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Mental Health NHS Foundation Trust

Pathways to Aggressive Behaviour During First Episode Psychosis

A Report from the UK National EDEN Study

Max Birchwood

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Christina Edkins inquiry finds missed opportunities to prevent killing

Report makes 51 recommendations after homeless man with mental health issues stabbed schoolgirl in Birmingham last year

Christina Edkins. Photograph: PA

Steven Morris

The report's findings include:

- Organisations failed to listen to and respond to carers and significant others consistently and adequately.
- The accessing and sharing of information between key agencies was ineffective.
- Organisations' information-recording and storage were not robust enough to allow good management and care.
- Services need to be more proactive in making it easier for a person with mental health issues to engage with them.

The chair of the investigation panel, Dr Alison Reed, said: "Many different organisations are associated with this very sad and complex case. It is clear that there were missed opportunities

not have been predicted. However, it is the conclusion of the panel that as Christina's death was directly related to [Simelane's] mental illness, it could have been prevented if his mental health needs had been identified and met."

Phillip Simelane. Photograph: PA

Christina, a bright pupil who hoped to become a nurse or carer, got on the number 9 bus in Birmingham city centre on the morning of 7 March last year and sat on the top deck. Simelane, wearing all the clothes he had for

- Why do individuals act on their delusions and others resist?
- What are the developmental pathways to harm to self or others?
- Why are there no interventions to reduce harm vs treating psychosis? Are they the same thing?
- Can we prevent such behaviour?

Original Investigation

Pathways to Violent Behavior During First-Episode Psychosis
A Report From the UK National EDEN Study

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IMPORTANCE Although many studies have explored the correlates of violence during first-episode psychosis (FEP), most have simply compared violent psychotic individuals with nonviolent psychotic individuals. Accumulating evidence suggests there may be subgroups within psychosis, differing in terms of developmental processes and proximal factors associated with violent behavior.

OBJECTIVE To determine whether there are subgroups of psychotic individuals characterized by different developmental trajectories to violent behavior.

DESIGN, SETTING, AND PARTICIPANTS The National EDEN (Evaluating the Development and Impact of Early Intervention Services in the West Midlands) Study longitudinal cohort assessed premorbid delinquency (premorbid adjustment adaptation subscale across childhood and adolescence), age at illness onset, duration of untreated psychosis, past drug use, positive symptoms, and violent behavior. Group trajectories of premorbid delinquency were estimated using latent class growth analysis, and associations with violent behavior were quantified. This study included 6 early intervention services in 5 geographical locations across England, with violent behavior information available for 670 first-episode psychosis cases.

MAIN OUTCOMES AND MEASURES Violent behavior at 6 or 12 months following early intervention services entry.

RESULTS Four groups of premorbid delinquency were identified: stable low, adolescent-onset high to moderate, stable moderate, and stable high. Logistic regression analysis, with stable low delinquency as the reference group, demonstrated that moderate (odds ratio, 1.97; 95% CI, 1.12-3.46) and high (odds ratio, 3.53; 95% CI, 1.85-6.73) premorbid delinquency trajectories increased the risk for violent behavior during FEP. After controlling for confounders, path analysis demonstrated that the increased risk for violence in the moderate delinquency group was indirect (ie, partially mediated by positive symptoms) (probit coefficient [β] = 0.12; P = .002); while stable high delinquency directly increased the risk for violence (β = 0.38; P = .05).

CONCLUSIONS AND RELEVANCE There appear to be diverse pathways to violent behavior during FEP. Stable high premorbid delinquency from childhood onwards appears to directly increase the risk for violent behavior, independent of psychosis-related risk factors. In addition to tackling illness-related risks, treatments should directly address antisocial traits as a potent risk for violence during FEP.

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ACTA PSYCHIATRICA SCANDINAVICA

Meta-analysis

A systematic review and meta-regression analysis of aggression during the First Episode of Psychosis

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Winsper C, Ganapathy R, Marwaha S, Large M, Birchwood M, Singh SP. A systematic review and meta-regression analysis of aggression during the First Episode of Psychosis.

