Do early symptoms and vital signs distinguish serious bacterial infection vs. self-limiting illness in primary care & paediatric assessment units?

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Each child seen by GP 3-4 times per year (x2 in < 4 yr) (Saxena 1999).

•40% for infections and respiratory disorders (Saxena, BMJ 1999. Eskerud, Fam Pract 1992)

•97-99% acute paediatric infections managed in primary care

•Over-referral of children overwhelms hospital paediatrics

•1% of infections in primary care are serious – of these pneumonia is most common (Van den Bruel 2006)

•50% children with meningococcal disease missed at 1st visit to Dr (Thompson & Ninis, Lancet 2006; Riordan BMJ 1996)

Serious infection = “needle in a haystack”

Symptoms predicting meningococcal disease in primary care

- GPs see few cases in their lifetime, most in hospital
- Limited primary care studies
  - Qualitative studies of GPs (Granier BMJ 1998. Brennan BJGP 2003)
    - Intuition, classical features often lacking
  - Clinical features reported by parents prior to hospital admission in 448 children with meningococcal disease
    - Children present with non-specific features
    - Classic features meningism uncommon (especially in infants) & relatively late
    - Pallor, cold extremities, leg pain early “red flag” features (Thompson & Ninis, Lancet 2006)

Vital signs

NICE Feverish child guideline (2007):
*"measure temperature, heart rate, respiratory rate, capillary refill…**routine** assessment of child with fever"*

Vital signs

For vital signs to be useful in primary care 3 essential criteria must be fulfilled:

	Temperature	Heart rate	Respiratory rate
Measurement accurate and reliable	+/-	+/-	+/-
Normal range known (& effects of interactions)	+	??	++
Predictive value	?	??	++

Aims

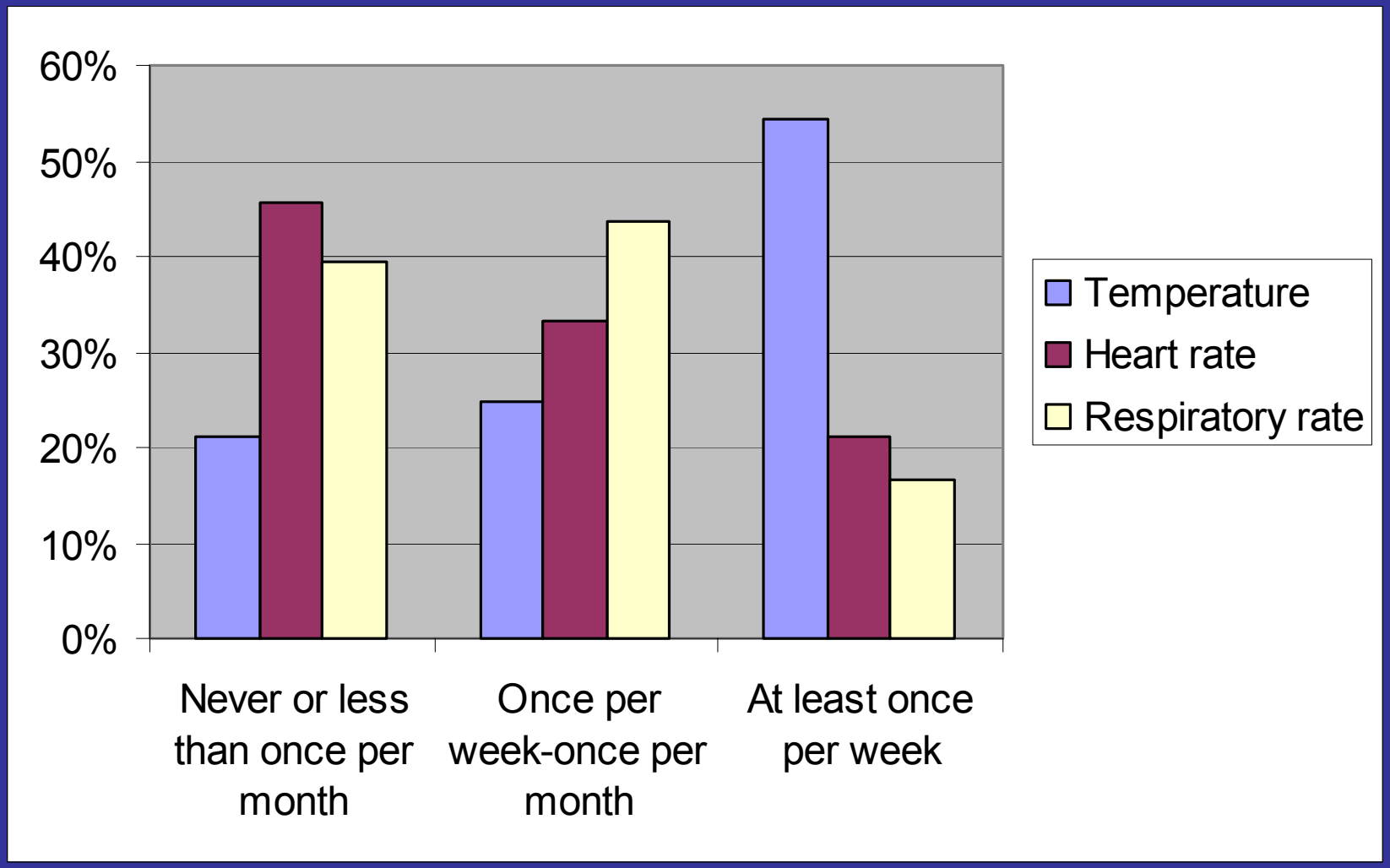
1) How do GPs assess children with acute infection?
2) Which presenting symptoms and vital signs predict SBI in a paediatric assessment unit?
3) Can temperature and age adjusted heart rate be used to predict SBI?

