Annex 1

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)[38]

Level		Therapy /Prevention. Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
I		At least one controlled clinical trial appropriately randomized				
	a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
	b	Individual RCT (with narrow Confidence Interval‡)	Individual inception cohort study with > 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
	c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses ††††

(.../...)

(.../...)

Level		Therapy /Prevention. Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
II	Cohort studies and studies of final outcomes					
	a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
	b	Individual cohort study (including low quality RCT; e.g., < 80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good††reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
	c	"Outcomes" research, ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research

(.../...)

(.../...)

Level		Therapy /Prevention. Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
III	Case-controls					
	a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
	b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
IV		Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	SCase-series or superseded reference standards	Analysis with no sensitivity analysis
V		Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Notes

Users can add a minus-sign "-" to denote the level of that fails to provide a conclusive answer because of:

- EITHER a single result with a wide Confidence Interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)
- OR a Systematic Review with troublesome (and statistically significant) heterogeneity.
- Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

(.../...)

(.../...)

* By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

† Clinical Decision Rule. (These are algorithms or scoring systems which lead to a prognostic estimation or a diagnostic category.)

‡ See note #2 for advice on how to understand, rate and use trials or other studies with wide confidence intervals.

§ Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

§§ By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

§§§ Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.

†† An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.

‡‡ Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.

††† Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.

†††† Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.

** Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.

*** By poor quality prognostic cohort study we mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in < 80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.

**** Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (eg 1-6 months acute, 1-5 years chronic)

Grades of recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies or extrapolations from level 1 studies
C	level 4 studies or extrapolations from level 2 or 3 studies
D	level 5 evidence or troublingly inconsistent or inconclusive studies of any level

"Extrapolations" sare where data is used in a situation which has potentially clinically important differences than the original study situation.

Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M. Levels of evidence and grades of recommendations, 1998. Review May 2001. Center for Evidence-Based Medicine (CEBM) of Oxford Available in English at: http://cebm.jr2.ox.ac.uk

Annex 2

Diagnostic criteria for ADHD according to DSM-IV[31]

A) Meets either Group 1 or Group 2 criteria.

A-Group 1) Six (or more) of the following symptoms of inattention must have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

	QUESTIONS ABOUT INATTENTION	Yes	No
1.	Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.	☐	☐
2.	Often has difficulty sustaining attention in tasks or play activities.	☐	☐
3.	Often does not seem to listen when spoken to directly.	☐	☐
4.	Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)..	☐	☐
5.	Often has difficulty organizing tasks and activities.	☐	☐
6.	Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort.	☐	☐
7.	Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools).	☐	☐
8.	Is often easily distracted by extraneous stimuli.	☐	☐
9.	Is often forgetful in daily activities.	☐	☐
	Total score (Number of affirmative answers)	_____	

A-Group 2) Six (or more) of the following symptoms of hyperactivity-impulsivity must have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

	QUESTIONS ABOUT HYPERACTIVITY	Yes	No
1.	Often fidgets with hands (for example: fluttering movements) or feet or squirms in seat.	☐	☐
2.	Often leaves seat in classroom or in other situations in which remaining seated is expected.	☐	☐
3.	Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).	☐	☐
4.	Often has difficulty playing or engaging in leisure activities quietly.	☐	☐
5.	Is often "on the go" or often acts as if "driven by motor".	☐	☐
6.	Often talks excessively.		

(.../...)

(.../...)

	QUESTIONS ABOUT IMPULSIVITY	Yes	No
7.	Often blurts out answers before questions have been completed.	☐	☐
8.	Often has difficulty waiting turn.	☐	☐
9.	Often interrupts or intrudes on others (e.g., butts into conversations or games).	☐	☐
	Total score (Number of affirmative answers)	_____	

B) At least some of the hyperactive-impulsive or inattentive symptoms that cause impairment must have been present before age 7 years.

C) There must be clear evidence of impairment in social, academic, or occupational functioning.

D) Some of the disturbances caused by the symptoms need to be present in two or more settings (e.g., at school [or work] and at home).

E) The symptoms must not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

CLASSIFICATION OF SUBTYPES

Combined. Meets criteria for attention deficit and hyperactivity and impulsivity.

Attention deficit alone or predominantly inattentive. Meets criteria for attention deficit, but not for hyperactivity and impulsivity.

Hyperactivity alone. Meets criteria for hyperactivity and impulsivity, but not for attention deficit.

Annex 3

Diagnostic questionnaire for dysfunctional voiding.

Clinical questionnaire on dysfunctional voiding. Farhat et al[86]

Name .....

Age ..... Sex: Boy/Girl .....

File number ..... Dates .....

Over the last month	Almost never or never	Less than half of the time	About half the time	Almost every time	Not available
1. I have had wet clothes or wet underwear during the day.	0	1	2	3	N/A
2. When I wet myself, my underwear is soaked.	0	1	2	3	N/A
3. I miss having a bowel movement every day	0	1	2	3	N/A
4. I have to push for my bowel movements to come out	0	1	2	3	N/A
5. I only go to the bathroom one or two times each day	0	1	2	3	N/A
6. I can hold onto my pee by crossing my legs, squatting or doing the "pee dance".	0	1	2	3	N/A
7. When I have to pee, I cannot wait.	0	1	2	3	N/A
8. I Have to push to pee.	0	1	2	3	N/A
9. When I pee it hurts.	0	1	2	3	N/A
10 Parents to answer. Has your child experienced something stressful like the example below?	No (0)		Yes (3)		

TOTAL .....

Examples:
- New baby
- New home
- New school
- School problems
- Abuse (sexual/physical)
- Home problems (divorce/death)
- Special events (birthday)
- Accident/Injury

Others: .....