Schizophrenia: early intervention and assessment

Rudolf Cardinal  
rudolf@pobox.com  
Clinical Lecturer, Department of Psychiatry, University of Cambridge  
Honorary SpR, Liaison Psychiatry, CPFT, Addenbrooke’s  

Cambridge MRCPsych course  
Ida Darwin Hospital, Fulbourn  
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Early intervention
Executive summary

- A long **duration of untreated psychosis (DUP)** is associated with poorer prognosis.

- The hope is that **early intervention** [in psychosis] (**EI**) reduces DUP, and that this improves the overall outcome for patients.

- EI is distinct from standard care in two ways: (1) early detection; (2) treatment specific to the early phase.

- There has been strong governmental and NICE support for EI services.

- Cochrane review (2011): “There is emerging, but inconclusive, evidence that people in the prodrome of psychosis can be helped by some interventions. There is some support for specialised early intervention services, but further trials would be desirable, and there is a question of whether gains are maintained. There is some support for phase-specific treatment focused on employment and family therapy, but again, this needs replicating with larger and longer trials... at present we have insufficient data to draw any definitive conclusions.”
Duration of untreated psychosis (DUP) and prognosis

  - Meta-analysis: 26 studies; total $n = 4490$; prospective cohorts; first-episode psychosis.
  - Longer DUP associated with worse outcomes at 6 and 12 months (total symptoms, positive symptoms, negative symptoms, depression/anxiety, overall functioning, social functioning, chance of remission).
  - Generally not fully explicable by premorbid functioning, where measured.

- Why?
  - Direct “toxicity” of psychosis?
  - Confound? e.g. maybe forms of psychosis characterized by insidious onset and social withdrawal cause (a) poorer outcome, and independently (b) delayed presentation and therefore longer DUP
Early intervention: government policy

- **NHS Plan (2000):** required mental health services to establish early intervention services for 14-35yo patients with a first presentation of psychotic symptoms, and 14-35yo patients during the first 3 y of psychotic illness.

- **Mental Health Policy Implementation Guide (2001):** set out tasks for early intervention services, including
  - “reducing stigma and raising awareness of symptoms of psychosis to reduce the duration of untreated illness;
  - developing engagement, providing evidence-based treatments and promoting recovery for young people who have experienced an episode of psychosis;
  - and working across the traditional divide between child and adolescent services and adult services as well as in partnership with primary care, education, social services, youth and other services.”

- **NICE (2009) Commissioning Guide:** “The key components of a schizophrenia service are: early intervention and early treatment...”

- **Dept of Health (2011):** “We... know that taking the right action through early intervention can make a long-lasting difference to people’s lives... we will... prioritise early intervention across all ages.”
Early intervention: NICE guidance on schizophrenia

- NICE (2002): “Because many people with actual or possible schizophrenia have difficulty in getting help, treatment and care at an early stage, it is **recommended that early intervention services are developed** to provide the correct mix of specialist pharmacological, psychological, social, occupational and educational interventions at the earliest opportunity.” *(Grading of recommendation: Good practice point [=based on the clinical experience of the guideline development group].)*


- NICE (2009): “**Offer early intervention services to all people with a first episode or first presentation of psychosis,** irrespective of the person’s age or the duration of untreated psychosis. Referral to early intervention services may be from primary or secondary care. **Early intervention services should aim to provide a full range of relevant pharmacological, psychological, social, occupational and educational interventions for people with psychosis, consistent with this guideline.**”
What is an EI service intended to achieve? (DH 2001)

Psychosis is a debilitating illness with far-reaching implications for the individual and his/her family. It can affect all aspects of life – education and employment, relationships and social functioning, physical and mental wellbeing. Without support and adequate care, psychosis can place a heavy burden on carers, family and society at large.

The mean age of onset of psychotic symptoms is 22 with the vast majority of first episodes occurring between the ages of 14 and 35. The onset of this disease is therefore often during a critical period in a person's development.

At present it can take up to two years after the first signs of illness for an individual and his/her family to begin to receive help and treatment. Lack of awareness, ambiguous early symptoms and stigma all contribute to the delay in appropriate help being offered and taken up.

Early treatment is crucial because the first few years of psychosis carry the highest risk of serious physical, social and legal harm. One in ten people with psychosis commits suicide - two thirds of these deaths occur within the first five years of illness.

Intervening early in the course of the disease can prevent initial problems and improve long term outcomes. If treatment is given early in the course of the illness and services are in place to ensure long-term concordance (co-operation with treatment), the prospect for recovery is improved.

An early intervention service should be able to:

- reduce the stigma associated with psychosis and improve professional and lay awareness of the symptoms of psychosis and the need for early assessment.
- reduce the length of time young people remain undiagnosed and untreated
- develop meaningful engagement, provide evidence-based interventions and promote recovery during the early phase of illness
What does an EI service look like? (DoH 2001) (1)

For population 1 million: ~150 new cases/year; ~450 caseload total; divided into teams with caseload 120–150. One team looks like:

<table>
<thead>
<tr>
<th>Table 5b</th>
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</thead>
<tbody>
<tr>
<td>Care co-ordinators</td>
</tr>
<tr>
<td>Key skills:</td>
</tr>
<tr>
<td>• High energy level</td>
</tr>
<tr>
<td>• Team player</td>
</tr>
<tr>
<td>• Ability creatively to engage service users</td>
</tr>
<tr>
<td>• Understanding of needs of service users, including specific needs related to cultural background/age/gender etc</td>
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<tr>
<td>• Able to co-ordinate care and provide broad range of interventions</td>
</tr>
<tr>
<td>• Works well with young people</td>
</tr>
<tr>
<td>Total 10 wte care co-ordinators with service user to care co-ordinator ratio maximum 15 to 1</td>
</tr>
<tr>
<td>Team leader must have an active caseload</td>
</tr>
<tr>
<td>Appropriate mix of psychiatric nurses, ASWs, OTs, psychologists needed to ensure that all the interventions listed can be provided within the team</td>
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<tr>
<td>Psychiatrists – adult mental health</td>
</tr>
<tr>
<td>• Active members of the team</td>
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<tr>
<td>• Dedicated sessions</td>
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<tr>
<td>0.5 wte adult consultant psychiatrist</td>
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<tr>
<td>1.0 wte non career grade psychiatrists</td>
</tr>
<tr>
<td>Psychiatrists – CAMHS</td>
</tr>
<tr>
<td>• Active members of the team</td>
</tr>
<tr>
<td>• Dedicated sessions</td>
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<tr>
<td>0.1 wte CAMHS consultant</td>
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</table>
What does an EI service look like? (DoH 2001) (2)