How do GPs assess pre-school children with acute infection in primary care?

(Thompson et al, BJGP under review)

- Postal survey of clinical techniques and vital signs used by GPs to assess pre-school children.
- 162 GPs in Oxfordshire (response rate 77%)

Frequency of measuring vital signs



Methods used to measure vital signs

- Heart rate
  - 88% auscultation, 28% palpate pulse, 8% use pulse oximeter
- Respiratory rate
  - 92% count rate, 91% auscultation, 19% use pulse oximeter
- Temperature
  - 86% aural thermometer, 48% touch
- Capillary refill time
  - Measured by 53%

Most useful features of "global" or overall severity of illness

Rank	Clinical feature	GPs rating as useful * *	
		n	%
1	Activity or behaviour (alertness, social interaction, interest in surroundings)	148	92
2	Skin colour (pallid, mottled, blotchy, cyanosed)	108	67
3	Temperature	103	64
4	Respiratory rate	85	53
5	Seeking specific focus of infection	83	52
6	Level of hydration	62	38
7	Peripheral circulation (capillary refill, peripheral perfusion, cold extremities)	62	38
8	Pulse rate	60	37
9	Body tone or handling	44	27
10	Feeding or appetite	18	11

Utility of vital signs in assessing respiratory status

Rank	Clinical feature	GPs rating as useful **	
		n	%
1	Work of breathing	140	86.4
2	Respiratory rate	114	70.4
3	Skin colour (i.e. pallor or cyanosis)	64	39.5
4	Activity or behaviour	42	25.9
5	Auscultation of chest	30	18.5
6	Pulse rate	15	9.3
7	Oxygen saturation	13	8.0
8	Presence of stridor	11	6.8
9	Temperature	7	4.3

Conclusions

- Basis of GP assessment of pre-school children with acute infection (still) involves assessment of behaviour, skin colour, work of breathing, hydration

- Vital signs infrequently measured
  - Seen as potentially useful
  - Measurement methods likely inaccurate
  - Knowledge of thresholds highly variable

Prospective cohort study of children presenting with acute infection to paediatric assessment unit in Coventry

University Hospitals Coventry and Warwickshire NHS trust

Department of Primary Health Care
University of Oxford

THE UNIVERSITY OF WARWICK

Aims

- Determine diagnostic value of presenting symptoms and vital signs for distinguishing serious bacterial infection (SBI) vs. minor infection in children attending a paediatric assessment unit

Methods

- Presenting symptoms
  - Parental questionnaire asking about 22 symptoms
- Vital signs
  - Axillary temperature, O_2 saturations, heart rate (using pulse oximeter), respiratory rate (clinical count)
- Investigations
  - Based on usual standard of care
- Usual clinical management & final diagnoses assigned by Consultant Paediatrician

