Executive Function Impairment in Patients with Medical Illness

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Disclosure

- Clinical Trials: Myriad, Pfizer, GSK, Neurochem
- CLOX and EXIT25 were developed at UTHSCSA

Learning Objectives

- To define executive function and give clinical examples of executive function impairment
- To describe potential causes of executive function impairment in patients with medical illness
- To describe the relationship between executive function impairment and functional status in elders

Executive Function

- The ability to think abstractly and to plan, initiate, sequence, monitor and stop complex behavior

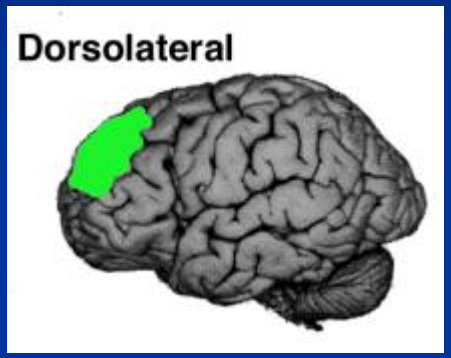
- Two Major Conceptual Themes
  - Frontal lobe function: insight, will, abstraction, and judgment
  - Behavioral regulation of nonexecutive processes

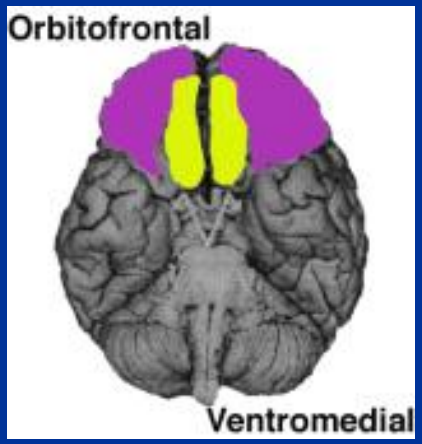
Executive Function

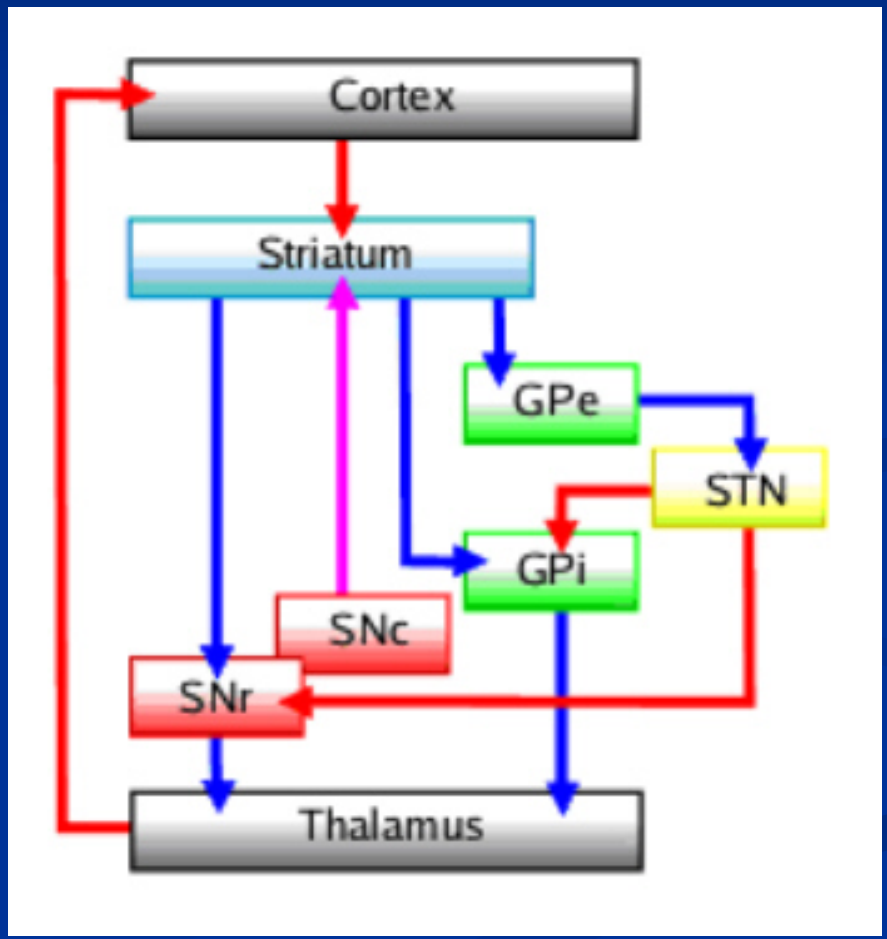
- That set of cognitive processes that allow one to behave independent of the environment instead of having behaviors mediated by the environment.

- Examples:
  - Cooking
  - Driving
  - Riding a bike

Prefrontal Circuits







Psychiatric Illness and Executive Impairment

- Dementia
- Depression
- Bipolar Disorder
- ADHD
- Substance Disorders
- Schizophrenia
- Personality Disorders

Medical Illness and Executive Impairment

- Peripheral arterial disease
- Hypertension
- Diabetes
- COPD
- OSA
- CHF
- HIV
- Lung cancer
- ESRD (dialysis)

Executive Function and Behavior

- Apathy
  - “Depression”
  - Perseveration
  - Impaired set shifting
- Disinhibition
  - Stimulus bound
  - Impulsivity
  - Aggression
  - Imitation Behavior

Examples of Executive Errors

- Perseveration: uncontrollable repetition
- Impulsivity: impaired self regulation
- Set Shifting
- Response inhibition

Bedside Executive Measures

- CLOX: An Executive Clock Drawing Task
- The Executive Interview (EXIT25)
- Controlled Oral Word Association Test
- Design Fluency Task
- Trailmaking Test, Part B

The Executive Interview (EXIT25)

- 25 item bedside scale
- Items derived from frontal lobe sequelae
- 15 minutes, lay interviewers
- Scored 0-50, higher scores worse
- 15/50 best discriminates healthy elderly from demented subjects (ROC, c=.93)
- Normal *young* adults rarely >07/50