<table>
<thead>
<tr>
<th>Specialist skills - adult</th>
<th>Specialist skills – CAMHS</th>
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<tbody>
<tr>
<td>• These skills should be available within the team either by employing a fully qualified practitioner or by training other team members</td>
<td>• OT/OT skills</td>
</tr>
<tr>
<td>• External supervision, support and training needed for ‘non specialists’ providing these interventions</td>
<td>• Psychologist/psychology skills</td>
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<tr>
<td></td>
<td>• ASW/strong links to social services and ability to undertake thorough assessment and activate services as needed</td>
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</tbody>
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<tr>
<th>Support workers</th>
<th>Programme support</th>
</tr>
</thead>
<tbody>
<tr>
<td>• People with health, social care or appropriate life experience or personal experience of mental health problems/treatment</td>
<td>• Number of support workers to be determined by the team</td>
</tr>
<tr>
<td></td>
<td>• Support workers to reflect the demography of the local population</td>
</tr>
<tr>
<td></td>
<td>• 1 wte administrative assistant</td>
</tr>
<tr>
<td></td>
<td>• IT, audit and evaluation support may also be needed</td>
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</table>
What does an EI service do? (DoH 2001) 1: general

- **Raising awareness of psychotic illness** (community-based programs to reduce stigma; symptoms awareness programmes for primary care, educational institutions, social services, etc.)

- **Focus on symptoms** (understand normality; know the variety of psychotic symptoms; encourage referral based on suspicion not certainty of psychosis; focus treatment on symptom management; “watch and wait” when diagnosis unclear)

- **Age-, culture-, and gender-sensitive service**
What does an EI service do? (DoH 2001) 2: assessment (a)

<table>
<thead>
<tr>
<th>ASSESSMENT</th>
<th>Training programmes and written guidance for GPs and other key agencies are needed on the importance of early detection and how to refer people with potential early psychosis</th>
<th>Pathways of care must be explicit and understood by all involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early detection</td>
<td>• Regular audit of effectiveness of referral pathways and training programmes</td>
<td>• Access to assessment should be easy and rapid</td>
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</tbody>
</table>
What does an EI service do? (DoH 2001) 2: assessment (b)

<table>
<thead>
<tr>
<th>Assessment</th>
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</table>
|  | • Service user centred, multidisciplinary assessment co-ordinated by care co-ordinator  
|  | • Sufficient time should be allowed to develop a relationship and let symptoms stabilise  
|  | • Physical Health Assessment where appropriate  |
|  |  |
|  | Comprehensive assessment to include as a minimum:  
|  | • Psychiatric history  
|  | • Mental state examination  
|  | • Risk - including suicide risk  
|  | • Social functioning and resource assessment  
|  | • Psychological assessment  
|  | • Occupational assessment  
|  | • Family/support assessment  
|  | • Service user's aspirations and understanding  
|  | • Contribution from people important to the service user  |
What does an EI service do? (DoH 2001) 2: assessment (c)

| Production of comprehensive care plan | • Initial care plan produced within a week of assessment  
• Initial care plan comprehensively reviewed at three months  
• Care plan updated at least six monthly | • Care plan flexible enough to adapt to changes in the level and type of care required |
<table>
<thead>
<tr>
<th>INTERVENTIONS</th>
<th>Early and sustained engagement</th>
<th>Lack of clear diagnosis should not lead to case closure. Instead an active ‘watching brief’ should be adopted if there is a suspicion of psychotic illness but no firm diagnosis.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Allocation of dedicated community-based care co-ordinator to each service user</td>
<td>• See Assertive Outreach Service Specification (section 4 of this guide) for more information on the assertive outreach approach</td>
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<tr>
<td></td>
<td>• Assessment should take place in the service user's home or other low stigma setting</td>
<td>• Focusing on the strengths and interests of the service user and the benefits that contact with the service can bring can help improve engagement and concordance (co-operation) with care</td>
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<tr>
<td></td>
<td>• Sustained engagement using an assertive outreach approach so that no service users are ‘lost to follow up’.</td>
<td>• Failure to engage in treatment should not lead to case closure.</td>
</tr>
<tr>
<td></td>
<td>• Failure to engage in treatment should not lead to case closure.</td>
<td></td>
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<tr>
<td>Medication</td>
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</tbody>
</table>
| • Use of **low** dose or atypical neuroleptics first line and consideration of mood stabilisers and antidepressants if appropriate  
• Service user involved in decision making and monitoring effects  
• Care designed to improve concordance  
• Standard side effect monitoring tools to be used regularly by staff and service user | 
| • Local evidence-based prescribing and therapy protocols should be developed and used  
• Choice of medication dependant on clinical condition  
• Specialist support from CAMHS expertise needed when prescribing for under 16 year-olds  
• Avoidance of and careful attention to side effects are important to ensure effective treatment and long term engagement with services |

“low dose or atypical”: FGA: e.g. haloperidol 1–4 mg/day, …  
SGA: risperidone 2–4 mg/d, quetiapine 350–400 mg/d, olanzapine 5–20 mg/d, aripiprazole…  
No clear superiority (FGA more EPS, SGA more metabolic side effects).
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<tr>
<th>Psychological therapies</th>
<th>Family/carers/Significant others involvement and support</th>
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<tbody>
<tr>
<td>• Use of cognitive behavioural therapy as appropriate</td>
<td></td>
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<tr>
<td>• Psycho-education</td>
<td></td>
</tr>
<tr>
<td>• Information provided to service user about local recovery or service user groups</td>
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<tr>
<td>• Cognitive behavioural therapy can be of considerable benefit to service users</td>
<td></td>
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<tr>
<td>• Promotion of coping skills is vital</td>
<td></td>
</tr>
<tr>
<td>• Family/carers/significant others should be involved in assessment and treatment process as early as possible</td>
<td></td>
</tr>
<tr>
<td>• Provision of psycho-education, family therapy and support</td>
<td></td>
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<tr>
<td>• At least monthly contact with family/carers/significant others</td>
<td></td>
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<tr>
<td>• Connexions workers</td>
<td></td>
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<tr>
<td>• Engagement of family/friends improves assessment, and the long term outcomes of the service user, and can alleviate stress within the family.</td>
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<tr>
<td>• Care must be taken to engage and support <strong>all</strong> those important to the service user. This is particularly important if the service user has left home</td>
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<tr>
<td>Addressing basics of daily living</td>
<td>Care plan should address all aspects of daily living</td>
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<td>---------------------------------</td>
<td>----------------------------------------------------</td>
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</table>
What does an EI service do? (DoH 2001) 3: interventions (f)