Objective: The First Episode of Psychosis (FEP) represents a period of heightened risk for aggression. However, it is not known whether this risk is significantly altered following contact with mental health services.
Method: Meta-analytic methods were used to estimate pooled prevalence of 'any' and 'serious' aggression during FEP, while meta-regression analyses were conducted to explore reasons for heterogeneity between studies.
Results: Fifteen studies comprising 3, 294 FEP subjects were analysed. Pooled prevalence of 'any aggression' before service contact was 28% (95% CI: 22–34) and following contact 31% (95% CI: 20–42). Pooled prevalence of 'serious aggression' was 16% (95% CI: 11–20) before service contact and 13% (95% CI: 6–20) following contact. Four studies reporting repeated assessments within the same cohort revealed that aggression rates did not significantly differ post and pre service contact: Odds Ratios for any aggression: 1.18 (95% CI: 0.46–2.99) and serious aggression: 0.61 (95% CI: 0.31–1.21).
Conclusion: Rates of aggression are high during FEP, both before and following initial service contact, and seem not to alter following contact. This conclusion remains tentative due to considerable heterogeneity between studies and a lack of prospective cohort studies.

Key words: First Episode Psychosis; serious aggression; any aggression; pooled prevalence

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Summations

- High rates of aggression are observed during first episode psychosis (FEP).
- Rates of aggression during FEP appear not to substantially alter following service contact.

Considerations

- Extant studies of aggression during FEP are heterogeneous in the assessment and reporting of aggressive acts.
- More prospective studies are needed in which the effects of specific interventions for aggression during FEP are evaluated within same patient cohorts.

Background

- Rates of violence/aggression during FEP do not appear to substantially decrease following service contact (Winsper et al. 2013)

- Mirrors concerns that treatments for psychosis do not tackle associated violent behaviour (Serper et al., 2011)

Background

- The aetiology of violent/aggressive behaviour during psychosis is heterogeneous.
  - The causes underlying the behaviour may differ
  - There are at least two distinct pathways:
    - Violence associated with premorbid conditions (e.g., antisocial traits)
    - Violence associated with acute psychopathology (e.g., positive symptoms)

It has been hypothesized that there are 3 groups of violent psychotic individuals:

1. The early starters display a pattern of antisocial behaviour emerging in childhood, which remains relatively stable across the lifespan.
2. An illness onset group displays no antisocial behavior prior to illness, then repeatedly engages in aggressive behavior.
3. A second illness onset group displays no antisocial behaviour prior to and for the first few decades of illness, then commits serious violence.

Hodgins S. Violent behaviour among people with schizophrenia. Philos Trans R Soc Lond B Biol Sci. 2008;363(1503):2505-2518.

In the Dunedin prospective study:

40% of individuals who developed schizophreniform disorder by age 26 years displayed conduct disorder prior to the age of 15.1 ($p<0.001$)

Kim-Cohen J, Caspi A, Moffitt TE, HarringtonHL ,Milne BJ, Poulton R. Prior juvenile diagnoses in adults with mental disorder. Arch Gen Psychiatry.2003;60(7):709-717.
12. Hodgins S, Cree A,

Research Questions

Are there distinct subgroups of FEP patients differing in premorbid delinquency patterns?

Do these subgroups differ in prevalence of violent behavior following EIS entry?

What are the direct and indirect (via mediators, e.g., positive symptoms) associations between premorbid delinquency and violent behavior?

Data Resource

National EDEN: Evaluating the Development and Impact of Early Intervention Services in the UK (more details see: Birchwood et al., 2014, EIP)

