimising residual disease rates.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Women treated for cervical intraepithelial neoplasia with excisional procedures have an increased risk of preterm delivery and low birth weight in future pregnancies

WHAT THIS STUDY ADDS

Women who become pregnant after treatment for cervical intraepithelial neoplasia with cold knife conisation and radical diathermy have an increased risk of perinatal mortality, severe preterm delivery, and extreme low birthweight infants

The commonly used loop excision is associated with mild but not with severe obstetric morbidity

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Pregnancy outcome in women before and after cervical conisation: population based cohort study

Susanne Albrechtsen,[1,2] Svein Rasmussen,[2,3] Steinar Thoresen,[4] Lorentz M Irgens,[2] Ole Erik Iversen[3]

EDITORIAL by Jakobsson and Bruinsma
RESEARCH, p 798

[1]Department of Obstetrics and Gynecology, Haukeland University Hospital, Institute of Clinical Medicine, University of Bergen, 5021 Bergen, Norway
[2]Medical Birth Registry of Norway, Locus of Registry Based Epidemiology, Department of Public Health and Primary Health Care, University of Bergen and the Norwegian Institute of Public Health, Norway
[3]Institute of Clinical Medicine, University of Bergen, Bergen, Norway
[4]Cancer Registry of Norway, Oslo, Section for Pathology, Gade Institute, University of Bergen, Norway
Correspondence to: S Albrechtsen
Susanne.Albrechtsen@Helse-Bergen.no

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ABSTRACT

Objectives To examine the consequences of cervical conisation in terms of adverse outcome in subsequent pregnancies.

Design Population based cohort study.

Data sources Data on cervical conisation derived from the Cancer Registry of Norway and on pregnancy outcome from the Medical Birth Registry of Norway, 1967-2003. 15 108 births occurred in women who had previously undergone cervical conisation and 57 136 who subsequently underwent cervical conisation. In the same period there were 2 164 006 births to women who had not undergone relevant treatment (control).

Results The proportion of preterm delivery was 17.2% in women who gave birth after cervical conisation versus 6.7% in women who gave birth before cervical conisation and 6.2% in women who had not undergone cervical conisation. The relative risk of a late abortion (<24 weeks' gestation) was 4.0 (95% confidence interval 3.3 to 4.8) in women who gave birth after cervical conisation compared with no cervical conisation. The relative risk of delivery was 4.4 (3.8 to 5.0) at 24-27 weeks, 3.4 (3.1 to 3.7) at 28-32 weeks, and 2.5 (2.4 to 2.6) at 33-36 weeks. The relative risk of preterm delivery declined during the study period and especially of delivery before 28 weeks' gestation.

Conclusion Cervical conisation influences outcome in subsequent pregnancies in terms of an increased risk of preterm delivery, especially in the early gestational age groups in which the clinical significance is highest. A careful clinical approach should be taken in the selection of women for cervical conisation and in the clinical care of pregnancies after a cervical conisation.

INTRODUCTION

Concern has been raised about the consequences of cervical conisation for cervical intraepithelial neoplasia and subsequent adverse pregnancy outcome. With some techniques, such as laser conisation and large loop methods, complications have been reported as less common.[1] Most studies, however, have been case control studies or were small, and randomised trials have not been performed. A recent meta-analysis showed a significantly increased risk of preterm delivery, low birth weight, and premature rupture of membranes,[1] but conclusions were based mostly on small numbers in the subgroups. With limited information on the effect of confounding factors, the question remains whether adverse outcomes are related to characteristics of women rather than to the treatment itself.

In Norway, we linked data from the medical birth registry and the cancer registry to perform a national

registry based cohort study with a large sample size. We assessed effects of cervical conisation on gestational age at delivery and birth weight. We also clarified whether the effects were related to the cervical conisation itself or to other factors. During the observation period methods of treatment changed and we wanted to assess secular trends.

METHODS

Exposure

Since 1953, the cancer registry has collected information on all cancer diagnoses as well as premalignant lesions, including intraepithelial neoplasia with staging. The method used—knife, laser, or large loop conisation—could not be identified in the individual woman. Until 1980, all treatment was knife conisation. Since 1985, laser based methods have been used to an increasing extent, and loop electrosurgical excision of the cervix was introduced in 1990-5. We included in the exposed group all women aged less than 45 at the time of cervical conisation.