| Providing pathway to valued education and occupation | • Vocational assessment (if required) should take place within 3 months of referral  
• An education or training plan/pathway to valued employment should be produced within 3 months | • Formal links with key agencies and schemes such as local careers advisory services, Connexions, New Deal, Training and Enterprise Agency, further education colleges, voluntary organisations etc. must be established.  
• Early referral is vital. The longer an individual remains out of work/education in the early phase, the harder it becomes to gain employment/participate in education later on. |
| Treating co-morbidity | Regular assessment of common co-morbidity’s particularly:  
|                       | - Substance misuse  
|                       | - Depression/suicidal thoughts  
|                       | - Anxiety disorders | • Early intervention team should have core skills to assess and deal with common co-morbidities.  
<p>|                       | | • Specialist help for any of these conditions should also be available. Care co-ordinator should co-ordinate provision of care as appropriate. If referral is necessary, early intervention team should continue to have overall responsibility for the service user. |</p>
<table>
<thead>
<tr>
<th>Relapse prevention plan</th>
<th>Crisis plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Individualised early warning signs plan developed and on file</td>
<td>- Changes in thought, feelings and behaviours precede the onset of relapse but there is considerable variation between service users. Development of individualised plans can be effective in reducing the severity of relapse.</td>
</tr>
<tr>
<td>- Relapse prevention plan agreed with service user and involve family/carers</td>
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<td></td>
<td>- Service user/family/carers know when and how to call for help</td>
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<td></td>
<td>- Intensive support in the community provided by the team during the crisis</td>
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<td></td>
<td>- If acute care is thought to be required, joint assessment should take place between early intervention team, crisis team and/or acute care team so that the least restrictive / stigmatising setting for care is arranged</td>
</tr>
<tr>
<td></td>
<td>- Avoidance of restrictive / stigmatising care wherever possible</td>
</tr>
<tr>
<td></td>
<td>- As much treatment provided in the community/service user’s home as possible</td>
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<tr>
<td></td>
<td>- Links with crisis team to ensure 24 hour crisis team available</td>
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</tbody>
</table>
### Inpatient and respite care

- Avoidance of hospitalisation if possible and provision of alternatives to hospital care e.g. community hostels, cluster homes, day care
- If hospitalisation is needed
  - Separate age, gender and culture appropriate accommodation should be provided
  - Regular, formal joint (inpatient and early intervention staff) review to ensure service user is transferred to the lowest stigma/restrictive environment as soon as clinically possible
- Early intervention team to be actively involved in discharge planning

- Avoidance of trauma and stigma associated with hospitalisation is important to reduce harm and ensure long term engagement
- Service user/family/carers involved in decision making and discharge planning as much as possible
- Primary care and other services to be involved in discharge planning as appropriate and kept informed of discharge plans
<table>
<thead>
<tr>
<th>What does an EI service do? (DoH 2001)</th>
<th>3: interventions (k)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regular review</strong></td>
<td></td>
</tr>
<tr>
<td>• Regular team review of effectiveness of care</td>
<td></td>
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<tr>
<td>• Second and third line pharmaceutical and range of psychological treatments considered where necessary</td>
<td></td>
</tr>
<tr>
<td>• Local evidence-based prescribing and therapy protocols should be developed and used</td>
<td></td>
</tr>
<tr>
<td>• Avoidance of and careful attention to side effects are important in ensuring effective treatment and long term engagement with services</td>
<td></td>
</tr>
<tr>
<td>• Service user actively involved in decision making and side effect monitoring</td>
<td></td>
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<tr>
<td>Discharge</td>
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<tr>
<td>The following discharge possibilities could be considered:</td>
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<tr>
<td>• If stable and well - discharge to primary care with yearly joint consultant/primary care review</td>
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<tr>
<td>• If unstable and fulfilling criteria for assertive outreach, refer to the Assertive Outreach Team</td>
<td></td>
</tr>
<tr>
<td>• If many negative symptoms and unwell, refer for rehabilitation and ongoing care</td>
<td></td>
</tr>
<tr>
<td>• If well but concerns about ability of primary care to care for service user - follow up as an outpatient</td>
<td></td>
</tr>
<tr>
<td>• If service user moves home before three years, the Early Intervention Team should continue care until care package established in new area</td>
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<p>| |</p>
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<tbody>
<tr>
<td>Usually a service user will require care from the Early Intervention Team for three years.</td>
</tr>
<tr>
<td>• There should however be flexibility regarding the ‘three years’ with early discharge arranged for stable service users and later discharge possible if engagement and stabilisation were problematical early in the course of illness</td>
</tr>
<tr>
<td>• Continuity of care is vital. Early intervention team should not disengage with the service user until adequate contact with other services has been established</td>
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</tbody>
</table>
Potential benefits of EI

- **Improving outcome in first-episode psychosis** (by detection and phase-specific treatment).
EI evidence: improving outcome in first-episode psychosis?

- Biggest study: integrated treatment (specialized team) v. standard care (OPUS-Scandinavia, RCT, $n = 547$) for 2 years (with follow-up also at 5y):
  - leaving study early: fewer people left in the specialized team group
  - attempted suicide: NS
  - compliance with treatment improved at 1y (RR stopped 0.20, NNT 9); NS at 2y
  - GAF symptom scores: favoured specialized team at 1y, NS by 2y, equivocal at 5y
  - GAF function scores: NS at 1y, favoured specialized team by 2y, equivocal at 5y
  - user satisfaction favoured specialized team
  - number of days in hospital at 1 year, 2y, 5y: NS
  - “has been hospitalized (yes/no)” by 5 years: NS
  - “living independently”: NS at 1y, NS at 2y; by 5 years favoured integrated treatment (RR 0.42, NNT 19)
  - unemployment: NS at 1y, favoured integrated treatment at 2y (RR 0.72, NNT 11), equivocal at 5y
Family therapy plus a specialised team for relapse: no effect (Netherlands); effect (China, RR for readmission 0.28, NNT 3).