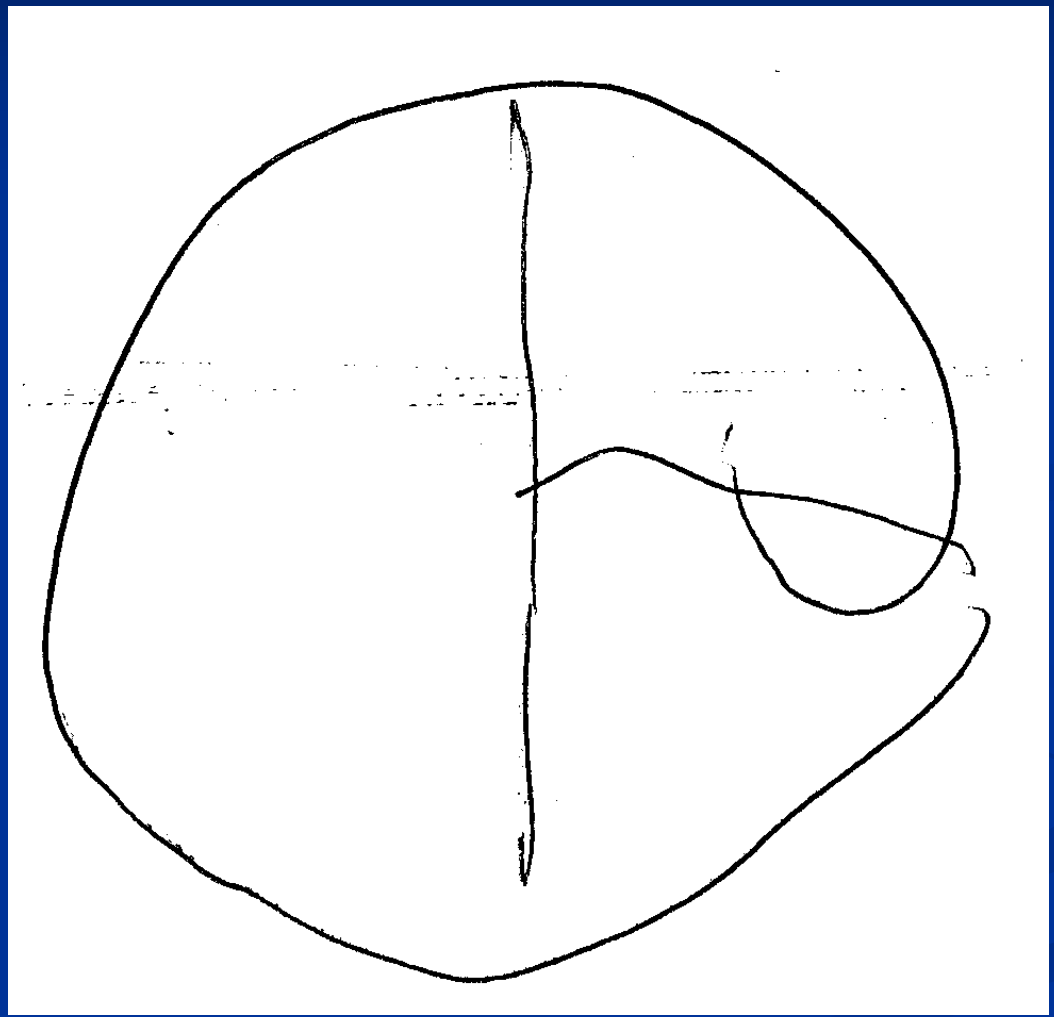
Instructions: CLOX1

1) Place the blank side of the CLOX form in front of the subject.
2) State “Draw me a clock that says 1:45. Set the hands and numbers on the face so that a child could read them.”
3) Once the subject begins the task, no further assistance is allowed (i.e. no prompting or repeat instructions)

Grading CLOX

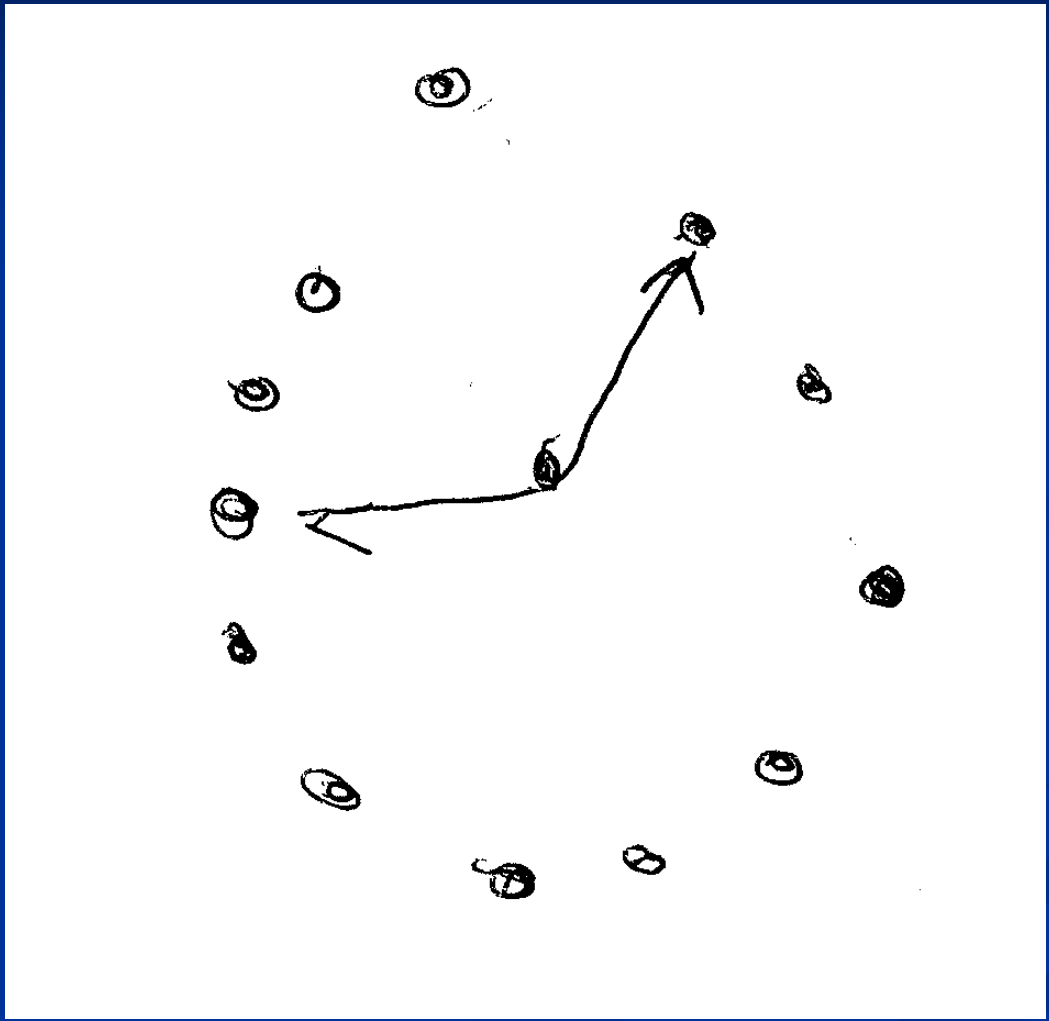
- Subject gets one point for each of the following 15 items

Does the figure resemble a clock?



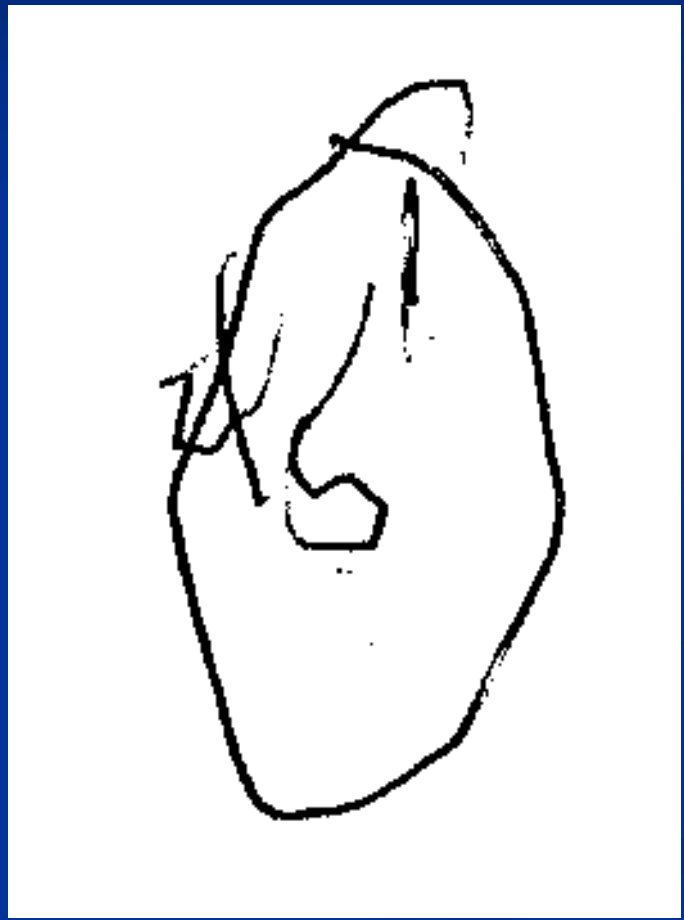
- 52yr with Depression NOS

Outer circle present?