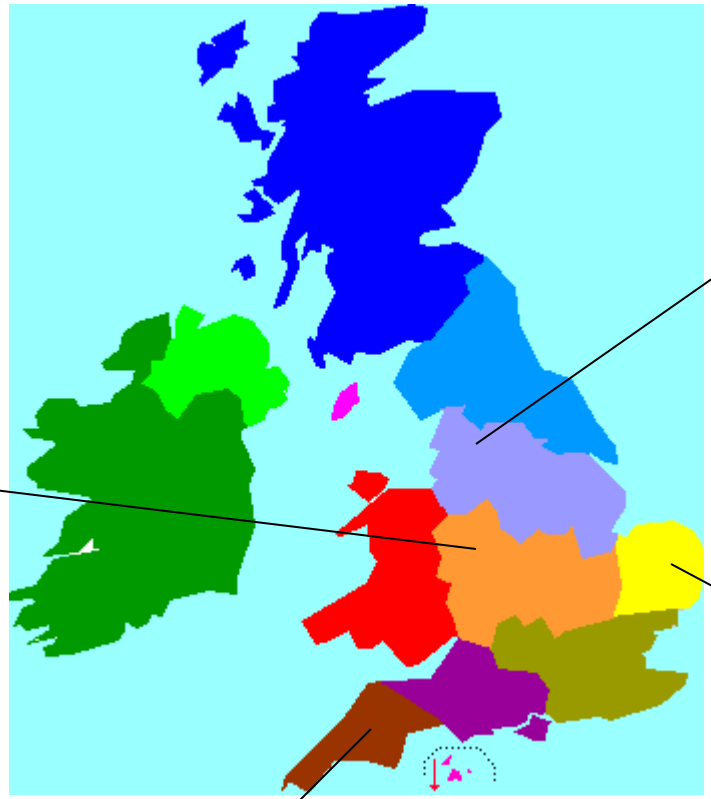
Longitudinal cohort of FEP patients across 5 sites in England. 1,027 patients at baseline.

- Baseline
- 6 months
- 12 months

The National/SUPER EDEN sites

Lancashire + Wirral
5 teams
(Marshall/Lewis/Sharma)

Birmingham
5 teams
(Birchwood/Lester)



East Anglia
4 teams
(Jones/Fowler)

Cornwall 2 teams
(Amos)

NIHR SUPEREDEN programme grant

Sustaining Positive Engagement and Recovery

The next step after Early Intervention for Psychosis

Lead: Birmingham and Solihull Mental Health Foundation Trust

Cambridgeshire and Peterborough NHS Foundation Trust EIS
Cheshire and Wirral Partnership NHS Trust EIS
Lancashire NHS Partnership Trust EIS
Norfolk & Waveney Mental Health Partnership Trust EIS
Devon and Cornwall Partnership Trust EIS
University of Birmingham
University of Bristol
University of Cambridge
University of East Anglia
University of Manchester
University of Warwick
King's College London

Rethink Mental Illness.

NHS
National Institute for Health Research

Assessments

- **Outcome:** Violent behaviour during EIS contact
  - "Adverse Outcomes Screening Questionnaire"
  - Dichotomous outcome (0=no violence; 1=violence at 6 or 12 months). Shortened version of the MacArthur study questionnaire.

- **Main predictor:** Premorbid delinquency
  - Premorbid Adjustment Scale (PAS) ("adaptation" subscale)
  - Continuous measure at baseline referring to: childhood, early adolescence, and late adolescence

Assessments: Confounders and mediators

- Past Drug Use
  - Continuous measure at baseline (0:no past drug use; 1:not more than 3 times; 2:less than weekly; 3:1 to 3 times weekly; 4: almost every day)

- Duration of untreated psychosis
  - Dichotomous measure (0:less than 6 months; 1: more than 6 months)

Assessments: Confounders and mediators

- Age of illness onset
  - Continuous measure reported at baseline
- Positive symptoms
  - Positive and Negative Syndrome Scale (PANSS)
  - Continuous measure reported at 6 months

Supplementary Table 1. Attrition analysis comparing those retained in analysis to those lost to follow-up

Risk factors for violence	Violent behaviour questions		Associations
	Retained [5]	Lost to follow-up	Available vs. not available OR (95% CI)
Premorbid delinquency[1]			
low	299 (49.2%)	154 (49.7%)	[reference]
adolescent onset	43 (7.1%)	30 (9.5%)	0.74 (0.45 to 1.22)
moderate	187 (30.8%)	84 (26.6%)	1.15 (0.83 to 1.58)
high	79 (13%)	48 (15.2%)	0.85 (0.56 to 1.28)
DUP[2]			
< 6 months	415 (62.7%)	234 (67.2%)	[reference]
> 6 months	247 (37.3%)	114 (32.8%)	1.22 (0.93 to 1.61)
Past drug use[3]			
Mean (SD)	2.00 (1.68)	2.03 (1.68)	1.09 (0.97 to 1.23)
Positive symptoms at 6 months[4]			
Mean (SD)	11.58 (4.34)	11.28 (4.72)	1.02 (0.98 to 1.05)
Age of onset of illness			
Mean (SD)	21.43 (5.09)	21.15 (4.78)	1.01 (0.99 to 1.04)