Vocational intervention: employment likelier (RR 0.39, NNT 2, Australia)

Other small studies:
- CBT, for suicidality
- CBT, for hospitalization
- Ethyl-eicosapentaenoic acid, for response
- Brief intervention, for admission NS
- Adherence Coping Education
- Cannabis and psychosis therapy
- Crisis assessment, for hospitalization
- Behavioural intervention, for weight
EI evidence: improving outcome in first-episode psychosis?

“Whilst there is a compelling theoretical case for early intervention, much of the supporting evidence is circumstantial (based on the correlation between duration of untreated psychosis and outcome) rather than definitive (based on improved outcome in clinical trials). If this discrepancy persists, the obvious risk is that, eventually, early intervention will become routine practice, without its efficacy ever being definitively established.”

(Marshall & Rathbone 2011.)
Potential benefits of EI

• Improving outcome in first-episode psychosis (by detection and phase-specific treatment).

• Prevention of psychosis for people with prodromal symptoms.
Psychotic prodrome (1)

- Prodromal or prepsychotic symptoms include
  - a disturbance in the perception of self;
  - overvalued (attenuated delusional) ideas;
  - extreme preoccupation with overvalued ideas (including philosophical and mystical or religious themes);
  - disturbances of simple perception (such as unusually vivid perception, and distorted body perception);
  - attenuated (brief or mild or simple) hallucinations;
  - mild thought disorder (difficulty with conc"/memory/thought flow);
  - emotional disturbances (depression, suicidal ideation, anxiety, panic, mood instability, social anxiety, sleep disturbance, tension or restlessness, irritability or rage);
  - a feeling of loss of inner control;
  - and coping responses (such as alcohol or drug use, social isolation, or trying to socialize to cope).

- Behavioural indications of a prodromal state include leaving or truanting from school, university, or a job; marked and lasting shift of interests; marked and lasting social passivity, withdrawal, or isolation; and a marked and lasting change in global appearance or behaviour.

- Some cognitive impairment may already be present.
Psychotic prodrome (2): typical operational criteria

- **Yung’s “Ultra High Risk” (UHR) criteria**, assessed by the Comprehensive Assessment of At Risk Mental State (CAARMS) tool: any of
  - attenuated psychosis within the previous 12 months (either of subthreshold intensity or subthreshold frequency for the diagnosis of a psychotic disorder),
  - brief limited intermittent psychotic symptoms (BLIPS) lasting <1 week that spontaneously resolved within the previous 12 months, or
  - “trait and state” risk factors: a “trait” vulnerability (a presumed genetic vulnerability to psychosis: first-degree FH of a psychotic disorder or schizotypal personality disorder in patient) plus persistent low general functioning for at least 1 month within the previous 12 months.

- There are other criteria for the prodrome; one set (for “psychosis risk syndrome”) is proposed in the draft DSM-V.

- Early study: sensitivity 83–92% and specificity 62–74% for predicting the development of (full-blown) psychosis (e.g. Yung et al. 2003, 2005, 2006).

- However, ~76% of UHR patients made no transition to psychosis over 6–40 months (Simon et al. 2011 systematic review) [PPV ≈ 24%]. *Ethics of treatment?*
### Diversion: classification table

From that sensitivity/specificity/PPV, the implied prevalence is about 10% (*above background; pre-selection effect*). Imagine 1000 people:

<table>
<thead>
<tr>
<th></th>
<th>Disease present (104)</th>
<th>Disease absent (896)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test positive</strong></td>
<td>91 (true+)</td>
<td>287 (false+, T1err)</td>
</tr>
<tr>
<td><strong>Test negative</strong></td>
<td>13 (false−, T2err)</td>
<td>609 (true−)</td>
</tr>
</tbody>
</table>

... PPV [P(present|+)]: 0.24

... NPV [P(absent|−)]: 0.98

Sensitivity: [P(+|present)] 0.88

Specificity: [P(−|absent)] 0.68
EI evidence: intervention in the prodrome?

- **olanzapine**+nonspecific supportive therapy (NSST) v. placebo+NSST (PRIME-USA): NS for conversion to psychosis

- **CBT**+NSST v. NSST (EDIE-UK, EIPS-Germany): NS for conversion to psychosis

- **risperidone**+**CBT**+specialized team (ST) v. ST (PACE-Australia): active group less likely to develop psychosis at 6 months (NNT 4); NS at 12 months. *(Delayed, not prevented?)*

- **amisulpride**+needs-focused interventions (NFI) v. NFI (LIPS-Germany, NB open label): PANSS positive symptom scores and Global Assessment of Functioning favoured amisulpride at 3 months

- **omega-3 fatty acids** v. placebo (Amminger-Austria): essential fatty acid group less likely to develop psychosis than placebo (NNT 6) over 3 months

*(Marshall & Rathbone 2011, Cochrane review. Their conclusion: further evidence needed before firm recommendations possible.)*
Even earlier intervention: prevention of psychosis?

- Primary prevention, via population-modifiable risk factors.
- No established methods.
- Some correlative studies raise the possibility. *For example:*
  - Psychotic symptoms in 33,000 Swedish women (general population; Hedelin et al. 2010 PMID 20504323):
    - relative risk of high-frequency symptoms 0.53 in those eating fish 3–4 times/week, compared to those who never ate fish
    - RR 0.78 for high (versus low) omega-6 polyunsaturated fatty acids
    - fatty fish: lowest risk at intermediate level of consumption
    - RR 0.63 for high (versus low) vitamin D intake
  - Vitamin D supplementation in first year of life in Finland (birth year 1966, \( n=9,114 \)); McGrath et al. 2004 PMID 14984883):
    - irregular or regular vitamin D supplementation reduced risk of later schizophrenia (RR 0.08 and 0.12 respectively, compared to none)
    - \( \geq 2,000 \text{ IU/day} \) had further RR of 0.23 compared to lower doses
Assessment
Assessment of psychosis: key factors

- Establishing the presence and nature of psychosis (and any other symptoms). *(History, collateral, MSE.)* Consider rating scales (such as BPRS, PANSS, SAPS/SANS).

- Referral: (a) to secondary psychiatric care; (b) to early intervention services.