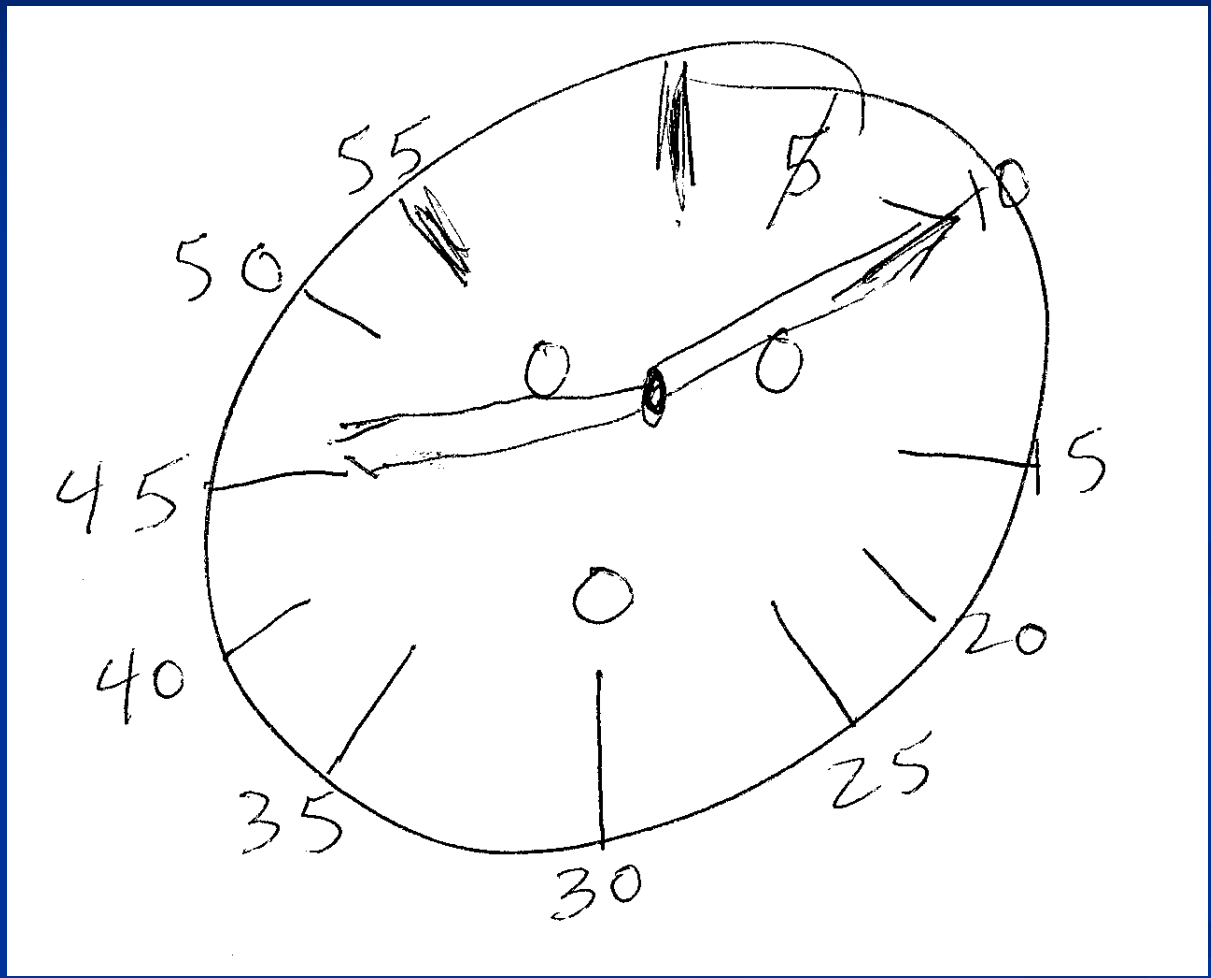
- 52yr with EtOH Dependence and Major Depression

Diameter greater than one inch?



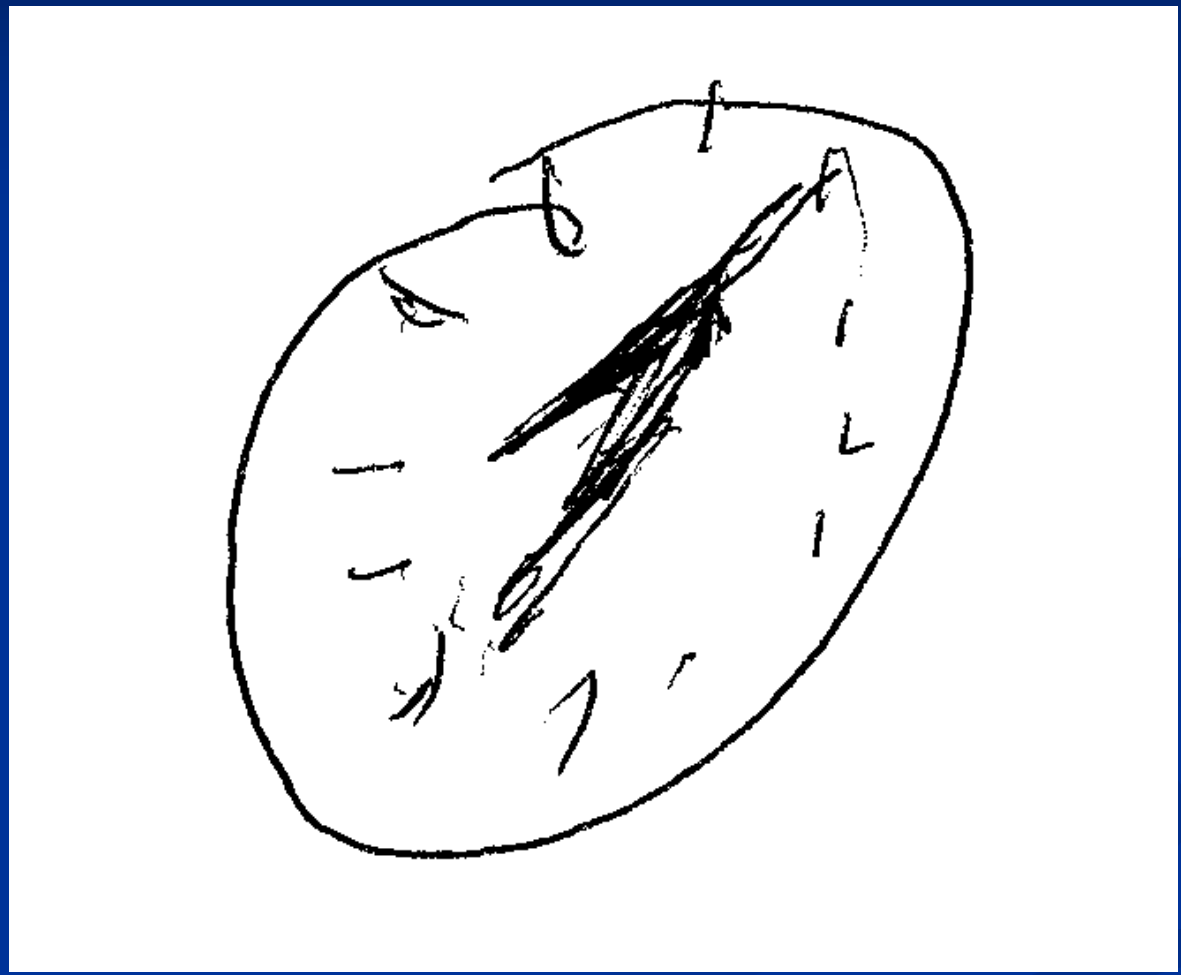
- 75yr with Vascular Dementia

All numbers in the circle?