Description of overall cohort (N = 700)

- Median age 37.5 months
- 54% male
- Ethnicity: 73% white, 12% Asian
- Referral
  - 51% referred by GPs
  - 28% self-referrals
  - 17% 999 calls
- 55% admitted
- Tests done:
  - Urine culture 21%
  - FBC 52%
  - Blood cultures 32%

Final diagnoses

Minor infection (n=339)	URTI , viral gastroenteritis, uncomplicated UTI, bronchiolitis, viral illness etc
Serious bacterial infection (n=108)	pneumonia (CXR confirmed) 67 appendicitis (pathology confirmed) 22 meningococcal 7 (2 clinical, 5 microbiol) mastoiditis 3 other bacteraemia 3 (S.typhi, pneumo, E.coli) meningitis 2 other 4
Intermediate infection (n=205)	viral illness needing hospital care 90, UTI with systemic symptoms 30, URTI with febrile seizure 26, cellulitis needing IV abx 21 LRTI diagnosed clinically 14, other 24
Not infection (n=48)	

Presenting symptoms

	Serious bacterial infection (n=93)	Minor infection (n=304)	Chi-square P-value	Unadjusted Odds Ratio (95%CI)
Fever	79 (85%)	228 (75%)	0.04	1.9 (1.01-3.5)
General aches	20 (21%)	36 (12%)	0.02	2.0 (1.1-3.7)
Drowsy	56 (60%)	137 (45%)	0.01	1.8 (1.2-3.0)
Confusion (>2 yr only)	12/68 (18%)	14/177 (8%)	0.03	2.5 (1.1-5.7)
Decreased appetite	61 (66%)	155 (51%)	0.01	1.8 (1.1-3.0)
Cough	61 (66%)	140 (46%)	0.001	2.2 (1.4-3.6)
Breathing difficulty	34 (37%)	77 (25%)	0.04	1.7 (1.01-2.8)
Pallor	58 (62%)	83 (27%)	<0.001	4.4 (2.7-7.2)
Cold hands/feet	28 (30%)	56 (18%)	0.02	1.9 (1.1-3.2)

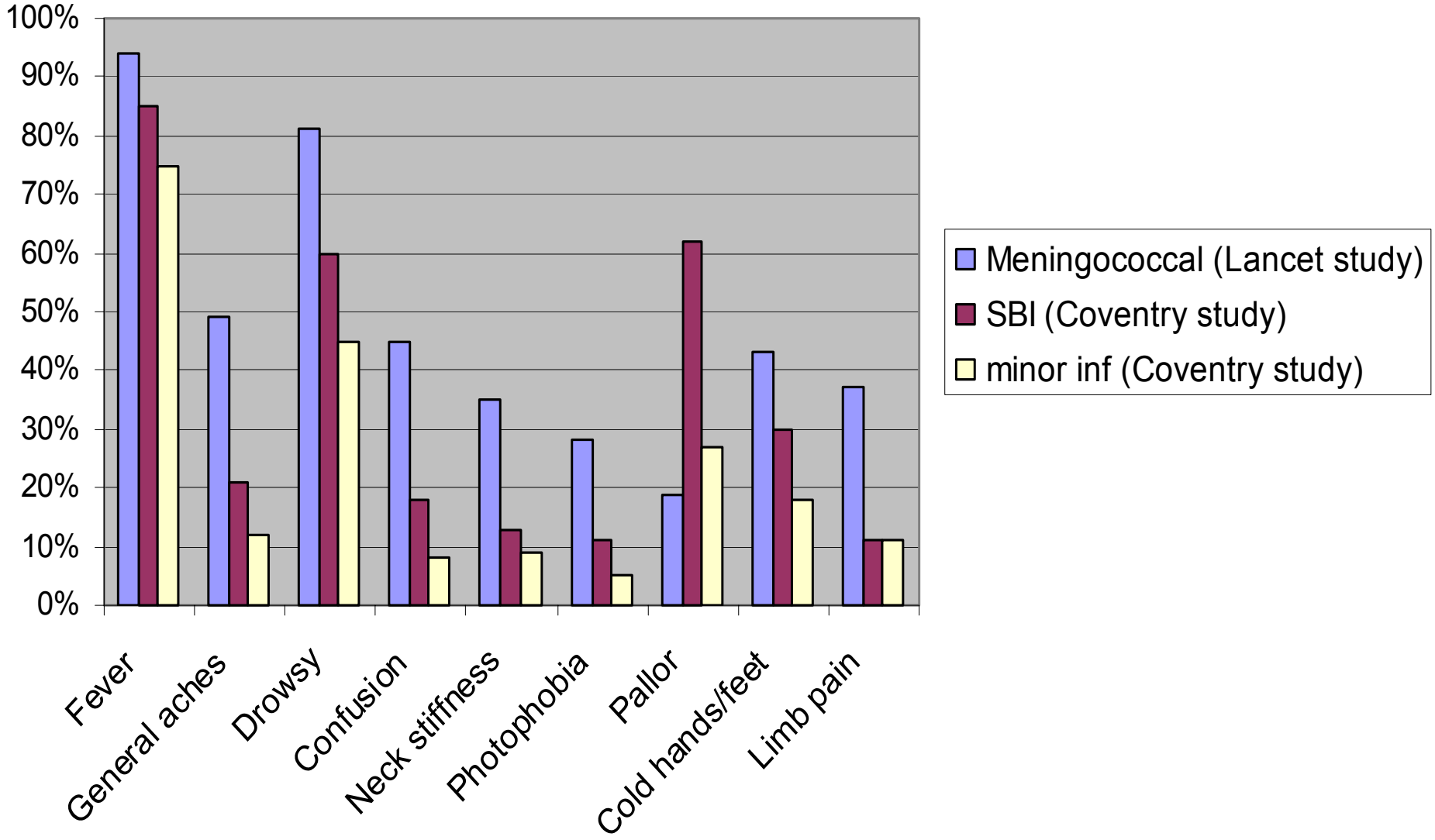
Notes: - 86% parents completed symptoms questionnaire.