- Diagnosing the cause(s). *(History, collateral, MSE, physical exam, Ix.)*

- Appreciation of the broader context the patient is in: biological, psychological, social factors (which overlap!). Think about the impact *on* disease (predisposing, precipitating, perpetuating factors), the impact *of* disease (e.g. on social functioning, physical health), and protective/relieving factors.

- Engagement, rapport and therapeutic relationship (patient and family/friends; psychiatrist and multidisciplinary team).

- Assess risks: self-harm, harm to others, risks to physical health.

- Treatments. *For schizophrenia* (NICE), start with: antipsychotic drug with appropriate monitoring, interventions regarding recreational drug use, CBT, family intervention, consider arts therapies, regular physical health monitoring.
... and remember the EI policy (DH 2001):

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Comprehensive assessment to include as a minimum:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Service user centred, multidisciplinary assessment co-ordinated by care co-ordinator</td>
<td></td>
</tr>
<tr>
<td>- Sufficient time should be allowed to develop a relationship and let symptoms stabilise</td>
<td></td>
</tr>
<tr>
<td>- Physical Health Assessment where appropriate</td>
<td></td>
</tr>
<tr>
<td>- Psychiatric history</td>
<td></td>
</tr>
<tr>
<td>- Mental state examination</td>
<td></td>
</tr>
<tr>
<td>- Risk - including suicide risk</td>
<td></td>
</tr>
<tr>
<td>- Social functioning and resource assessment</td>
<td></td>
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<tr>
<td>- Psychological assessment</td>
<td></td>
</tr>
<tr>
<td>- Occupational assessment</td>
<td></td>
</tr>
<tr>
<td>- Family/support assessment</td>
<td></td>
</tr>
<tr>
<td>- Service user's aspirations and understanding</td>
<td></td>
</tr>
<tr>
<td>- Contribution from people important to the service user</td>
<td></td>
</tr>
</tbody>
</table>
Eliciting psychotic symptoms: examples from the PSE (1)

**Hallucinations**
- I should like to ask you a routine question which we ask of everybody. Do you ever seem to hear noises or voices when there is no one about, and nothing else to explain it?
- Have you had visions, or seen things other people couldn’t see?
- Is there anything unusual about the way things feel or taste or smell?

**Other perceptual abnormalities**
- Do you ever get the feeling that something odd is going on which you can’t explain?

**Thinking, thought reading/insertion/echo/broadcast**
- Can you think clearly or is there any interference with your thoughts?
- Are you in full control of your thoughts?
- Can people read your mind?
- Is anything like hypnotism or telepathy going on?
Eliciting psychotic symptoms: examples from the PSE (2)

**Delusions**
- Do you feel under the control of some force or power other than yourself?
- Do people seem to drop hints about you or say things with a double meaning, or do things in a special way so as to convey a meaning?
- Do things seem to be specially arranged?
- Is someone deliberately trying to harm you, such as trying to poison you or kill you?
- Do you think that people are organising things specially to help you?
- Is there anything special about you? Do you have special abilities or powers?
- Are you a very religious person?
- How do you explain the things that have been happening? *(SPECIFY)* Is anything like hypnotism, telepathy, or the occult going on? What is the explanation?
- Do you have any reason to be jealous of anybody?
- Have you had any unusual experience or adventure recently?
- Do you have committed a crime, or sinned greatly, or deserve punishment?
- Do you think your appearance is normal? Is there anything the matter with your brain? Is there anything the matter with your body?
- Do you have the feeling that something terrible is going to happen?
Eliciting psychotic symptoms: examples from the PSE (3)

Delusion or overvalued idea?

• Even when you seem to be most convinced, do you really feel in the back of your mind that it might well not be true, that it might be imagination?

For a likely delusion:

• How did it come into your mind that this was the explanation? (Did it happen suddenly? How did it begin?)

Insight

• Do you think there is anything the matter with you?
• What do you think it is? Could it be a nervous condition? What do you think the cause is? Why did you need to come to hospital?
• Do you think (specify delusions or hallucinations) were part of a nervous condition?
Eliciting psychotic symptoms (4)


Good summary.

(Though not everything listed as a “symptom of psychosis” here is a symptom of psychosis!)

Table 1. Symptoms of psychoses
- Positive symptoms
  - delusions and hallucinations
  - formal thought disorder
- Negative symptoms
  - flat affect
  - poverty of thought
  - lack of motivation
  - social withdrawal
- Cognitive symptoms
  - distractibility
  - impaired working memory
  - impaired executive function
- Mood symptoms
  - depression
  - elevation (mania)
- Anxiety/panic/perplexity
- Aggression/hostility/suicidal behaviour

Table 3. Questions for eliciting psychotic symptoms

<table>
<thead>
<tr>
<th>Anxiety</th>
<th>Have you been feeling especially nervous or fearful? Have you felt tense and shaky, or experienced palpitations?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood</td>
<td>Have you been feeling sad or ‘down in the dumps’ recently, not enjoying activities as much as before?</td>
</tr>
<tr>
<td>Elevated mood</td>
<td>Have you been feeling especially good in yourself, more cheerful than usual and full of life?</td>
</tr>
<tr>
<td>Auditory hallucinations</td>
<td>Do you hear voices of people talking to you even when there is no-one nearby?</td>
</tr>
<tr>
<td>Thought insertion</td>
<td>Have you felt that thoughts are being put into your mind? Do you experience telepathy?</td>
</tr>
<tr>
<td>Thought withdrawal</td>
<td>Have you experienced thoughts being taken out of your mind?</td>
</tr>
<tr>
<td>Thought broadcasting</td>
<td>Have you felt that other people are aware of your thoughts?</td>
</tr>
<tr>
<td>Thought echo</td>
<td>Have you experienced voices or people echoing your thoughts?</td>
</tr>
<tr>
<td>Delusion of control</td>
<td>Have you felt under the control or influence of an outside force?</td>
</tr>
<tr>
<td>Delusions of reference</td>
<td>Do programs on the television or radio hold special meaning for you?</td>
</tr>
<tr>
<td>Delusions of persecution</td>
<td>Do you feel that you are being singled out for special treatment? Is there a conspiracy against you?</td>
</tr>
<tr>
<td>Delusions of grandeur</td>
<td>Do you feel special, with unusual abilities or power?</td>
</tr>
<tr>
<td>Delusions of guilt</td>
<td>Do you believe that you have sinned or have done something deserving punishment?</td>
</tr>
</tbody>
</table>
SCHIZOPHRENIA. ICD-10 criteria for schizophrenia [10]. Layout as before. Further explanation of individual symptoms is given in italics.

