Confusion in the General Hospital

S O'Keeffe

Galway University Hospitals

Why Does Cognitive Impairment Matter?

- Common
- Atypical presentation of illness in aged
- Unpleasant
- Serious consequences

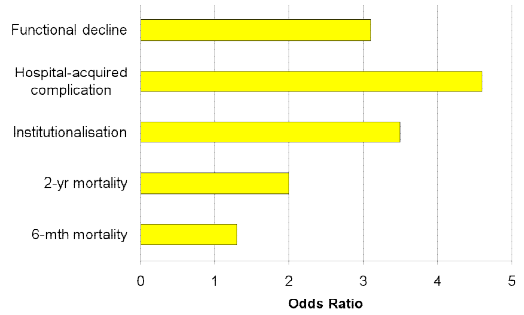
Atypical Presentation of Acute Illness

	Well Older N=67	Frail Older N=117
% atypical present	25%	59%
Delirium	**32%**	**61%**
Falls	37%	9%
Immobility	5%	6%
Functional decline	26%	19%

Jarrett et al. Arch Int Med 1995

Outcomes of Delirium

(adjusted for confounding variables)



Even worse if....Delirium superimposed on dementia: a systematic review. Fick et al. JAGS 2002

BJPsych The British Journal of Psychiatry (2009) 195, 61–66. doi: 10.1192/bjp.bp.108.055335

Dementia in the acute hospital: prospective cohort study of prevalence and mortality

Elizabeth L. Sampson, Martin R. Blanchard, Louise Jones, Adrian Tookman and Michael King

Table 4 Cox proportional hazard models for death during index admission associated with cognitive impairment and dementia in people over 70 years of age during acute hospital admission

			Mortality during index admission					
			Unadjusted			Adjusted[a]		
	Median survival, days	Deaths, % (n=75)	Hazard ratio (95% CI)	χ^2 (d.f.=1)	P	Hazard ratio (95% CI)	χ^2 (d.f.=1)	P
MMSE score								
24–30 (n=321)	18	7.5	1			1		
16–23 (n=141)	12	10.0	1.57 (0.73–3.39)			1.34 (0.60–3.15)		
0–15 (n=155)	11	24.0	4.02 (2.24–7.36)	22.50	<0.001	2.62 (1.28–5.39)	34.14	<0.001

Recoverable Cognitive Dysfunction In Older Persons During Acute Illness

Inouye et al, J Gen Intern Med 2006

- Defined as an MMSE score that improved by 3 or more points by discharge
- RCD in 179 of 460 (39%) consecutive 70y+ patients
- 80% did not meet criteria for delirium, and 81% cases did not meet criteria for dementia
- RCD was independently predictive of 1-year mortality (adjusted OR 1.82 (95% CI 1.03-3.20).

Why Do People with Cognitive Impairment Do Badly?

- Dementia and delirium have adverse physical and mental consequences
- Acute illness as a stress test for the brain - delirium (?RCD) is a marker for physical and mental frailty
- Failure of hospital systems and design
- Failure of 'health care professionals'
  - Poor recognition and delayed treatment
  - Preventative and environmental measures not used
  - Misuse of medications, restraints
- Failure of the 'experts'
  - Limited evidence base
  - Poorly taught

Cognitive impairment

Incontinence/ Catheter

Falls, instability

Functional decline
Institutional care
Prolonged stay
Mortality

Poor nutrition

Restraints/ Psychoactive meds

Nosocomial infections

Poor hydration

Skin breakdown

Detection of Cognitive Impairment

Is Cognitive Impairment Missed?

- Dementia: 50% acute hospitals (Bynum, JAGS 2004)
- Delirium
  - General wards: 40-60%
  - Hip fracture patients: 90% missed (Milisen, J Geront Nurs 2002)
  - Emergency dept: 83% (Hustey, Ann Emerg Med 2002)

Why?

- Cognition, except orientation, not assessed
- Style of interaction by nurses minimises chance of detecting problems (Treloar & MacDonald, J R Soc Med 1995)
- Hypoactive delirium easily misdiagnosed as depressed
- Hyperactive delirium difficult to miss but labelled as 'confused' 'demented' 'agitated'

How to miss delirium

- Keep any talk with patients to a minimum and do not assess cognitive function
- If by mischance you identify cognitive impairment, assume it is long-standing
- Never talk to nurses, especially night staff
- If patient is withdrawn, start an antidepressant
- If patient is noisy, start a benzodiazepine

Pejorative labels instead of diagnosis?