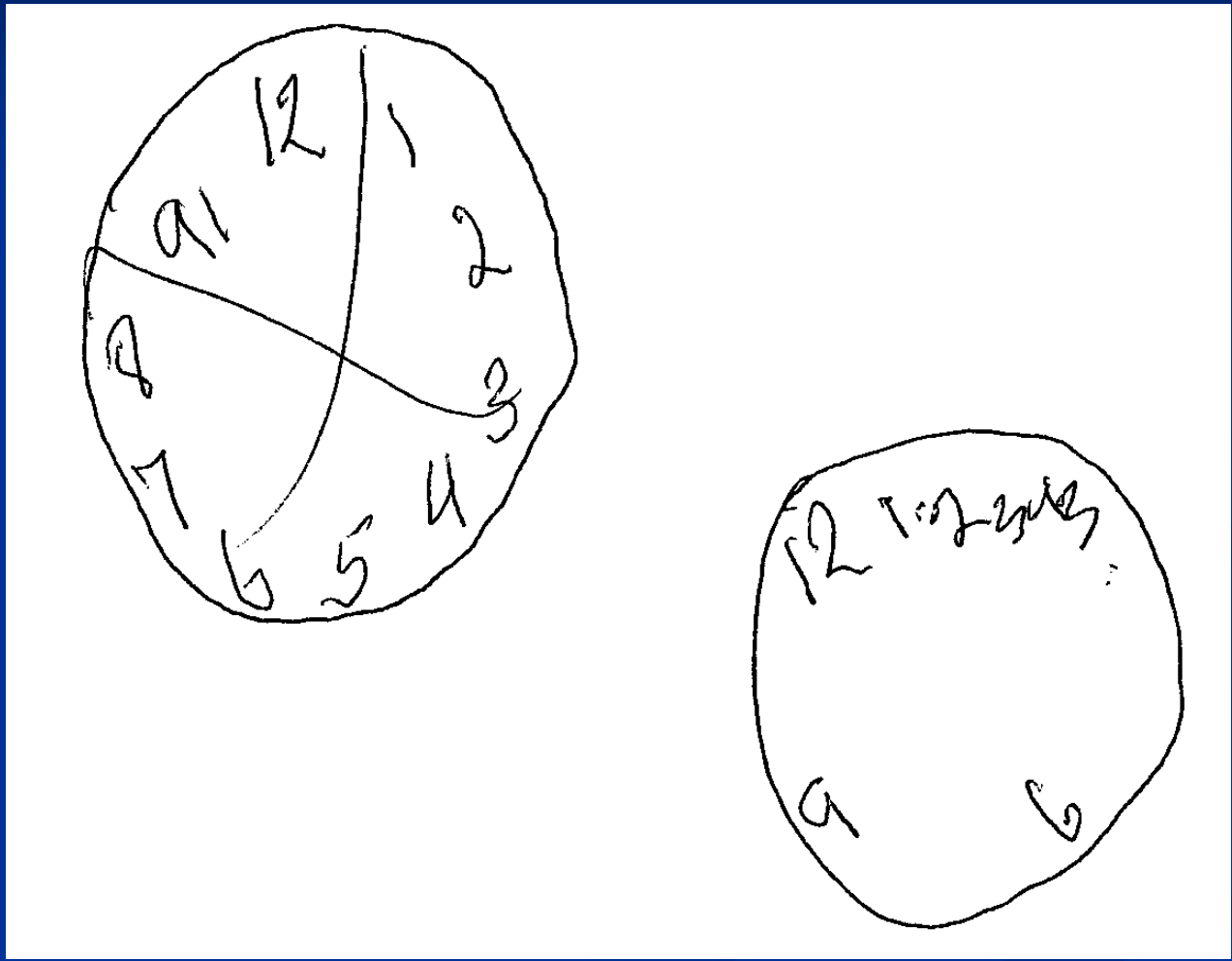
- 37yr with Mood d/o secondary to HIV

No sectoring or tic marks?



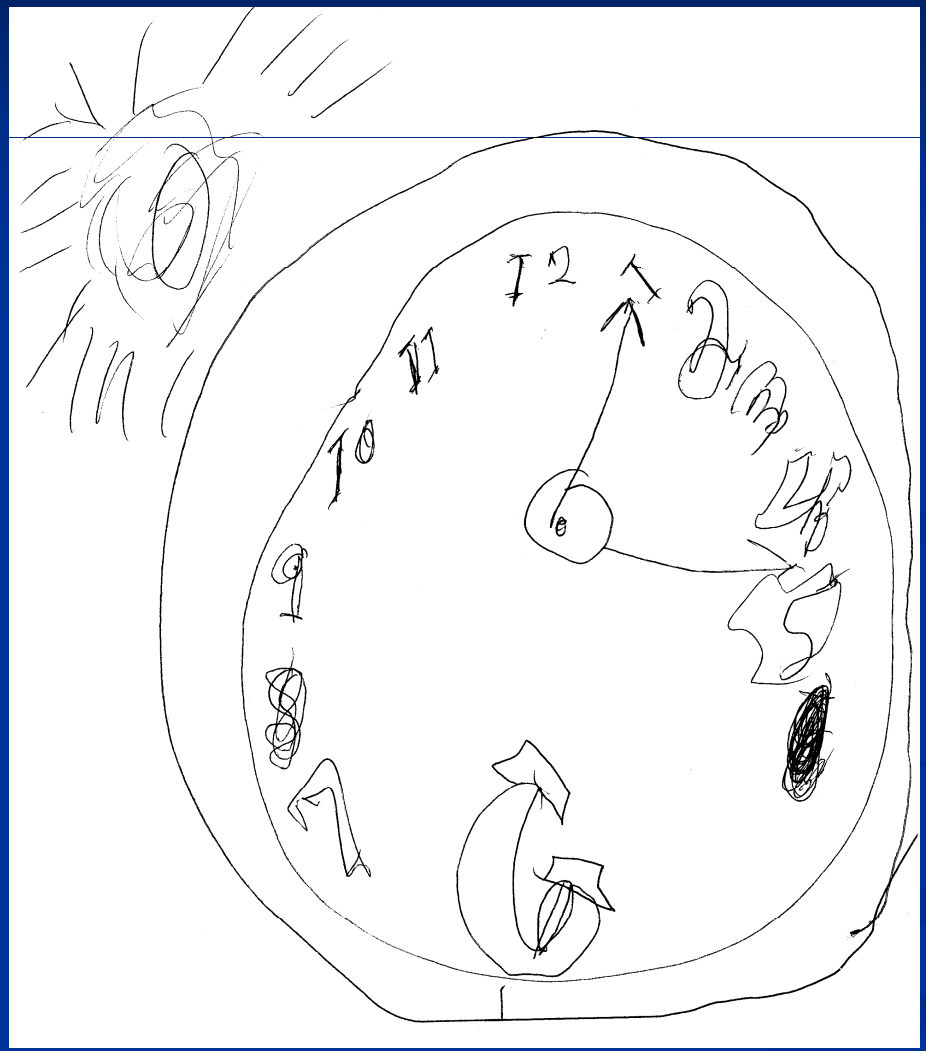
- 23yr with End-Stage Renal Disease

12, 6, 3, and 9 placed first?