Outcome

Established in 1967, the birth registry comprises compulsory notification of all live births and stillbirths in Norway from 16 completed weeks of gestation. The notification form includes demographic variables and data on maternal health, reproductive history, complications during pregnancy and delivery, and neonatal outcome.

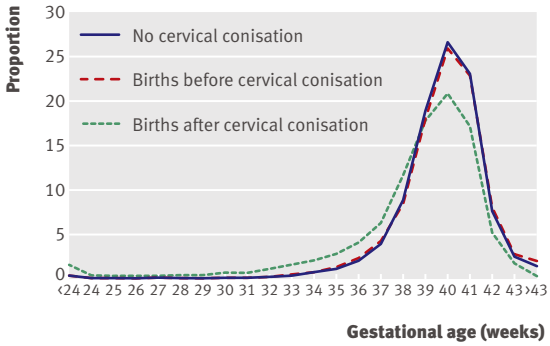
Calculation of gestational age was based on the first day of the last menstrual period. The proportion of women with missing data on gestational age was 5.3%, while data on birth weight were almost complete. All fetuses delivered at <24 weeks' gestation or with birth weight <500 g were classed as late abortion. Fetuses delivered at 24-36 weeks' gestation or with birth weight 500-2499 g were classed as preterm delivery.

We categorised women with a cervical conisation according to whether they had been treated before or after the delivery; most (99.7%) were treated before the start of the index pregnancy. To control for confounding factors we followed two reference cohorts with respect to preterm birth: women who had never had cervical conisation (non-exposed) and women who underwent cervical conisation after delivery.

The present study included births from 1967 to 2003. See bmj.com for table of birth related characteristics. The national identification number allowed linkage with the Central Population Registry and the Cause of Death Registry, ensuring complete ascertainment of all births as well as perinatal deaths.

Statistics

We used relative risk to estimate associations of preterm birth with cervical conisation and adjusted odds ratios, obtained from logistic regression, to calculate approximate adjusted relative risks. The population attributable risk percentage (PAR%) was calculated and refers to the percentage of cases attributable to the cervical conisation. We compared z scores of birth weight in women with a conisation before and after pregnancy or not. See bmj.com.



Births before and after cervical conisation or with no cervical conisation by gestational age, Norway 1967-2003

RESULTS

From 1967 to 2003, 0.7% of the births in the population studied occurred in women who had undergone a cervical conisation before the index pregnancy and 2.6% after. Births after a cervical conisation were more common in older women and with higher birth orders. The proportion of preterm birth (delivery before 37 weeks' gestation) was 17.2% (95% confidence interval 16.6% to 17.8%) in women who gave birth after cervical conisation, 6.7% (6.5% to 6.9%) in women who gave birth before cervical conisation, and 6.2% (6.2% to 6.3%) in women who did not have conisation.

The relative risk of premature delivery in women after a cervical conisation compared with women who did not have cervical conisation increased with decreasing gestational age (table). Also, the risk of late abortion was higher after a cervical conisation. The relative risk decreased slightly after adjustment for maternal age and birth order. The same pattern was observed according to birth weight.

Births in women without cervical conisation and with conisation after delivery had similar distribution according to gestational age, whereas delivery at lower gestational ages was more common in women with cervical conisation (figure). Birth weight in women who gave birth after conisation was lower than in those who had not had conisation. The relative risk of a preterm birth, however, was lower when compared with women with a conisation after delivery.

Infants born to women who had a conisation after delivery were lighter than those born to women without a conisation. In women with no cervical conisation, z scores were on average 0.004 (95% confidence interval 0.002 to 0.005) compared with −0.04 (−0.058 to −0.023) in births after a conisation (data not presented). The lowest z score −0.135 (−0.144 to −0.127) was found in births before a conisation.