(O'Keeffe Eur Ger Med 2011)

Dx	'Vague' (N=28)	'Poor historian' (N=76)	'Poorly motivated' (N=21)
Cognitive	16 (57%)	44 (58%)	8 (38%)
Depressed	3 (11%)	10 (13%)	14 (67%)
Either	17 (61%)	51 (67%)	18 (86%)

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Patient Deemed Poor Historian

Unable to identify five causes of Pelopponesian Wars

PHILADELPHIA, PA--COPD sufferer Hank Spencer was found to be an extremely poor historian by admitting house staff.

Dr. Karen Filmer, a junior resident, was one of the first to evaluate Spencer in the Medical Emergency Department.

"*He knew something about post-Civil War American history. But when it came to the ancient civilizations of Egypt, Greece, and Rome, he simply didn't have a clear grasp of the basic principles underlying the important events in those eras*."

How not to diagnose delirium

Impairment	DSM 3	DSM 3R	DSM4
Attention	+	+	+
Acute onset	+	+	+
Fluctuations	+	+	+
Consciousness	+	+	+
Memory	+	+	+
Orientation	+	+	+
Perception	+	+	+
Language	+	+	+
Sleep-wake	+	+	±
Psychomotor	+	+	±
Emotional	-	-	±
Organic cause	+	+	-
	2/4	2/6	1/4

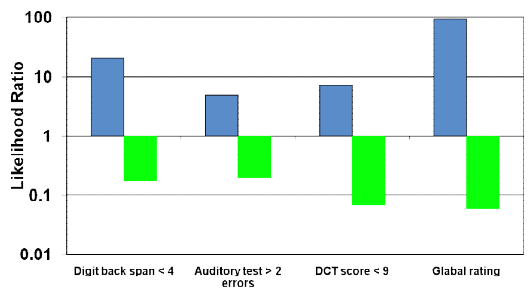
Diagnostic Tools

	Sensitivity	Specificity
• CAM	0.5 - 0.9	0.90
Acute onset & fluctuating course; inattention; disorganized thinking; altered level of consciousness		
• Serial AMT*	0.9	0.85
• Serial MMSE*	0.9	0.9

*Fall of 2 or more points

Inouye 1990, Trepzacz 1998, Jitapunkel 1992, Ni Chonchubhair 1995, O'Keeffe 2005

Formal tests *versus* Global assessment of attentiveness for the diagnosis of delirium (N=87)



O'Keeffe & Gosney, JAGS 1998

How to diagnose delirium

- Delirium as default diagnosis if 'agitated', 'confused', 'vague', 'uncooperative', or 'poor historian'
- History from informant usually gives diagnosis
- Impairment of attentiveness & consciousness the primary cognitive deficits
  - Dementia: patient alert and pays attention to examiner (even if performs poorly)
  - Delirium: patient not alert and unable to pay attention for long, may be lethargic or distractible

If You Can't Beat Em.....

(O'Keeffe et al JNNP 2011)

Orientation to time as a guide to the presence and severity of cognitive impairment in older hospital patients

Emma O'Keeffe, Osman Mukhtar, Shaun T O'Keeffe

ABSTRACT

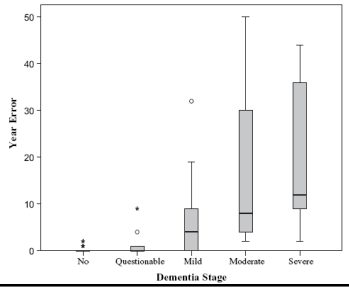
Background Testing of orientation to time is an important part of mental status examination. The validity of errors in different aspects of temporal orientation was examined in older hospital patients as a guide to the presence of dementia or delirium and as a measure of the severity of dementia, as defined by the Global Deterioration Scale.

aged between 65 and 84 years (1981).[4] Nevertheless, the frequency of temporal disorientation in their study was 1% in 90 patients aged 65–74 years and 6% in 72 patients aged 75–84 years. Brotchie *et al* used a different questionnaire to study temporal orientation in 235 hospital visitors aged 50–84 years.[5] They noted that less than 2% misstated the year or month but that errors in