- total of 22 symptoms included in parental questionnaire, only significant differences presented in table

Diagnostic characteristics: symptoms

	Sensitivity	Specificity	PPV	NPV
Fever	85%	25%	26%	84%
General aches	22%	88%	36%	79%
Drowsy	60%	55%	29%	82%
Confusion	18%	92%	46%	74%
Decreased feeding	66%	49%	28%	82%
Cough	66%	54%	30%	84%
Breathing difficulty	37%	75%	31%	79%
Pallor	62%	73%	41%	86%
Cold hands/feet	30%	82%	33%	79%

Comparison with symptom frequency: meningococcal (n=448) (Thompson & Ninis, Lancet 2006)



Vital signs

	SBI	Minor infection	Chi-square P-value	Unadjusted Odds Ratio
Temperature >39°C	33/106 (31%)	48/335 (14%)	0.001	2.7 (1.6-4.5)
Increased respiratory rate for age	62/108 (57%)	127/339 (38%)	<0.001	2.3 (1.4-3.5)
Increased heart rate for age	67/108 (62%)	148/339 (44%)	0.001	2.1 (1.4-3.3)
Oxygen saturations <95%	31/105 (30%)	22/327 (7%)	<0.001	5.8 (3.2-10.6)
Capillary refill time > 2 sec	6/61 (10%)	1/193 (0.5%)	0.005	21 (2.5-177)

Diagnostic characteristics: vital signs

	Sensitivity	Specificity	PPV	NPV
Temperature > 39°C	31%	86%	41%	80%
Fast respiratory rate	57%	63%	33%	82%
Fast heart rate	62%	56%	31%	82%
O_2 saturations < 95%	30%	93%	58%	80%
Capillary refill > 2 secs	10%	99%	86%	78%

Binary logistic regression (SBI vs. minor infection)

Logistic regression model	**Variables included**	Adjusted Odds ratio (95%CI)	
Symptoms only +age	Fever, general aches, drowsy, confusion, decreased feeding, nausea, cough, breathing difficulty, photophobia, cold hands/feet. Pallor	ns 3.0 (1.8-5)	 p<0.001
Symptoms + vital signs +age	Fever, general aches, drowsy, confusion, decreased feeding, nausea, cough, breathing difficulty, photophobia, cold hands/feet. Abnormal respiratory rate Abnormal heart rate Pallor Temperature >39°C Oxygen saturations <95%	ns ns ns 4.2 (2.3-7.6) 3.1 (1.6-5.7) 7.4 (3.6-15)	 p<0.001 p<0.001 p<0.001