During the study period, the excess risk of a preterm delivery in women who underwent cervical conisation decreased, particularly the risk of delivery before 28 weeks. In women aged under 25 at the time of treatment, preterm delivery was no more common

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Numbers and proportions of preterm deliveries with relative risks (95% confidence intervals) in births of women with cervical conisation and no cervical conisation by gestational age in Norway, 1967-2003

Gestational age (weeks)	Births after cervical conisation	Births before cervical conisation	No cervical conisation	Births after *v* births before cervical conisation			Births after cervical conisation *v* no cervical conisation	
				RR (95% CI)	Adjusted*	Adjusted†	RR (95% CI)	Adjusted*
Late abortion	226 (1.5)	209 (0.4)	8501 (0.4)	4.0 (3.3 to 4.8)	3.2 (2.6 to 3.8)	3.2 (2.6 to 3.9)	4.0 (3.3 to 4.8)	3.3 (2.9 to 3.7)
24-27	234 (1.5)	263 (0.5)	7757 (0.4)	3.3 (2.8 to 4.0)	3.3 (2.7 to 3.9)	3.0 (2.5 to 3.7)	4.4 (3.8 to 5.0)	4.3 (3.8 to 4.9)
28-32	535 (3.5)	614 (1.1)	22 945 (1.1)	3.3 (3.0 to 3.7)	3.2 (2.9 to 3.6)	3.0 (2.6 to 3.4)	3.4 (3.1 to 3.7)	3.4 (3.1 to 3.7)
33-36	1599 (10.6)	2724 (4.8)	95 764 (4.4)	2.3 (2.2 to 2.4)	2.2 (2.0 to 2.3)	2.2 (2.0 to 2.3)	2.5 (2.4 to 2.6)	2.4 (2.3 to 2.5)

*Adjusted for birth order (1 *v* >1) and maternal age at delivery.
†Adjusted for birth order (1 *v* >1) and maternal age at treatment.

than in older women. The population attributable risk percentage of preterm delivery attributable to cervical conisation before 28, 33, and 37 weeks of gestation was 2.0%, 1.7%, and 1.2%, respectively.

DISCUSSION

In this cohort study, based on 15 108 births to women who had undergone cervical conisation, we found an increased risk of preterm delivery after a cervical conisation because of intraepithelial neoplasia. The excess risk was highest for late abortion and for preterm delivery before 33 weeks, in agreement with a cohort study from Finland.[2] In previous studies on pregnancy outcome after a cervical conisation, the small numbers of cases have hampered the ability to detect significant differences between gestational age groups.[3-5]

The population attributable risk percentage of preterm birth because of cervical conisation was not high. Women who have had cervical conisation might benefit from closer surveillance during pregnancy. Also, optimised surgical treatment of the cervix to avoid or reduce cervical damage might be beneficial.

Strengths and weaknesses

Information bias was low in our study, which included all births in Norway. The exposure, cervical conisation, was clearly defined. Complete follow-up of all exposed women represents another strength. The two reference cohorts enabled us to control for confounding factors that otherwise could be difficult to account for. Smoking is a potential confounding variable, and relevant data were not available in the registries. In the present study, births in women who later underwent cervical conisation virtually had the same distribution of gestational age as births in women who never had cervical conisation, though with birth weight shifted to the left, consistent with different smoking habits. Several studies have used birth weight as an outcome variable.[1467] Our results indicate that the effect of cervical conisation could be overestimated if birth weight is used as an outcome variable, possibly because of confounding by smoking.

The time trend described could be explained by the fact that over the period studied, smaller amounts of cervical tissue were removed as new methods of conisation were introduced. The time trend was not explained by a trend in the general population towards fewer preterm births as the opposite has been observed.[8]

In the study period, the mean maternal age at delivery increased in all birth orders and women had fewer births.[8] The influence of birth order and maternal age on the risk of preterm birth was rather limited. Because of the increasing mean maternal age at delivery, a higher number of pregnant women would have had a previous cervical conisation. The study underscores the need for a careful clinical approach to women with a previous cervical conisation when they become pregnant.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Evidence from smaller studies suggests a significant increased risk of preterm delivery and low birth weight after cervical conisation

WHAT THIS STUDY ADDS

Cervical conisation increases the risk of preterm delivery, especially in the early gestational age groups, in which the clinical significance is highest

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