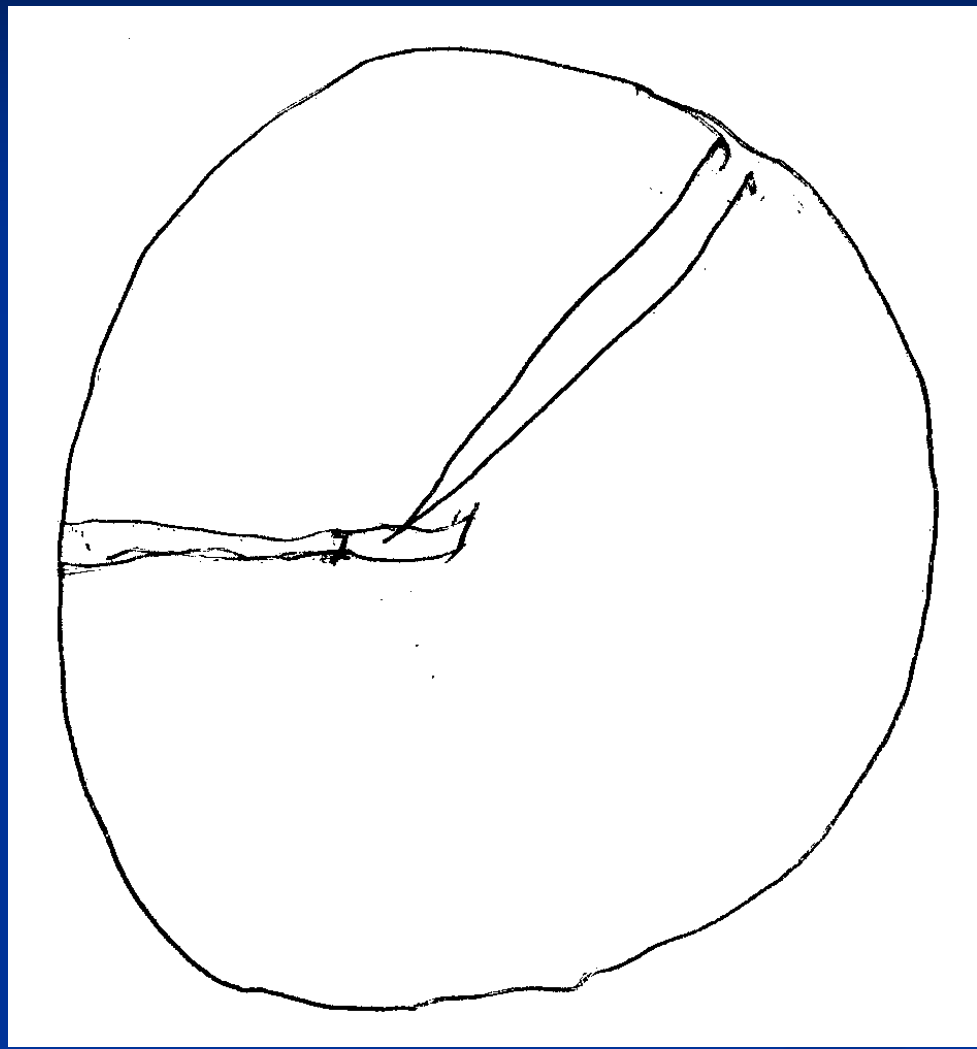
- 43yr with Schizophrenia

Spacing intact?



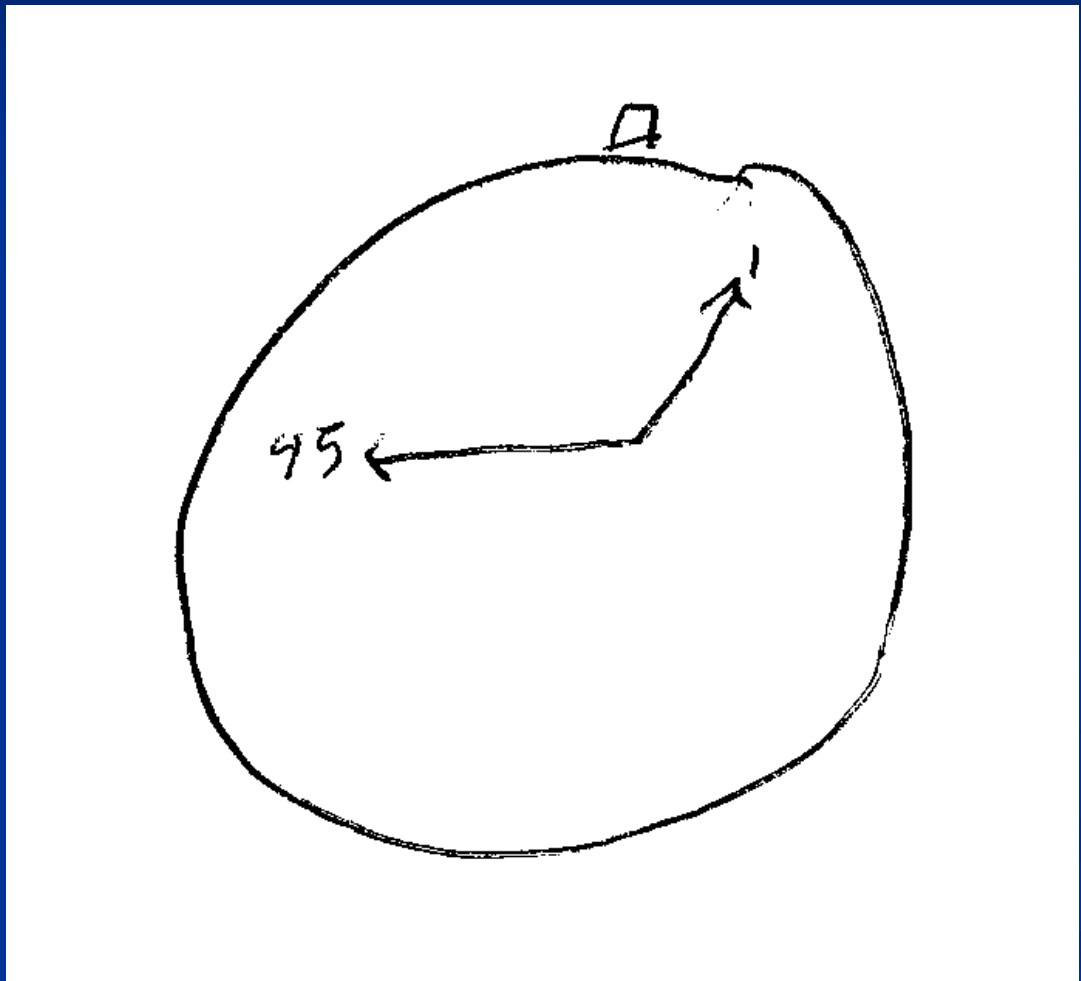
- 52yr with Schizoaffective d/o, bipolar type

Only Arabic numerals?



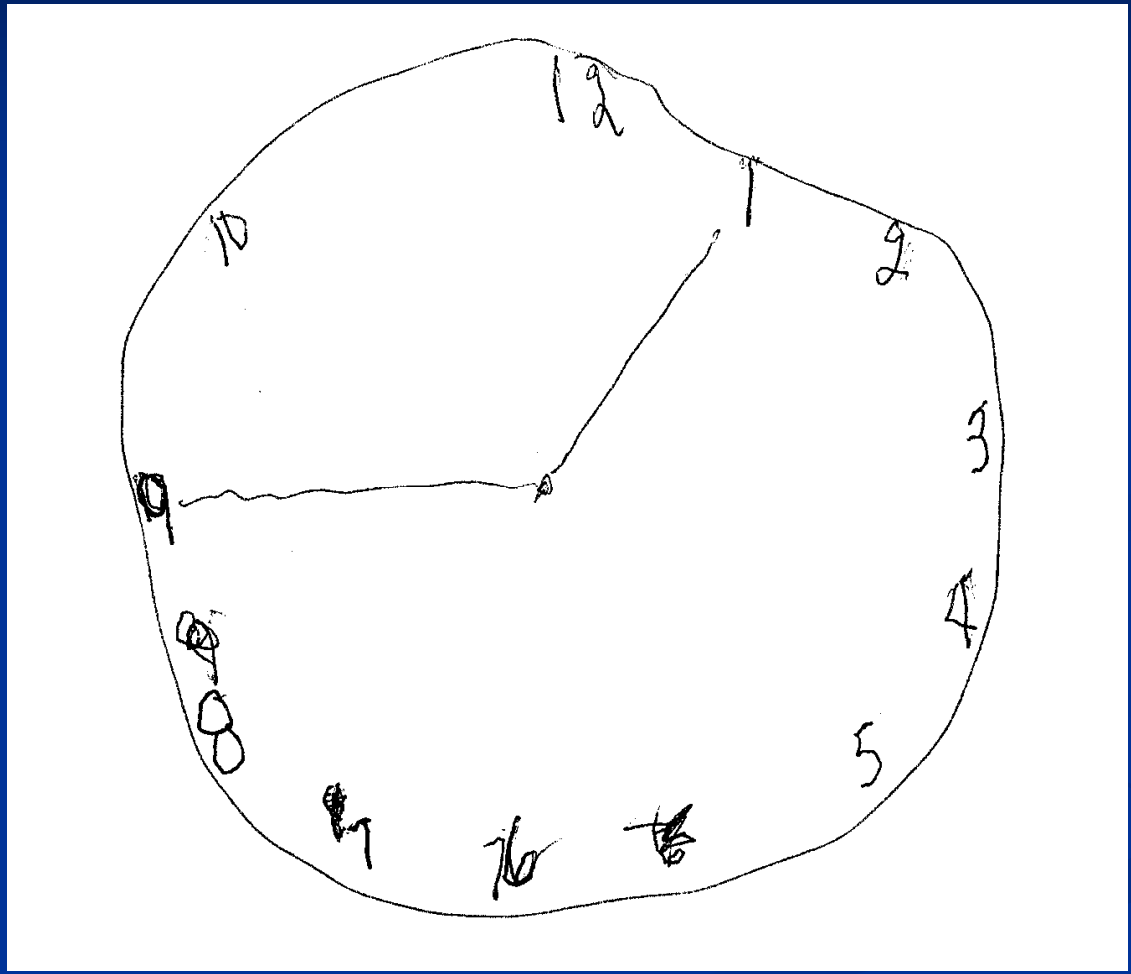
- 60yr with Schizoaffective d/o, bipolar type