Presence of one or more of: Pallor, temperature >39C, oxygen saturations <95%

SBI	Minor infection	Sensitivity	Specificity	PPV	NPV
82/104 (79%)	124/323 (38%)	79%	62%	40%	90%

Study limitations

- Recruitment non-consecutive
- Clinical staff not blinded to symptoms, vital signs etc
- Clinical diagnoses not standardised
- Spectrum of patients
  - SBI (mostly pneumonia) ≠ meningococcal disease
  - generalisable to primary care?

Conclusions

- Symptoms relatively insensitive at discriminating SBI vs. minor infection
  - Confusion & general aches highest specificity
  - Pallor only symptom independently associated with SBI.
  - Compared to *meningococcal disease,* children with minor infection less likely to have drowsiness, confusion, meningism, cold extremities, leg pains
- Children with SBI more likely to have higher temperature, tachycardia, tachypnoea, low saturations, prolonged capillary refill time, than those with minor infection
  - Sensitivities low
  - Specificities highest for capill refill time, decreased saturations
- Presence of low saturations, pallor, and/or fever = sens 79%, spec 62%

Does pulse rate predict serious infection in children?

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Background

1) Tachycardia is an objective marker of serious infection/complications (SIRS, sepsis, hypoxia, dehydration)
2) Current cut-off values for tachycardia do not incorporate effect of temperature… limited value
3) Incorporating measurement of heart rate with clinical assessment of children will improve recognition of serious infection

Aims

- Create age-specific charts of pulse rate expected at given temperature of children presenting with self-limiting infection in primary care
- Compare with currently used definitions of tachycardia (Advance Paediatric Life Support, APLS)
- *Determine whether children with serious infections are more tachycardic than expected for temperature & age*

Methods

- Convenience sample
- Age 1month-12yr
- Presenting to Nurse/GP with self-limiting infection
  - Axillary temperature
    - WelchAllyn SureTempPlus
  - Heart rate
    - Pulse oximeter
  - GP diagnosis, re-presentation, hospitalisation within 7 days
- Surgeries
  - GP surgeries in Oxfordshire, Buckinghamshire, Somerset

Centile charts

- Smoothed lines showing how measure (e.g. weight) changes when plotted against independent variable (e.g. age)
- Balance between adequate goodness of fit and smoothness
- LMS method of Cole & Green/WHO