[1] PAS assessed at baseline; [2] Duration of untreated psychosis assessed at baseline; [3] Past drug use assessed at baseline; [4]PANSS scale assessed at 6 months; [5] Complete violent behavior information available.

Methods: 3 stages

- Latent Class Growth Analysis: LCGA (Question 1)
  - To group individuals according to patterns of delinquent behavior *across time* from childhood to late adolescence
- Logistic Regressions (Question 2)
  - To assess unadjusted associations between delinquent groups (identified in the LCGA) and violent behavior during EIS contact
- Path Analysis (Question 3)
  - To assess direct and indirect (via possible mediators, e.g., positive symptoms) associations between delinquent groups and violent behavior

Aggression post FEP

- 13.7% at 6 or 12 months
- 8.6% at 6 months; 8.5% at 12 months

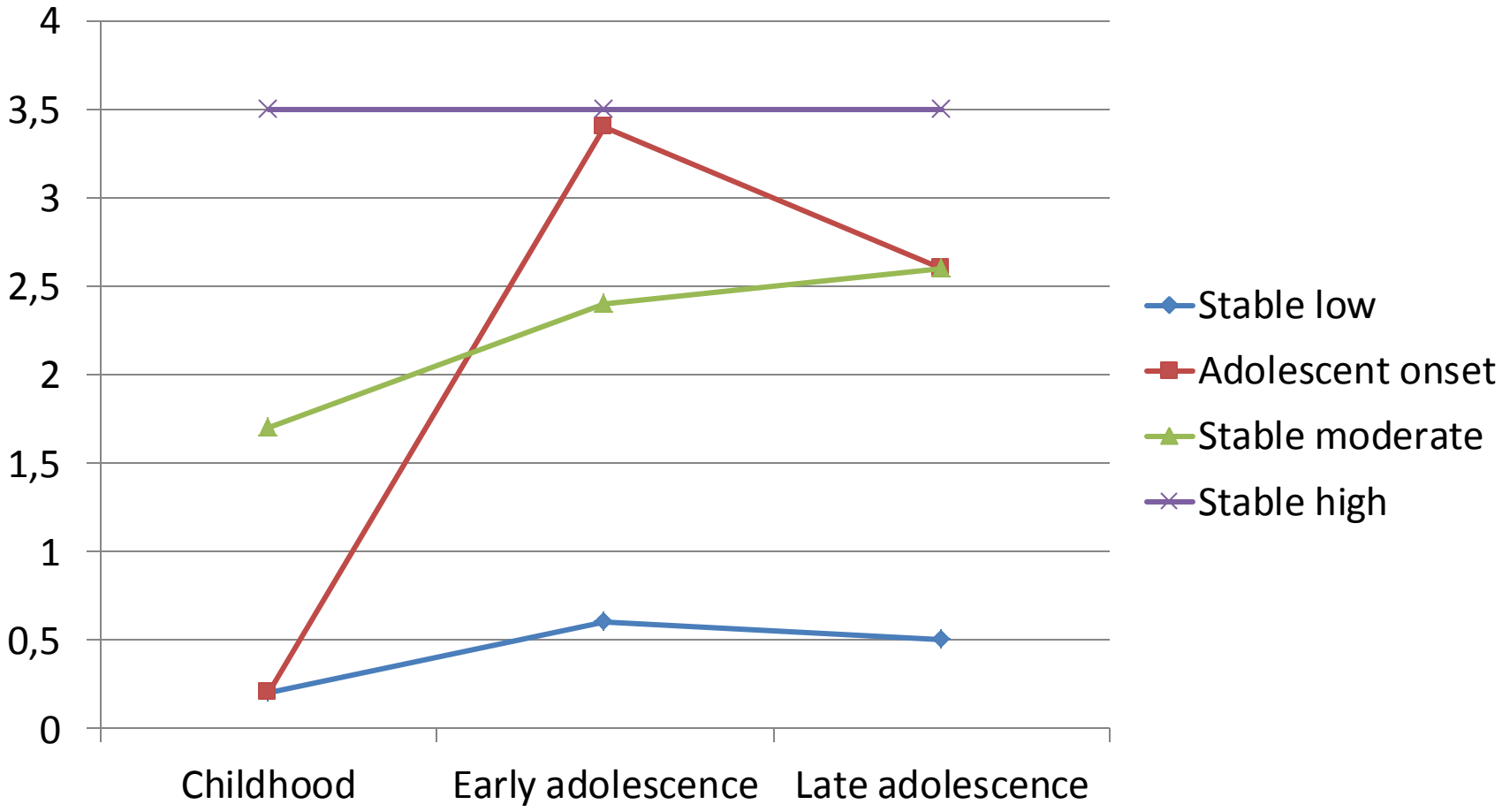
Supplementary Table 2. Descriptive statistics of violent behavior following EIS contact