Table 1 Sensitivity, specificity and likelihood ratios (with 95% CIs) of temporal orientation tests

Test	Sensitivity	Specificity
Year (any error)	0.86 (0.78 to 0.91)	0.94 (0.92 to 0.96)
Month (any error)	0.69 (0.60 to 0.78)	0.86 (0.83 to 0.89)
Date (any error)	0.95 (0.88 to 0.98)	0.38 (0.36 to 0.39)
Day of week (any error)	0.58 (0.48 to 0.68)	0.82 (0.79 to 0.85)
Time of day (≥1 h error)	0.77 (0.67 to 0.86)	0.70 (0.66 to 0.72)

LR, likelihood ratio.

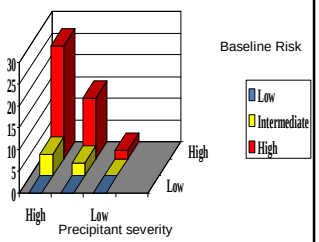


Treat contributing/ exacerbating factors?

Treat Cause of Delirium?

- Blaming the final straw for breaking the camel's back
- Causation in younger people:
  - Principle of parsimony or Occam's razor
  - "*Pluralitas non est ponenda sine neccesitate*" William of Ockham (14th C)

- Causation in older people
  - Usually multifactorial
  - Inverse relationship between baseline vulnerability and severity of precipitant needed to provoke illness



Inouye, JAMA 1996

Delirium: A Useless Differential Diagnosis

TABLE 3. Possible causes of delirium

Medications
- Psychotropics (anxiolytics, sedative-hypnotics, barbiturates, antidepressants, antipsychotics, lithium)
- Anticonvulsants
- Analgesics
- Anticholinergics (antihistamines, antispasmodics, antiparkinsonian agents)
- Antiarrhythmics
- Antihypertensives
- Aminoglycoside antibiotics
- Miscellaneous (cimetidine, steroids, nonsteroidal anti-inflammatory drugs, salicylates)

Drugs of abuse (phencyclidine and hallucinogenic agents)

Alcohol

Poisons (heavy metals, organic solvents, methyl alcohol, ethylene glycol, insecticides, carbon monoxide)

Withdrawal syndromes
- Alcohol
- Sedatives and hypnotics

Cardiovascular
- Congestive heart failure
- Cardiac arrhythmia
- Myocardial infarction

Neurologic
- Head trauma
- Space-occupying lesions: tumor, subdural hematoma, abscess, aneurysm
- Cerebrovascular diseases: thrombosis, embolism, arteritis, hemorrhage, hypertensive encephalopathy
- Degenerative disorders: Alzheimer disease, multiple sclerosis
- Epilepsy

Infection
- Intracranial: encephalitis and meningitis (viral, bacterial, fungal, protozoal)
- Systemic: Pneumonia, septicemia, subacute bacterial endocarditis, influenza, typhoid, typhus, infectious mononucleosis, infectious hepatitis, acute rheumatic fever, malaria, mumps, diphtheria, AIDS

Metabolic
- Hypoxia
- Hypoglycemia
- Acid–base imbalance: acidosis, alkalosis
- Electrolyte imbalance: elevated or decreased sodium, potassium, calcium, magnesium
- Water imbalance: inappropriate antidiuretic hormone, water intoxication, dehydration
- Failure of vital organs: liver, kidney, lung
- Inborn errors of metabolism: porphyria, Wilson disease, carcinoid syndrome
- Remote effects of carcinoma
- Vitamin deficiency: thiamine (Wernicke encephalopathy), nicotinic acid, folate, cyanocobalamin

Endocrine
- Thyroid: thyrotoxicosis, myxedema
- Parathyroid: hypo-and hyperparathyroidism
- Adrenal: Addison disease, Cushing syndrome
- Pancreas: hypoglycemia, diabetes
- Pituitary hypofunction

Hematologic
- Pernicious anemia

Delirium: A Useful Differential Diagnosis

- Meds
- Meds
- Meds
- Infection
- Hypoxia
- Metabolic problems
- Some combination
- Something else

Acute disturbance in dementia

+Pain

+Full bladder

Rockwood & MacKnight, 2001

Cholinergic system and cognition

- Affected by age and Alzheimer's disease
- Sensitive to metabolic insults e.g. hypoxia, thiamine deficiency, hypoglycaemia
- Involved in regulation of memory, attention and sleep
- Anticholinergic medications a common cause of delirium