Results

2123 recruited

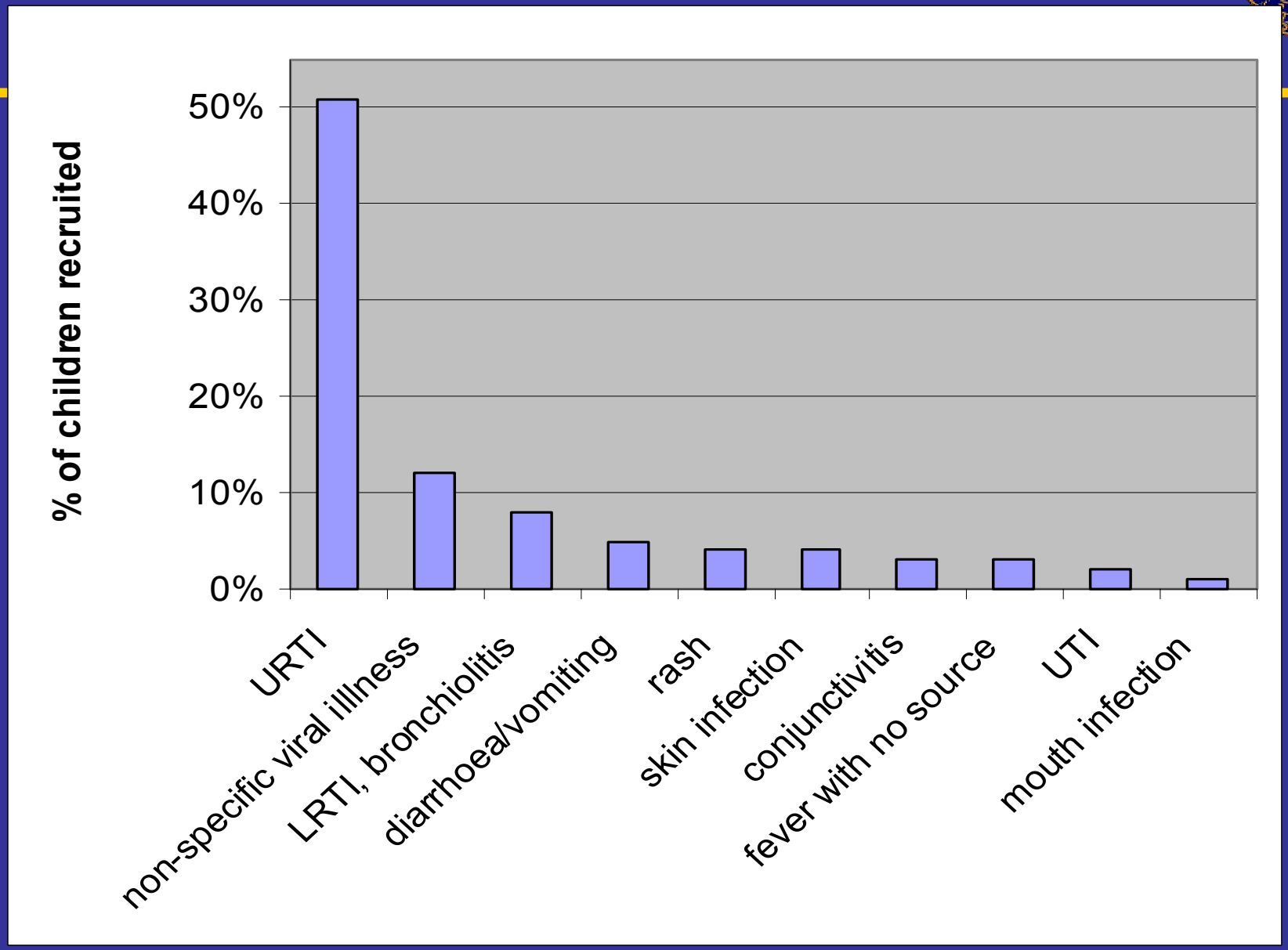
186 excluded: repeat presentation (112), no heart rate (30), no temperature (35), no DOB (9)