<table>
<thead>
<tr>
<th>A. Core symptoms of schizophrenia*</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Passivity:</strong> delusions of control, influence, or passivity, clearly referred to body or limb movements…</td>
<td></td>
<td></td>
</tr>
<tr>
<td>… or to specific thoughts, actions, or sensations.</td>
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<tr>
<td><strong>Third-person auditory hallucinations:</strong> hallucinatory voices giving a running commentary on the patient’s behaviour</td>
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<td></td>
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<tr>
<td>… or discussing the patient among themselves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>… or other types of hallucinatory voices coming from some part of the body.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delusions:</strong> persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world).</td>
<td></td>
<td></td>
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<tr>
<td>Delusional perception (a normal perception, delusionally interpreted [1298])</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thought echo</strong> (hearing one’s own thoughts aloud, just before, just after, or simultaneously with the thought [1298])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>… thought <strong>withdrawal</strong> (the feeling that one’s thoughts have been removed by an outside agency [1298])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>… thought <strong>insertion</strong> (the feeling that one’s thoughts have been placed there from outside [1298])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>… or thought <strong>broadcasting</strong> (the feeling that one’s thoughts leave oneself and are diffused widely [1298], or are audible to others, or that others think the same thoughts in unison [1299])</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Other positive symptoms of schizophrenia</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hallucinations:</strong> persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thought disorder:</strong> breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Catatonia:</strong> catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor (see template for catatonia).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Read the ICD-10 original, too.
<table>
<thead>
<tr>
<th>C. Negative symptoms of schizophrenia</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative symptoms: “negative” symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. Additional criteria used in the diagnosis of simple schizophrenia</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>A significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marked decline in social, scholastic, or occupational performance.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Schizophrenia** requires at least 1 of group A, or at least 2 of groups B+C, present for most of the time for a month.
- Other diagnoses are used if these symptoms are present for less than a month (see Chapter 28.1).
- Exclusion criteria apply:
  - If the patient also meets criteria for a manic episode or depressive episode, the criteria for schizophrenia must have been met before the disturbance of mood developed.
  - The disorder is not attributable to organic brain disease or to alcohol or drug intoxication, dependence, or withdrawal.
- Subtypes of schizophrenia are shown on the next page.

* These core symptoms of schizophrenia are essentially Schneider’s first-rank symptoms of schizophrenia [18], with the addition of persistent delusions not relating to passivity. The first-rank symptoms are audible thoughts, voices arguing or discussing, voices commenting on the patient’s action, delusional perception, somatic passivity, made thoughts, made impulses, made volitional acts, made feelings, thought insertion, thought withdrawal, and thought broadcasting [1298, 1300].

(simple schizophrenia: C+D for 1 year)
Psychosis. “It’s schizophrenia.” Is it?

Know what else it might be. Think in categories. Some examples:

- **Primary psychiatric.** Affective (manic, depressive) psychosis (can have Schneiderian first-rank symptoms). Schizoaffective disorder. Persistent delusional disorder. Acute and transient psychotic disorders. Personality disorders with stress-induced psychotic symptoms.
- **Toxins,** e.g. drug-induced psychosis (recreational, therapeutic).
- **Delirium,** which isn’t a final diagnosis (carry on...).
- **Developmental disorders,** e.g. velocardiofacial syndrome.
- **Neurodegenerative disorders,** e.g. Alzheimer’s disease, frontotemporal dementia, Huntington’s disease.
- **Focal neurological disease,** e.g. stroke, tumours, epilepsy-associated psychosis, multiple sclerosis.
- **Infection,** e.g. viral encephalitis, malaria.
- **Autoimmune,** e.g. systemic lupus erythematosus, anti-NMDA receptor encephalitis.
- **Endocrine** (e.g. severe thyroid disease).
- **Metabolic** (e.g. porphyria, Niemann–Pick C, hypercalcaemia).
- **Nutritional** (e.g. pellagra).
- … etc.
Section 1: The causes of psychosis
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5 Neurodegenerative disorders 16
6 Focal neurological disease 25
7 Malignancy 38
8 Infectious and postinfectious syndromes 40
9 Endocrine disease 60
10 Inborn errors of metabolism 68
11 Nutritional deficiency 82
12 Other acquired metabolic disorders 89
13 Autoimmune rheumatic disorders and vasculitides 99
14 Other autoimmune encephalopathies 113
15 Poisoning 118
16 Sleep disorders 140
17 Sensory deprivation and impairment 142
18 Miscellaneous 143
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25.1 Suggested initial investigations in psychosis
The basic set of investigations is debated (e.g. [1256, 1257]), and we could find no good evidence as to which tests should be performed; this area is one dominated by a range of opinions. We suggest one initial set of investigations below, divided into “always do” and “always consider”, and then discuss the rationale for the tests. Tests have been included in this list only if they might be expected to yield an identifiable cause for psychosis or contribute substantially to general medical management or the drug treatment of psychosis.

<table>
<thead>
<tr>
<th>Always do:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <em>Bedside</em>: pulse oximetry, ECG*</td>
</tr>
<tr>
<td>• <em>Urine testing</em>: urine screen for common drugs of abuse (typically, cannabinoids, opiates, cocaine, amphetamines, MDMA, PCP, benzodiazepines, barbiturates); urinary βHCG in females who could be pregnant*</td>
</tr>
<tr>
<td>• <em>Haematology</em>: FBC, ESR</td>
</tr>
<tr>
<td>• <em>Biochemistry</em>: U&amp;E, BFT, LFT, CRP, TSH (with free T4 ± T3 if TSH abnormal), CK, vitamin B₁₂, red cell folate, random or fasting glucose*, random or fasting lipid profile*</td>
</tr>
<tr>
<td>• <em>Microbiology</em>: syphilis serology</td>
</tr>
<tr>
<td>Always consider from the outset:</td>
</tr>
<tr>
<td>• <em>Bedside</em>: fingerprick capillary glucose, urine dipstick</td>
</tr>
<tr>
<td>• <em>Haematology</em>: clotting (PT and APTT)</td>
</tr>
<tr>
<td>• <em>Biochemistry</em>: Mg</td>
</tr>
<tr>
<td>• <em>Immunology</em>: ANA (with subtyping if positive)</td>
</tr>
<tr>
<td>• <em>Radiology</em>: MRI brain (T1, T2, and FLAIR sequences)</td>
</tr>
<tr>
<td>• <em>Neurophysiology</em>: EEG</td>
</tr>
</tbody>
</table>