	Frequency (%)	
Type of violent behavior	**6 months assessment**	**12 months assessment**
Pushed anyone	39 (5.8%)	47 (6.6%)
Slapped anyone	11 (1.6%)	13 (1.8%)
Used knife	2 (0.3%)	3 (0.4%)
Choked anyone	4 (0.6%)	6 (0.8%)
Beaten anyone	43 (6.3%)	49 (6.9%)
Hit with blunt instrument	7 (1.0%)	7 (1.0%)
How often harmed others		
Once	43 (65.2%)	36 (56.9%)
2 to 5 times	18 (27.3%)	22 (33.8%)
Over 5 times	5 (7.6%)	6 (9.2%)
Who harmed		
Family	23 (34.3%)	28 (42.4%)
Friend	11 (16.4%)	6 (9.1%)
Healthcare/staff	1 (1.5%)	3 (4.5%)
Stranger	25 (37.3%)	21 (31.8%)
Other	7 (10.4%)	8 (12.1%)

Results 1: Latent Class Growth Analysis

- Four groups of premorbid delinquency were identified:
  - Stable low (48.5%)
  - Stable moderate (28.7%)
  - Stable high (13.2%)
  - Adolescent onset (9.7%)

Trajectories of Premorbid Delinquency (LCGA)



Assessed using the "adaptation" subscale of the PAS

Results 2: Logistic Regressions

- Stable moderate delinquency significantly increased risk of violent behavior:

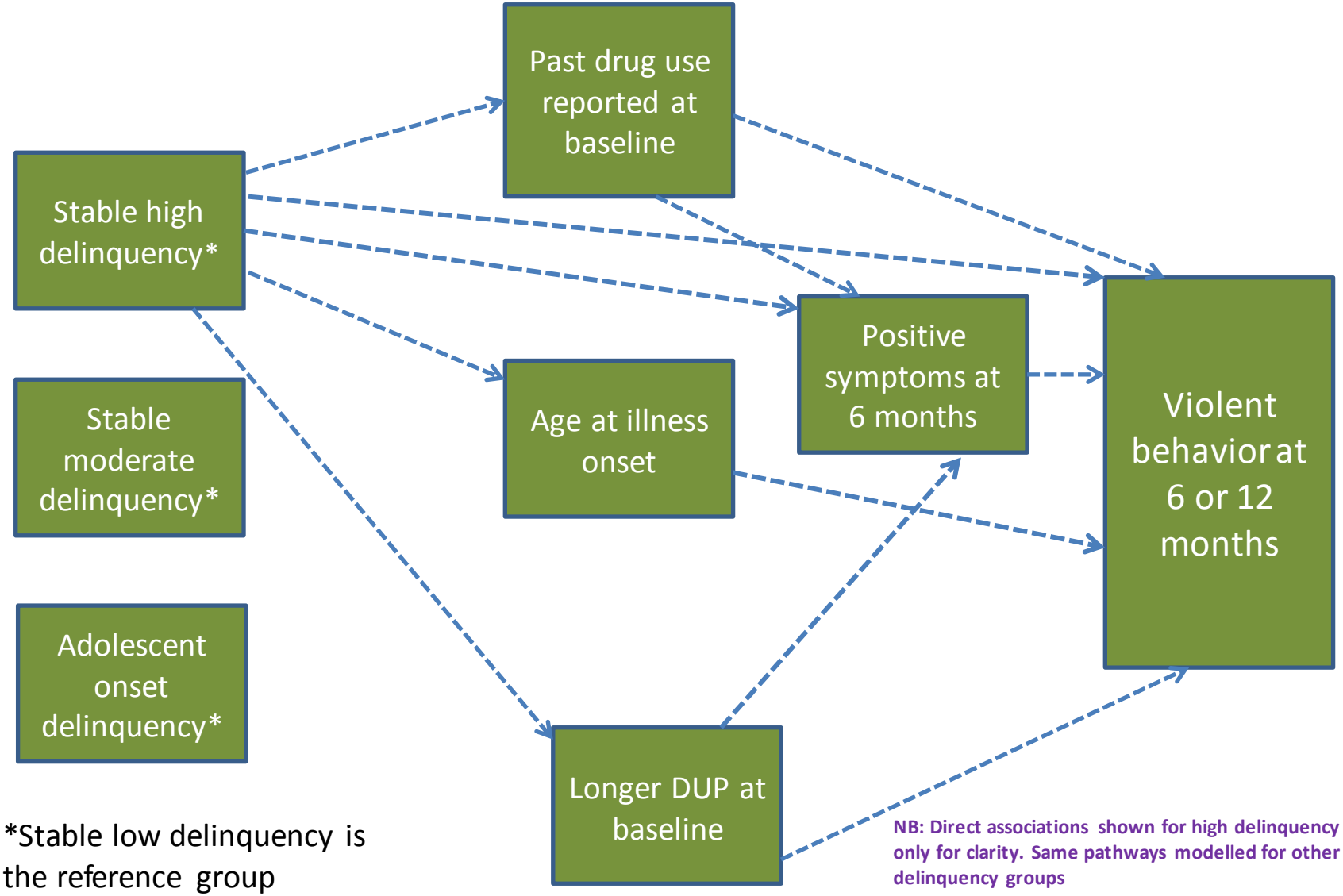
  OR=1.97 (95% CI=1.12-3.46)*

- Stable high delinquency most strongly increased risk of violent behavior:

  OR=3.53 (95% CI=1.85-6.73)*

* Stable low delinquency used as the reference group. These associations are unadjusted