Final sample N = 1937

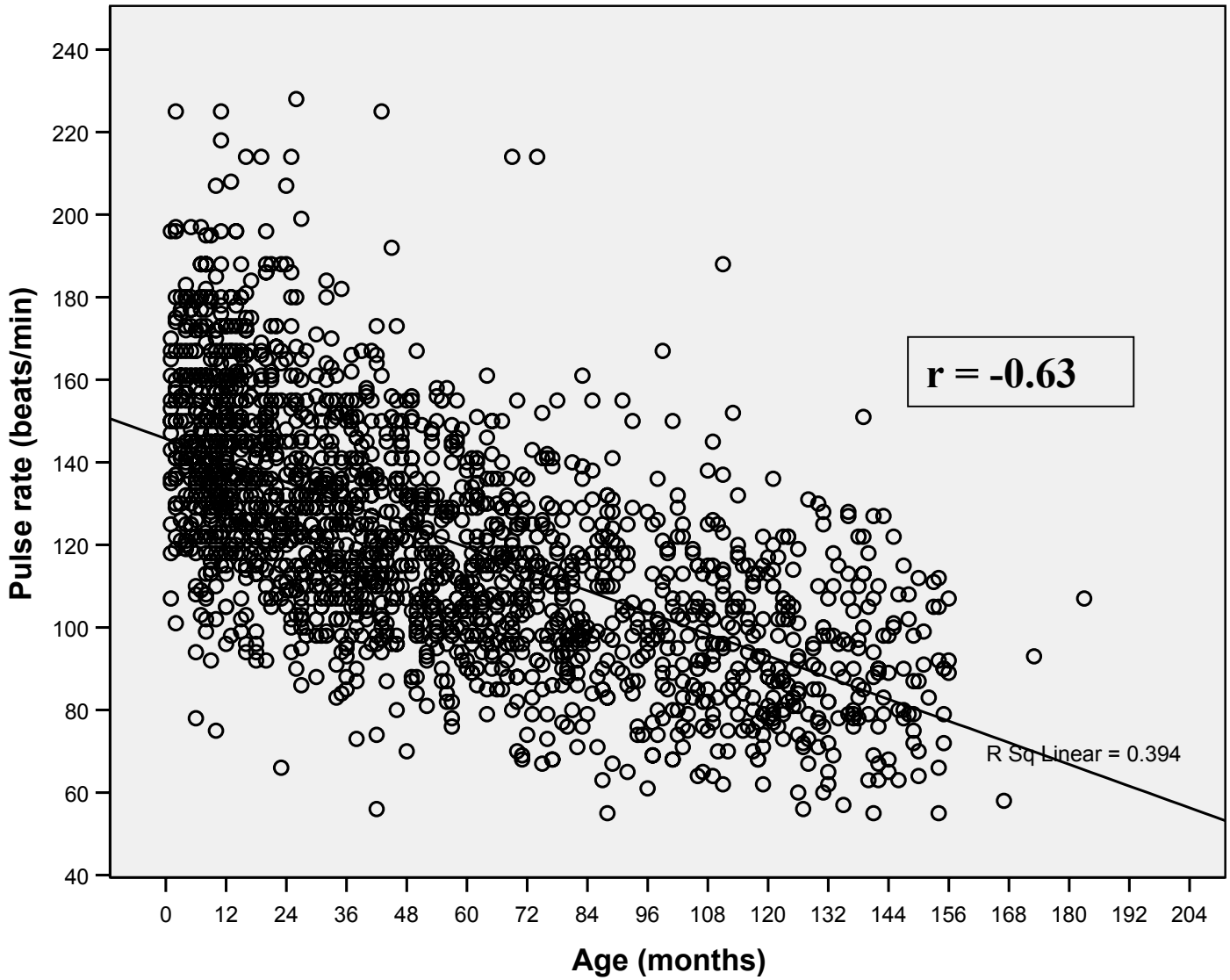
Description of sample (N=1937)

- Age
  - <1yr: 314 (16.1%)
  - 1-2 yr: 294 (15.1%)
  - 2-5 yr: 605 (31.1%)
  - 5-12 yr: 685 (35.2%)
- 53% male
- Hospital referrals & admission
  - 67 (3.4%) referred to hospital by GP
  - 106 (5.4%) actually seen in hospital – 53 admitted, 53 sent home