Only numbers 1-12 among the Arabic numerals present?



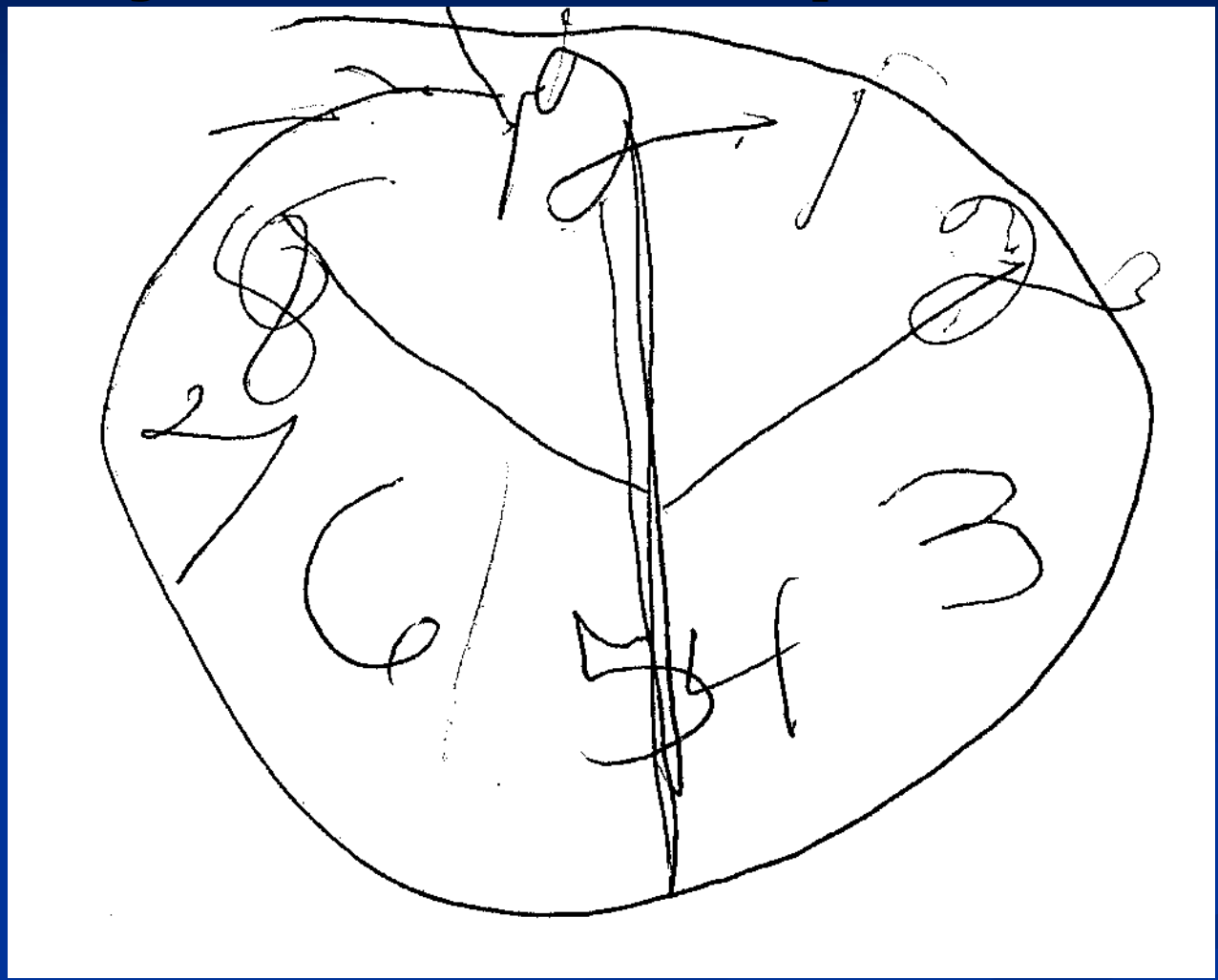
- 51yr with Schizoaffective d/o

Is the sequence 1-12 intact?



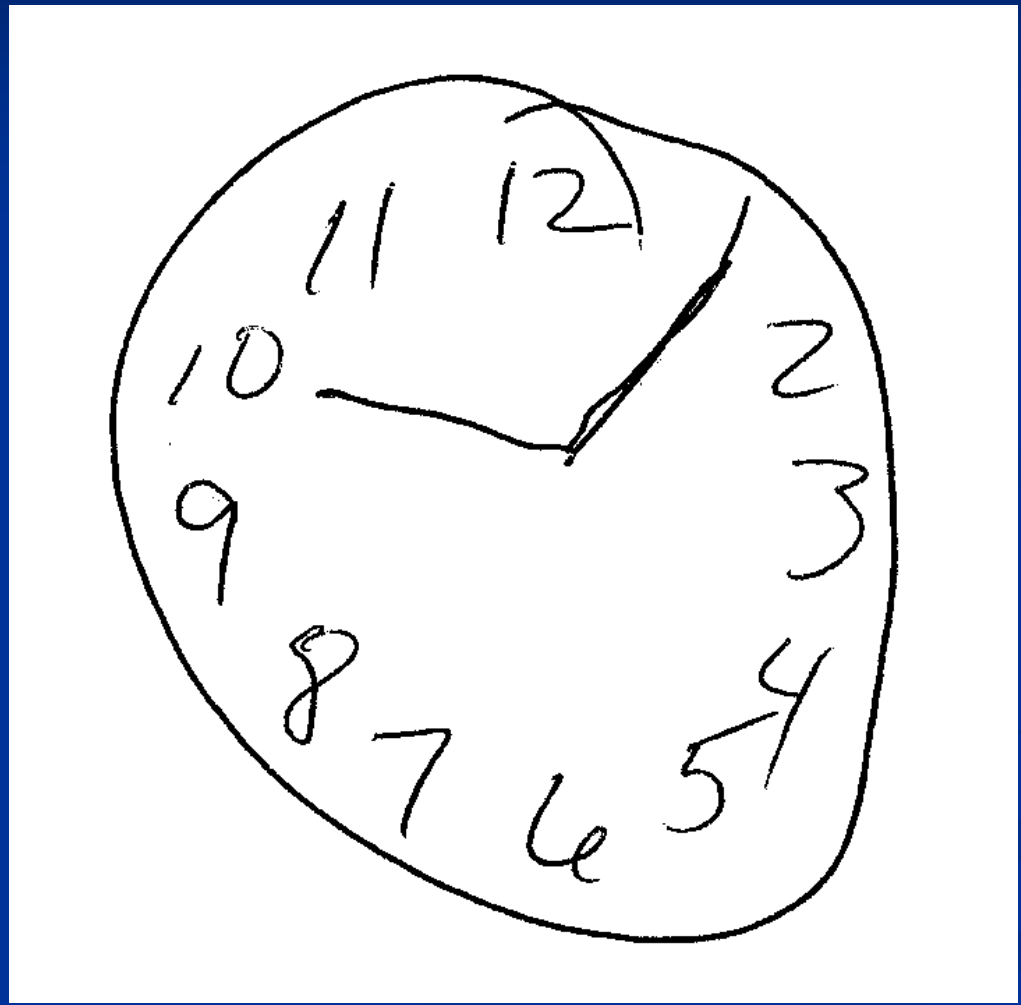
- 77yr with Depression secondary to GMC (bile duct cancer)

Only two hands present?