Investigations marked (*): rationale
These investigations are infrequently relevant to the diagnosis of psychosis without suggestive features in the history or examination, but have significant implications for choice of antipsychotic treatment [1256].
Early Intervention within CPFT

Contact us

If you need more information, advice or help from the CAMEO team, please get in touch with us by phone, e-mail, fax or letter. Our contact details are below. You could also check out our website:

www.cameo.nhs.uk

**CAMEO South**
Block 7, Ida Darwin, Fulbourn, Cambridge CB21 5EE

**T** 01223 884360  
**F** 01223 884362  
**E** cameosouth@cpft.nhs.uk

**CAMEO North**
53 Thorpe Road, Peterborough, Cambs PE3 6AN

**T** 01733 318102  
**F** 01733 318114  
**E** cameonorth@cpft.nhs.uk

For information about CPFT services or to raise an issue, contact the Patient Advice and Liaison Service (PALS) on Freephone 0800 376 0775, or e-mail pals@cpft.nhs.uk

Cambridge and Peterborough NHS Foundation Trust
Understanding mental health, understanding people

Cameo
Early Intervention Services
April 2010

For people with early symptoms of psychosis
Schizophrenia in the exams
A patient saw a cat cross the road and knew immediately that there was a conspiracy by the government to kill him. What is this psychopathological phenomenon termed?

A. passivity phenomenon
B. phobia
C. delusional mood
D. delusional perception
E. functional hallucination
Paper 1: smaller

Which structure is proportionally smaller in schizophrenia?

A. Lateral ventricles
B. Striatum
C. Left inferior frontal lobe
D. Prefrontal cortex
E. Hippocampus
Paper 1: passivity

A young man has passivity phenomena and third-person auditory hallucinations. Which is the most likely risk factor?

A. losing mother before age 14
B. alcohol abuse
C. HLA-DQB1/DQA1
D. immigrant status
E. childhood sexual abuse
Paper 1: poison

You are interviewing a patient for the first time. She tells you that her neighbours have given her a poison that has made her intestines stop working. Which should you do?

A. Ask her to tell you more about the problem.
B. Offer blood tests, an intestinal workup.
C. Agree that some poisons can do this.
D. Tell her that this is very unlikely.
E. Suggest she contact the police.
Which of these is not classified under F20 (Schizophrenia) in ICD-10?

A. disorganized schizophrenia
B. post-schizophrenic depression
C. schizoaffective disorder
D. residual schizophrenia
E. simple schizophrenia
Paper 1: direction

A patient shows marked changes in direction of thought between grammatically correct, coherent individual sentences. What is this termed?

A. Deviation  
B. Derailment  
C. Drivelling  
D. Verbigeration  
E. Wittering
A young man was admitted for treatment of an acute psychotic episode 3 days ago. Today you find him febrile and sweating with tachycardia and muscular rigidity. Which is the most likely diagnosis?

A. hyperthyroidism
B. varicella zoster virus encephalitis
C. serotonin syndrome
D. neutropenic sepsis
E. neuroleptic malignant syndrome
Paper 1: persecution

A man is admitted to your unit. He has delusions of persecution and feels guilty about past misdeeds. He also complains of low mood, and his concentration is poor; he does not enjoy his customary pursuits. His appetite is reduced, he has lost weight, and he is not sleeping well. What is the most likely diagnosis?

A. depressive episode
B. schizophrenia
C. bipolar affective disorder
D. hyperparathyroidism
E. delusional disorder
A patient has the experience of hearing his own thoughts out loud a few seconds after he thinks them. What is this termed?

A. Gedankenlautwerden
B. Gegenhalten
C. Mitmachen
D. Vorbeigehen
E. Wahnstimmung
Paper 1: choice of therapy

A. cognitive–behavioural therapy
B. dialectical–behavioural therapy
C. family intervention
D. cognitive–analytical therapy
E. eye movement desensitization
F. psychodrama
G. relationship counselling
H. motivational interviewing
I. Gestalt therapy

Which would you advise for (pick ONE each):

A young man with bizarre delusions and social withdrawal who is just being discharged from hospital; his mother thinks he’s lazy.

...
Paper 1: thought disorder

A. Fusion  
B. Asyndesis  
C. Condensation  
D. Drivelling  
E. Substitution  
F. Clang association  
G. Neologism  
H. Tangentiality  
I. Perseveration

Which ONE?

* A major thought stops and is replaced by a minor thought.  
* Heterogeneous elements of thought are interwoven with each other.  
* There is a lack of connection between successive thoughts.
A drug has zero-order kinetics. How many half-lives does it take to reach steady state?

A. 3
B. 5
C. 7
D. 9
E. 11
Paper 2: least likely

Which is LEAST likely to be true of schizophrenia?

A. Prenatal infections predispose to schizophrenia.
B. Visual hallucinations do not invalidate the diagnosis.
C. Abnormalities on neurological examination are consistent with the diagnosis of schizophrenia.
D. Dopamine and glutamate abnormalities contribute to the development of psychosis.
E. Tau mutations cause schizophrenia.
A patient with schizophrenia has liver disease and a glomerular filtration rate of 120 ml/min. He needs an antipsychotic. Pick the best:

A. chlorpromazine
B. clozapine
C. olanzapine
D. amisulpride
E. risperidone
A patient with schizophrenia has read that schizophrenics perform badly on the Hayling test, and asks you to explain this to him. What process does it test?