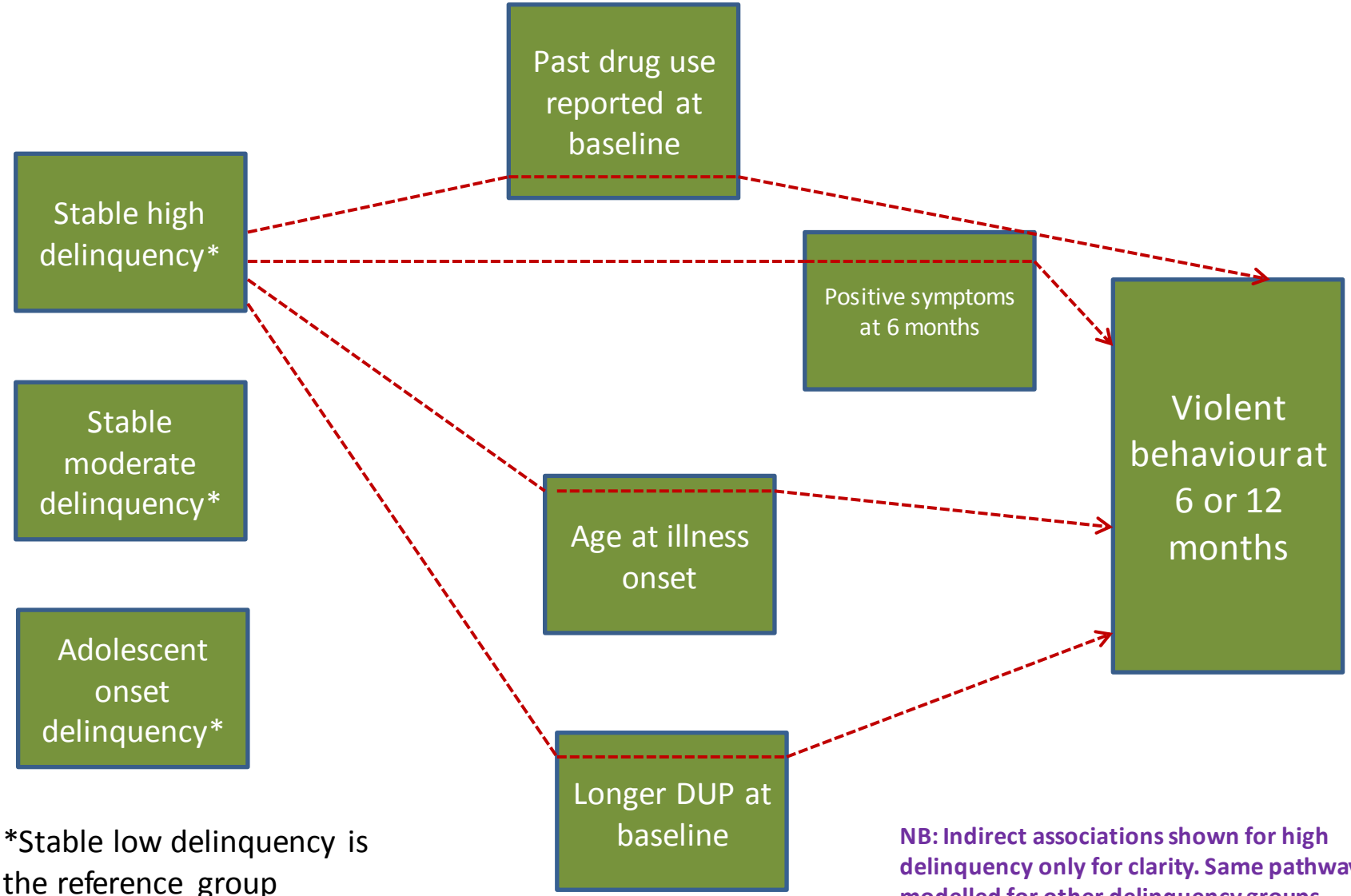
Results 3: Direct pathways modelled



*Stable low delinquency is the reference group

NB: Direct associations shown for high delinquency only for clarity. Same pathways modelled for other delinquency groups

Results 3: Indirect pathways modelled



*Stable low delinquency is the reference group

NB: Indirect associations shown for high delinquency only for clarity. Same pathways modelled for other delinquency groups

Results 3: Direct Associations

Three factors were independently (i.e., all other factors controlled for) associated with violent behaviour:

Stable high delinquency: $\beta = 0.379$, $p=.05$

Positive symptoms: $\beta = 0.074$, $p<.001$

Early onset of illness: $\beta = -0.044$, $p=.003$

Results 3: Indirect Associations

- Stable moderate delinquency was indirectly associated with violent behavior via positive symptoms: $\beta = 0.119$, $p=.002$

- Stable moderate delinquency increased the risk of violent behavior by increasing the risk of positive symptoms rather than being directly related

Summary

Stable high delinquency independently increased risk of violent behaviour

Stable moderate delinquency only increased risk of violent behavior via positive symptoms (there was no direct association)

Conclusions

Individuals demonstrating antisocial behaviour from childhood onwards may be especially likely to engage in violent behavior during FEP

Violent behavior in this subgroup appears to be independent of psychosis-related risks (e.g., positive symptoms)

In addition to tackling illness related risks, treatments should directly address antisocial traits

Long-term Effects of Nurse Home Visitation on Children's Criminal and Antisocial Behavior

15-Year Follow-up of a Randomized Controlled Trial

David Olds, PhD; Charles R. Henderson, Jr; Robert Cole, PhD; John Eckenrode, PhD; Harriet Kitzman, RN, PhD; Dennis Luckey, PhD; Lisa Pettitt, PhD; Kimberly Sidora, MPH; Pamela Morris; Jane Powers, PhD

Context.—A program of home visitation by nurses has been shown to affect the rates of maternal welfare dependence, criminality, problems due to use of substances, and child abuse and neglect. However, the long-term effects of this program on children's antisocial behavior have not been examined.