Anticholinergic Burden

- Cumulative effect of multiple medications acting on the cholinergic nervous system
- Factors that may influence ACh burden:
  - Multiple medications with ACh effects
  - Drug exposure and ACh potency and muscarinic receptor subtype selectivity for each individual agent
  - Co-morbid conditions (such as dementia)
  - Pharmacokinetic changes with aging
  - Drug interactions
  - Blood-brain barrier integrity

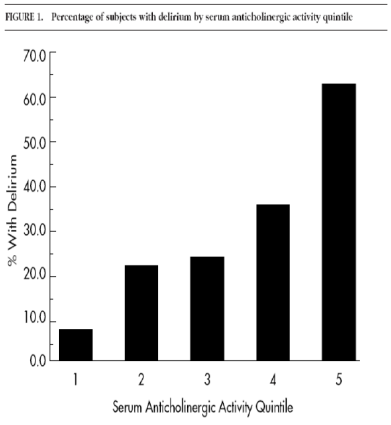
Drugs Producing Anticholinergic Activity (based on in vitro ACh binding)

Tune LE. J Clin Psychiatry 2001

Theophylline	Dipyridamole
Prednisolone	Furosemide
Cimetidine	Hydrochlorothiazide
Ranitidine	Hydralazine
Codeine	Isosorbide mononitrate
Diazepam	Methyldopa
Flurazepam	Nifedipine
Oxazepam	Triamterene
Oxycodone	Warfarin
Phenelzine	Alprazolam
Captopril	Chlordiazepoxide
Chlorthalidone	Ampicillin
Digoxin	Gentamycin
Diltiazem	

Clinical Impact of ACh Burden

- Strong predictor of mild cognitive impairment in elderly people (Ancelin et al. BMJ 2006)
- Predicts clinical severity of delirium symptoms in older medical inpatients (Han et al. Arch Intern Med 2001
- Increased risk of anticholinergic adverse effects, including delirium, in older inpatients (Rudolph et al. Arch Intern Med 2008
- Bidirectional prescribing cascades involving cholinesterase inhibitors and anticholinergic drugs (Gill et al. Arch Intern Med 2005; Noyen et al, Biol Psychiatry. 2003)



Flacker JM et al. Am J Geriatr Psychiatry 1998;6:31-41.

What are we treating? And why?

- Relieve distress
- Treat psychotic symptoms
- Shorten duration delirium
- Improve cognitive function?
- Hyperactive vs hypoactive?

Delusions in Delirium (N=123)

	Normal (58)	Dementia (65)
Distressing	42 (72%)	48 (74%)
Harm from staff	20 (53%)	16 (24%)
Abandonment	21 (36%)	40 (62%)
Theft	10 (17%)	21 (31%)
Bizarre/complex	20 (34%)	8 (12%)
Party/entertainment	11 (19%)	4 (6%)
Recall after delirium	21/42 (50%)	5/40 (13%)

Visual hallucinations in Delirium (N=155)

Multiple visual hallucinations	108 (70%)
Simple (Lights/shapes)	7 (5%)
Panoramas	10 (6%)
Objects	8 (5%)
Complex	149 (96%)
'Presence'/'Passage'	18 (12%)
People	104 (67%)
Animals	62 (40%)
Hybrids	5 (3%)
Body parts	11 (7%)

Animals (N=62)

- Dogs (12)
  – 3 familiar
- Cats (5)
  – 2 familiar
- Cattle (15)
- Sheep (8)
  – 1 familiar

- Rats (8)
- Snake (5)
- Bats (4)
- Spiders (3)
- Ants (2)
- Birds (2)
- Frogs (1)
- Tiger (1)
- Giraffe (1)
- Monkey (1)
- Zoo/farm scene (6) – 'like Noah's Ark'

General themes

- Fighting
- Fornicating
- Eating
  - Other patients
  - Each other

People (N=104)

- Family/friends (45)
  - Dead (25)
- Strangers (63)
- Public figures/Others (9)
- Ghostly figures (6)

- Lilliputian – 18 (17%)
- Giants – 2 (2%)
- Distorted – 24 (23%)

Strangers (N=63)

- Children (19)