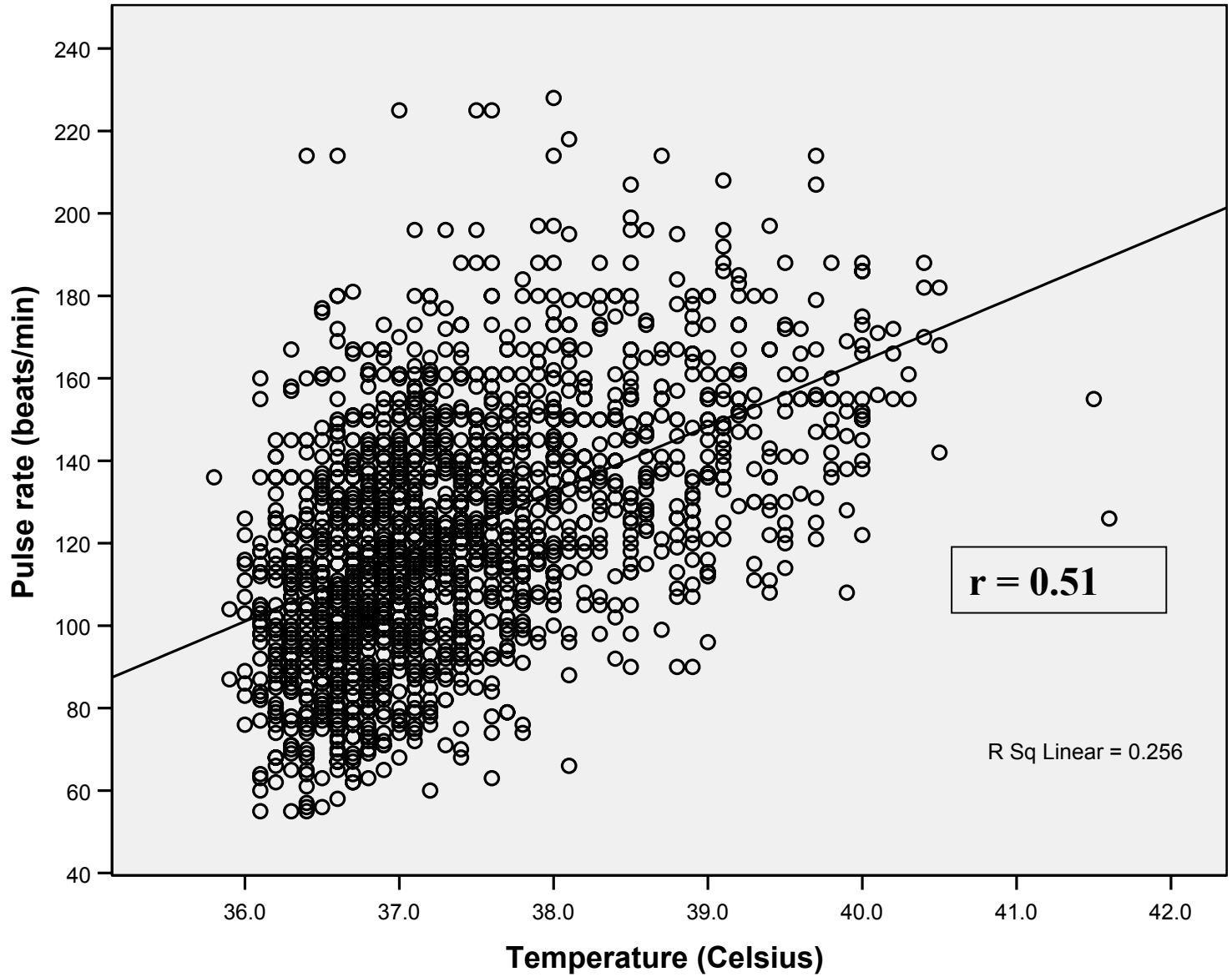
Diagnoses


% of children recruited
50%
40%
30%
20%
10%
0%
URTI
non-specific viral illness
LRTI, bronchiolitis
diarrhoea/vomiting
rash
skin infection
conjunctivitis
fever with no source
UTI
mouth infection

Correlation of heart rate & age



Correlation of heart rate & temperature



Limitations

- Convenience sample
- Measurement error
  - Heart rate, temperature subject to measurement error
  - Single measurements
- Effects of medications, anxiety, environment

Conclusions

- Linear relationship between heart rate and temperature: increase of x beats per min/1C rise temperature
- Centile charts better define relationship between heart rate and temperature
  - Allows “cut-off” values for tachycardia defined, using e.g. 90th or 97th centile for age and temperature band
- Current cut-off levels of tachycardia (e.g. APLS) are exceeded in majority of febrile children with self-limiting infections
- Heart rate differences small, unlikely that manual measurements would identify

Overall conclusions

Overall conclusions

- Incidence & spectrum of serious infection changed fundamentally in UK
- Primary care assessment of children with infection relies on clinical intuition & minimal use of diagnostic technology
- Symptoms of pallor, cold extremities, mental status changes, difficulty breathing, leg pain may be helpful
- Vital signs generally low sensitivity, but several have high specificity (e.g. cap refill, low saturations)…useful for **targeted** assessment of children

Future research directions 1.

- Diagnostic value of presenting symptoms of children in primary care with acute infections
  - Compare frequency of presenting symptoms in primary care, with paeds assessment unit & meningococcal studies
  - Prospective study primary care funded by MRF 2007-8

Future research directions 2.

- Predictive value of heart rate
  - Do children with sepsis have heart rates at upper centiles of normal?
  - Need data from children with sepsis …….!

Future research directions 3.

- Electronic measurement and interpretation of vital signs
  - Clinical feasibility & diagnostic value using data fusion to interpret combinations of vital signs in a single instrument in real time

Collaborators: Oxford Dept Electrical Engineering, Oxford BioSignals Ltd.

Oxford BioSignals

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  - Clinical Chemistry: Steve Smith, Julie Stinson
- 1000s of parents & children! GPs

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