Objective.—To examine the long-term effects of a program of prenatal and early childhood home visitation by nurses on children's antisocial behavior.

Design.—Fifteen-year follow-up of a randomized trial. Interviews were conducted with the adolescents and their biological mothers or custodial parents.

Setting.—Semirural community in New York.

Participants.—Between April 1978 and September 1980, 500 consecutive pregnant women with no previous live births were recruited, and 400 were enrolled. A total of 315 adolescent offspring participated in a follow-up study when they were 15 years old; 280 (89%) were born to white mothers, 195 (62%) to unmarried mothers, 151 (48%) to mothers younger than 19 years, and 186 (59%) to mothers from households of low socioeconomic status at the time of registration during pregnancy.

Intervention.—Families in the groups that received home visits had an average of 9 (range, 0-16) home visits during pregnancy and 23 (range, 0-59) home visits from birth through the child's second birthday. The control groups received standard prenatal and well-child care in a clinic.

Main Outcome Measures.—Children's self-reports of running away, arrests, convictions, being sentenced to youth corrections, initiation of sexual intercourse, number of sex partners, and use of illegal substances; school records of suspensions; teachers' reports of children's disruptive behavior in school; and parents' reports of the children's arrests and behavioral problems related to the children's use of alcohol and other drugs.

Results.—Adolescents born to women who received nurse visits during pregnancy and postnatally and who were unmarried and from households of low socioeconomic status (risk factors for antisocial behavior), in contrast with those in the comparison groups, reported fewer instances (incidence) of running away (0.24 vs 0.60; $P = .003$), fewer arrests (0.20 vs 0.45; $P = .03$), fewer convictions and violations of probation (0.09 vs 0.47; $P < .001$), fewer lifetime sex partners (0.92 vs 2.48; $P = .003$), fewer cigarettes smoked per day (1.50 vs 2.50; $P = .10$), and fewer days having consumed alcohol in the last 6 months (1.09 vs 2.49; $P = .03$). Parents of nurse-visited children reported that their children had fewer behavioral problems related to use of alcohol and other drugs (0.15 vs 0.34; $P = .08$). There were no program effects on other behavioral problems.

Conclusions.—This program of prenatal and early childhood home visitation by nurses can reduce reported serious antisocial behavior and emergent use of substances on the part of adolescents born into high-risk families.

JAMA. 1998;280:1238-1244

JUVENILE CRIME is a significant problem in the United States. In 1996, law enforcement agencies made 2.9 million arrests of juveniles (children <18 years). Moreover, 19% of all arrests and 19% of all violent crime arrests were accounted for by juveniles. Although the number of juvenile Violent Crime Index arrests (ie, for murder, forcible rape, robbery, and aggravated assault) declined in both 1995 and 1996, the rate in 1996 was still 60% higher than the 1987 level.[1]

For editorial comment see p 1271.

Antisocial behavior can be classified according to its time of onset: prior to puberty (childhood onset) vs after puberty (adolescent onset).[2,3] Childhood onset is characterized by more serious behavioral disruption, such as violent behavior toward classmates and cruelty toward animals beginning as early as age 3 years, but occurs less frequently. The adolescent-onset variety, although sometimes expressed as aggression toward peers, is generally less serious (eg, shoplifting, lying to teachers and parents) and occurs so frequently that some consider it normative.[3] Childhood-onset antisocial behavior is associated with neuropsychological deficits (eg, impaired language and intellectual functioning, attention-deficit/hyperactivity disorder) and harsh, rejecting parenting early in the child's life.[4,5] The

From the University of Colorado Health Sciences Center, Denver (Drs Olds and Luckey); Cornell University, Ithaca, NY (Mr Henderson, Drs Eckenrode and Powers, and Ms Morris); the University of Rochester, Rochester, NY (Drs Cole and Kitzman and Ms Sidora); and the University of Denver (Dr Pettitt).

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Opportunity for prevention in those at risk?

Thank you.

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