- Nuns (9)
  - Good ones (3)
  - Not so good ones (6)
    - Carrying gun
    - Two headed
    - Drinking pints
    - Naked below waist

- 'Nurses' with a difference (7)
  - Naked/semi-naked (3)
  - Murderous/weapon-carrying (2)
  - Drinking (2)
  - Flying (1)

- 'Doctors' with a difference (4)
  - Armed with hatchet
  - Three legged
  - Tiny head 'like acorn'
  - Deliberately vomiting on patients

Response to hallucination

Unpleasant

Snakes/rats/spiders
Nuns
Nurses
Doctors
Devil

Puzzling

Domestic /farm animals
Children
Look alikes
Body parts

Pleasant

Lilliputian figures
Family/friends

Delirium-related distress predicted by…

- Psychotic symptoms (delusions > hallucinations)

- Uncorrected visual impairment

- Prior history anxiety or depression

Randomized Double Blind Trials?

- 1 × Treatment:
  - Haloperidol vs lorazepam vs chlorpromazine in delirious HIV patients (N=30) (Breitbart et al Am J Psychiatr 1996) → haloperidol and chlorpromazine superior
- 7 × Prevention:
  - Haloperidol (1.5mg/d) reduced duration, not incidence, of delirium hip-surgery pts (N=430) (Kalisvaart et al. JAGS 2005)
  - Donepezil no effect in 2 studies in orthopedic pts (Liptzin 2005, Sampson 2007)
  - Gabapentin reduced delirium in 22 spinal surgical pts (Leung et al, Neurology 2006)
  - Dexmedetomidine less delirium than midazolam, 3 ICU studies (eg Riker et al, JAMA 2009)

Using Antipsychotics

- ? Only for agitated/ psychotic patients
  - Distress/psychosis in quiet delirium also
- Haloperidol
  - Remains gold standard
  - Little anticholinergic, sedative, hypotensive or arrhythmic; highest potency
  - Can be administered po, im and iv (unlicensed)
  - EPS - prolonged use, > 3mg /d
  - Effect in 2 hours for oral, 45 min for i.m.
- Olanzapine if sedation needed; quetiapine if EPS

Safety of Antipsychotics?

- Risks
  - Oversedation, disinhibition
  - ? Prolong cognitive impairment
  - Arrhythmias (torsades de pointes)
  - Parkinsonism (esp PD, Lewy body disease)
- Relevance of concerns in dementia? mortality, strokes, cardiac events
  - Cohort study 27,000 matched pairs (Gill et al, Ann Intern Med 2007): Mortality ↑↑ for conventional, ↑ for atypical vs nonusers, **present by 30 days** and persisted

American Psychiatric Association guidelines

- Monitor ECG if using antipsychotics for delirium.
- Reduce or discontinue if QTc >450ms or 25% increase from baseline

BUT (QT interval, JAMA 2003)

- Gene/environment interaction likely
- Poor reliability of measuring QT interval (+ cannot rely on automated readings)
- Clinical significance of QT in individuals unproven for most drugs

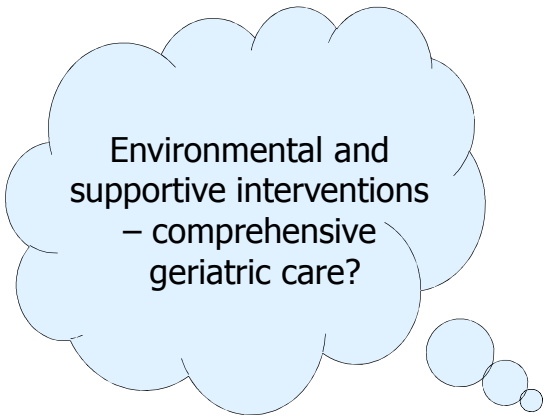
Real life pharmacotherapy

- Antipsychotics: Too much, too late
  - Intermittent chemical cosh' rather than regular low-dose treatment
  - No dose titration, and disregard of age, weight, sex
- Overuse of benzodiazepines
  - Routine use of sleeping tablets on prn sheet
  - Primary use to treat delirium

Judge not, lest ye be judged….?

Carnes et al, JAGS 2003

- 275 physician members AGS given delirium vignettes
- For severe delirium
  - 180 chose haloperidol alone,
  - 55 chose lorazepam alone
  - 23 chose lorazepam in combination with haloperidol
  - 12 wrote in another drug.
- 61% of those selecting haloperidol chose a dose greater than that recommended for older patients.