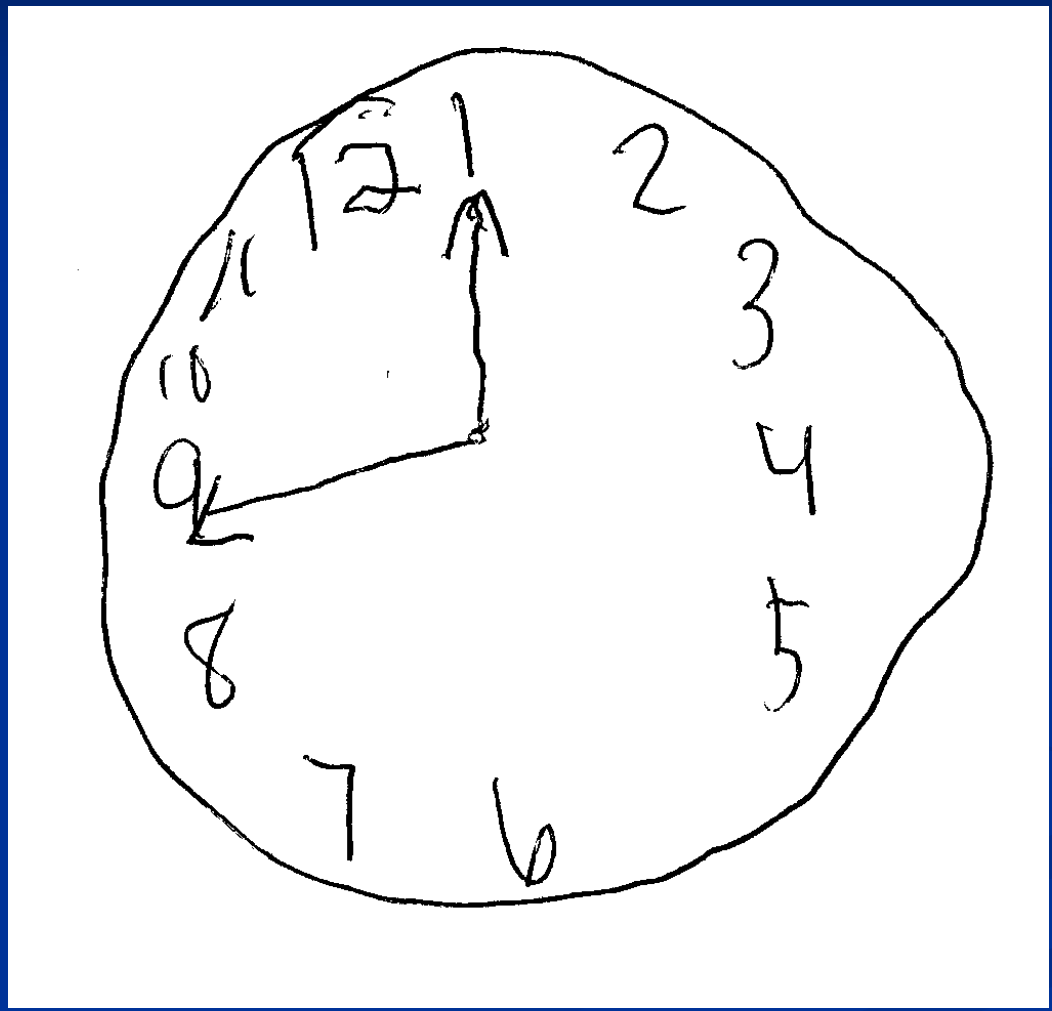
- 53yr with Depression secondary to GMC (s/p CVA)

All hands represented as arrows?



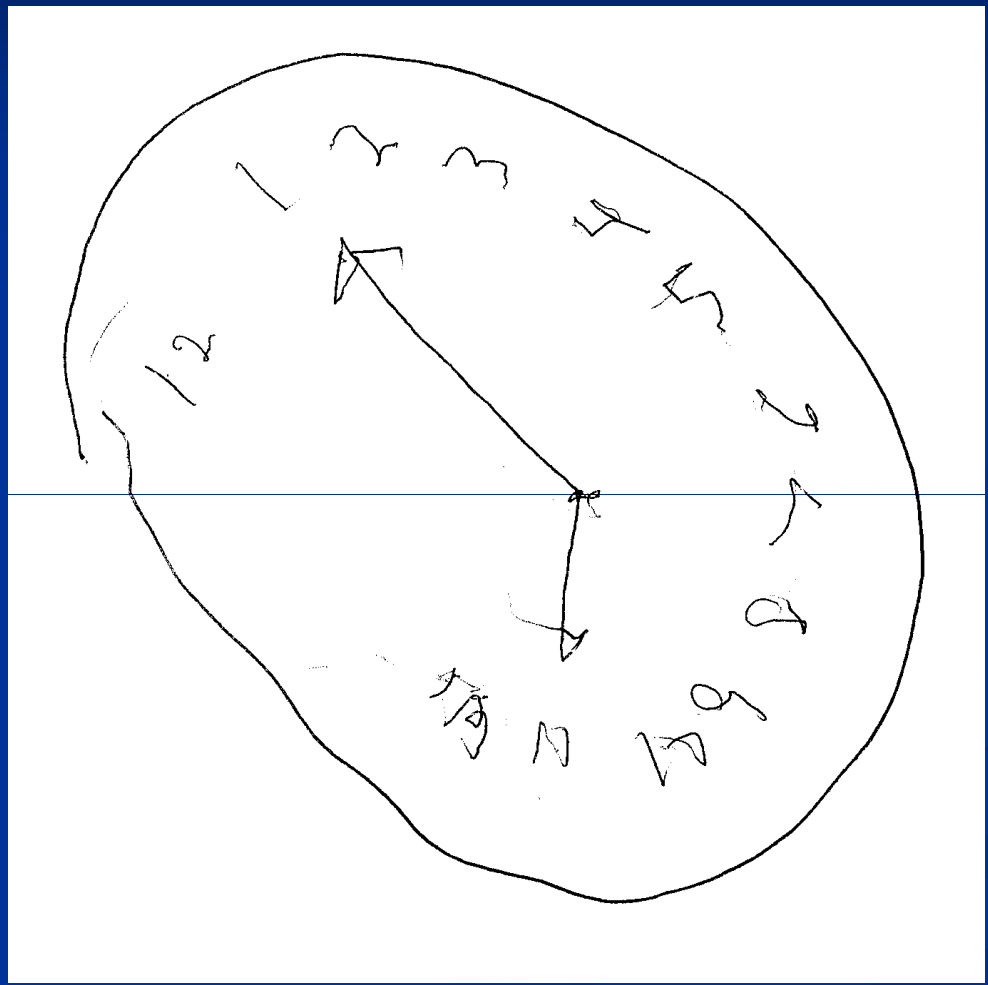
- 42yr with Heroin Dependence

Hour hand between 1 and 2 o'clock?



- 20yr with Schizophrenia

Minute hand longer than hour hand?