A. visual short-term memory
B. phonological priming
C. immediate recall
D. delayed recall
E. response inhibition
Here are some frequencies:

A) 1–5%
B) 5–15%
C) 15–25%
D) 25–35%
E) 35–45%
F) 45–55%
G) 55–65%
H) 65–75%
I) 75–85%
J) 85–95%

A 30-year-old woman has had bizarre delusions and disorganised speech. She has now recovered and asks you about risks to her family. What is the risk of the same condition developing in (pick ONE each):

- her healthy 12-year-old son when he is an adult?
- her 28-year-old sister?
- her sister’s son, who has Down’s syndrome, when he is adult?
Paper 2: mutations

A) microtubule-associated protein tau (MAPT)
B) DISC1
C) dysbindin (DTNBP1)
D) Notch
E) presenilin 1
F) presenilin 2
G) leucine-rich repeat kinase 2 (LRRK-2)
H) neuregulin-1 (NRG1)
I) alpha-synuclein (SNCA)
J) PTEN-induced putative kinase 1 (PINK-1)

Mutations of which genes are associated with:
• Schizophrenia (THREE)?
Subjects are recruited to a randomized controlled trial of psychosis and given new treatment drug X or usual treatment of chlorpromazine. Patients are randomly allocated to one of the two treatments. In this study, 15% of patients given drug X decide to stop and switch to the usual treatment, and of those that remain, 120 out of 300 have extrapyramidal side effects and the treatment is effective in 55%. In contrast, all patients given chlorpromazine finish the study, and of them, 225 out of 450 have extrapyramidal side effects and the treatment is effective in 60%.

What should be done about the patients that were allocated to treatment X but dropped out?

a) they should be analysed as if they had continued on drug X
b) they should be analysed as if they had been in the control group
c) their data should be dropped from the study entirely
d) their data should be replaced by data from randomly selected patients on drug X who completed the study
e) their data should be replaced by the mean final measure for patients on drug X who completed the study
Paper 3: schizophreniform

Which of the following diseases can cause a schizophreniform psychosis?

A. acromegaly
B. generalized anxiety disorder
C. anorexia nervosa
D. Huntington’s disease
E. severe pain
Paper 3: learning disability

What is the risk of schizophrenia in someone with learning disability?

A. 1%
B. 3%
C. 5%
D. 7%
E. 9%
CASC

STATION 1.

Mr John Hathaway is a 16-year-old who has been referred to you by his GP, who is concerned he may have psychotic symptoms.

* Assess his mental state.
* In the next station, you will discuss your management plan with your consultant.

STATION 2.

Relevant physical examination and investigations are all normal.

* Discuss the case and your management plan with Dr Wilbur, your consultant.
References (PMID = PubMed ID)


- **OPUS at 5y.** Bertelsen et al. (2008) PMID 18606949.


- **Differential diagnosis.** Cardinal & Bullmore (2011) *The Diagnosis of Psychosis,* CUP.

- **Present State Examination (PSE).** Wing et al. (1974), CUP.


Paper 1: ANSWERS

Cat: D (delusional perception).
Smaller: not sure (somewhat duff question); E best? Hippocampus smaller (PMID 9596046, meta-analysis); lateral ventricles larger (e.g. PMID 9850225); striatal sub-nuclei can be smaller (15539860, 17306506, 19616411); lots of cortical regions can be smaller (see 21312403).
Passivity: D? Diagnosis is SZ. A/B/C irrelevant. Immigrant status: incident rate ratios 2.3 (1st gen), 2.1 (2nd gen) (PMID 20663257). Childhood sexual abuse: data not as good; psychotic disorders, RR ~2; schizophrenia, maybe closer to 1? (reviews PMID 22033827, 18003630).
Poison: A.
F20: C (schizoaffective disorder is F25); A is a synonym listed in ICD10 for F20.1 (hebephrenic SZ); B is F20.4; D is F20.5; E is F20.6.
Direction: B (derailment = Entgeleisen = knight’s move).
Febrile: E (NMS).
Persecution: A. Depressive psychosis is the most likely.
Out loud: A. Gedankenlautwerden = écho de la pensée = hearing thoughts out loud. (Wikipedia 26/1/12 opts for Gedankenlautwerden = hearing thoughts at the same time and é.d.l.p. = hearing thoughts after the thought, but historically they were simply coined in different countries, translate to more or less the same thing, and have been used in overlapping ways, so caveat Wikipedior.) (One of the “foreign languages” questions.) (Blom 2010 A Dictionary of Hallucinations.)
Choice of therapy: probably C (family interventions). The question suggests schizophrenia; CBT and family interventions are effective; the question emphasizes (adverse) expressed emotion, which is a predictor of relapse, and a target of family interventions. (NICE CG82.)
Thought disorder: E (substitution), A (fusion), B (asynodesis = loosening of association).
**Kinetics: broken question.** There’s no such thing as a half-life when kinetics are zero-order. (Zero-order kinetics = like alcohol, e.g. ~1 unit metabolized per hour, regardless of starting level.) Don’t get upset more than briefly; guess; move on. (For first order kinetics, which is probably what they meant, the strictly correct answer is infinity, but the practical answer is usually given as 5 half-lives, at which point you’re $1 - 0.5^5 = 97\%$ of the way to steady state, so guess B).

**Least likely: E (tau mutations);** tau mutations cause frontotemporal dementia with parkinsonism (FTDP-17) and perhaps other tauopathies (PMID 18948254).

**Comorbid: D (amisulpride).** BNF: All antipsychotic drugs can precipitate coma if used in hepatic impairment; phenothiazines are hepatotoxic. BNF/eMC: amisulpride is the best choice (weakly metabolised, renally excreted).

**Hayling: E (response inhibition/suppression)** is tested by the Hayling Sentence Completion Test (complete the sentences // complete the sentences with a nonsense word).

**Family: B, B, A.** SZ. Son = children: 9.7–12.3%. Sister = siblings: 6.7–13.8%. Nephew with Down’s: harder. Nephew/nieces 2.3%. Learning disability ~3%, Down’s specifically ~1.6% (PMID 6996080, 1422617, 19267267 = 19048420.)

**Mutations: B (DISC1), C (dysbindin), H (neuregulin).**
**Paper 3: ANSWERS**

**Design:** A. The last-observation-carried-forward (LOCF) technique is the standard measure in the psychiatric literature. (Not perfect, though: Saha & Jones 2008 doi:10.1016/j.jspi.2008.04.017)

**Schizophreniform:** D. Huntington’s disease can cause schizophreniform psychosis; no evidence for the others. (PMID 8929949; Cardinal & Bullmore 2011.)

**Learning disability:** B. 3% would be a good overall estimate. (PMID 19267267 = 19048420, page 28, summarizes other studies with frequencies, of SZ occurring in LD, of 3.7%, 6.2%, 3.2%, 3.4%, 1.8%, 3%, 3%, 1.3%, and [70.8%,18.7%,2.1%, overall 8.3%] depending on LD severity.)