Prevent harm

- Maintain nutrition & hydration
  - Oral if possible, ? nutritional supplements
  - SC route
  - Thiamine/ multivit supplements in alcohol abuse, ? Others
- Avoid unnecessary interventions
- Delirium patients may benefit from subintensive care (delirium unit, own nurse) (Flaherty, J Geront 2004)

Provide a supportive environment

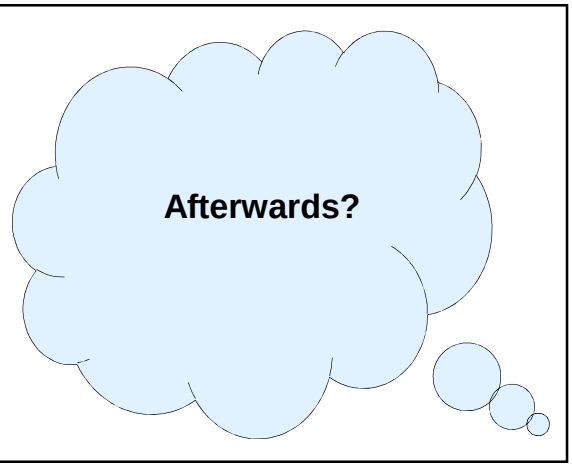
- Communicate clearly
- Repeated orientation and reassurance
- Involve family
- Control sources of excess noise
- Correct sensory problems: glasses, hearing aid
- Encourage self care, mobility
- Calender, clocks, orientation, photos may help
- Send home as soon as possible

What really happens

- Environmental strategies rarely used Meagher et al, Br J Psych 1996
- Fluids often out of reach (Simpson, Age Ageing 1996)
- Weight loss common (Inouye, Am J Med 1998)
- Catheter if incontinent or dehydrated
- Aggression answered with aggression
- 'Agitated confusion' predicts use of and risk of injury from bedrails
- Easier to get MRI than glasses, hearing aids, etc

Effectiveness of these measures?

- Prevention: Reduced frequency and severity of delirium (Inouye et al, NEJM 1999)
- Few RCTs on comprehensive treatment
  - Cole et al. CMAJ 2002: geriatric consultation in delirium (N=227) → no effect cognition, survival, hospital stay, Barthel, length of delirium
  - Lundström et al. JAGS 2005: staff education (N=125)→ delirium resolved faster, length of stay↓
  - Pitkala et al. J Gerontol 2006: comprehensive geriatric care (N=174): delirium resolved faster, cognition improved, no effect on institutionalization/mortality
- Wrong question – humane care



Prolonged cognitive impairment after delirium

- Residual impairment at 6 months in 80% of 125 delirium patients (Levkoff 1991)
- Mean 2 year decline in MMSE: 3.3 with and 0.6 without delirium (Francis 1992)
- Persistent delirium at 6 months in a third of 412 patients (Kiely et al, JAGS 2009)
- New dementia during 3 year follow up: 23/124 (19%) non-delirium and 9/15 (60%) delirium (Rockwood 1999)

Need to 'Debrief' Patients?

- Characteristic anterograde amnesia for period of delirium *(Roth, Int Psychoger 1991)*

BUT

- Post-traumatic stress disorder – case reports, ICU pts
- 101 cancer pts post-delirium *(Breitbart et al, Psychosomatics 2002)*
  - Recall in 62% younger and 33% older pts
  - Mean distress (0-4): 3.2 patients if recall
  - Distress related to presence of delusions or hallucinations
  - Distress did not vary with delirium subtype

Recall?

	N.
Hallucinations	54/105 (51%)
Delusions	41/105 (39%)
Poor insight	12/80 (15%)
Fear of recurrence	34/80 (43%)
Distress 6 months	5/53 (9%)

Where do we go?

- Develop evidence base
- Education: attitudes & knowledge
  - Undergraduate to postgraduate
  - Medical and nursing
  - Repetition
- Research into how to achieve

To fail to recognize delirium is to practise with an unsatisfying disengagement with one's patients' lives…. Who would accept looking at a young trauma patient with numerous injuries and giving only a half-hearted effort ?

Rockwood, CMAJ 2002