- 37yr with Substance Induced Psychosis

None of the Following:

1). Hand pointing to 4 or 5 o'clock?

2). "1:45" present?

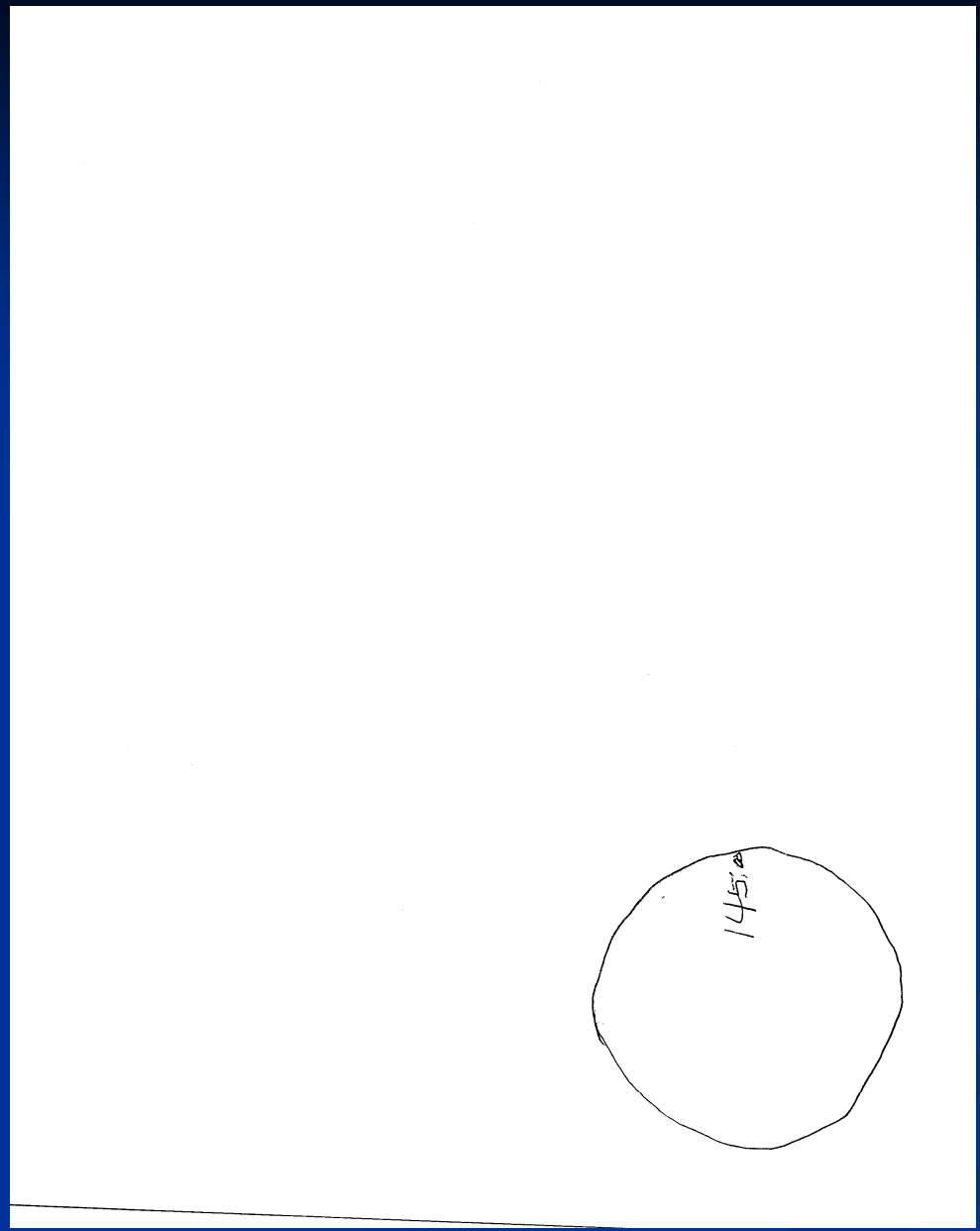
3). Any other notations (e.g. 9:00)?

4). Any arrows point inward?

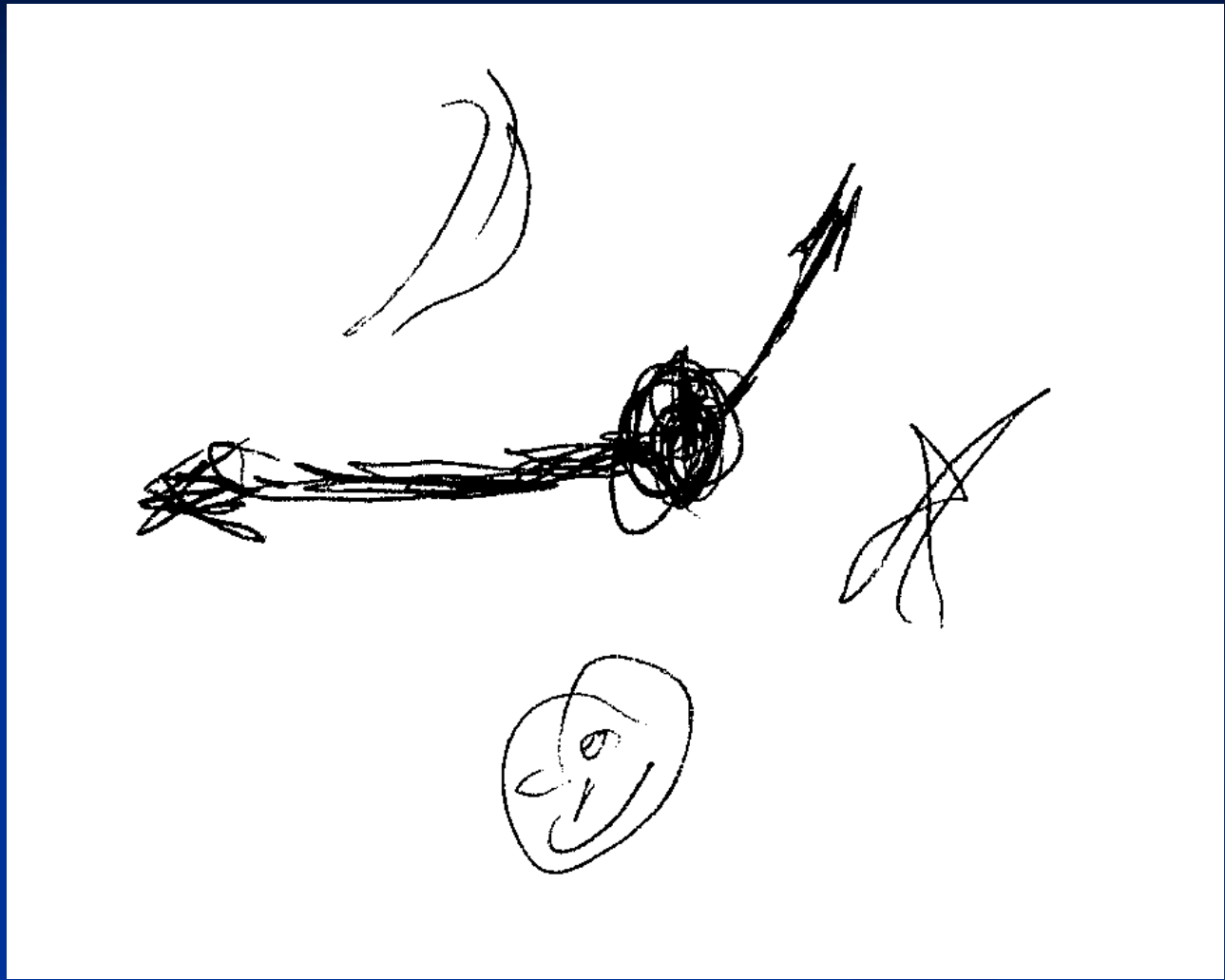
5). Intrusion from hand or face present?

6). Any letters, words, or pictures?

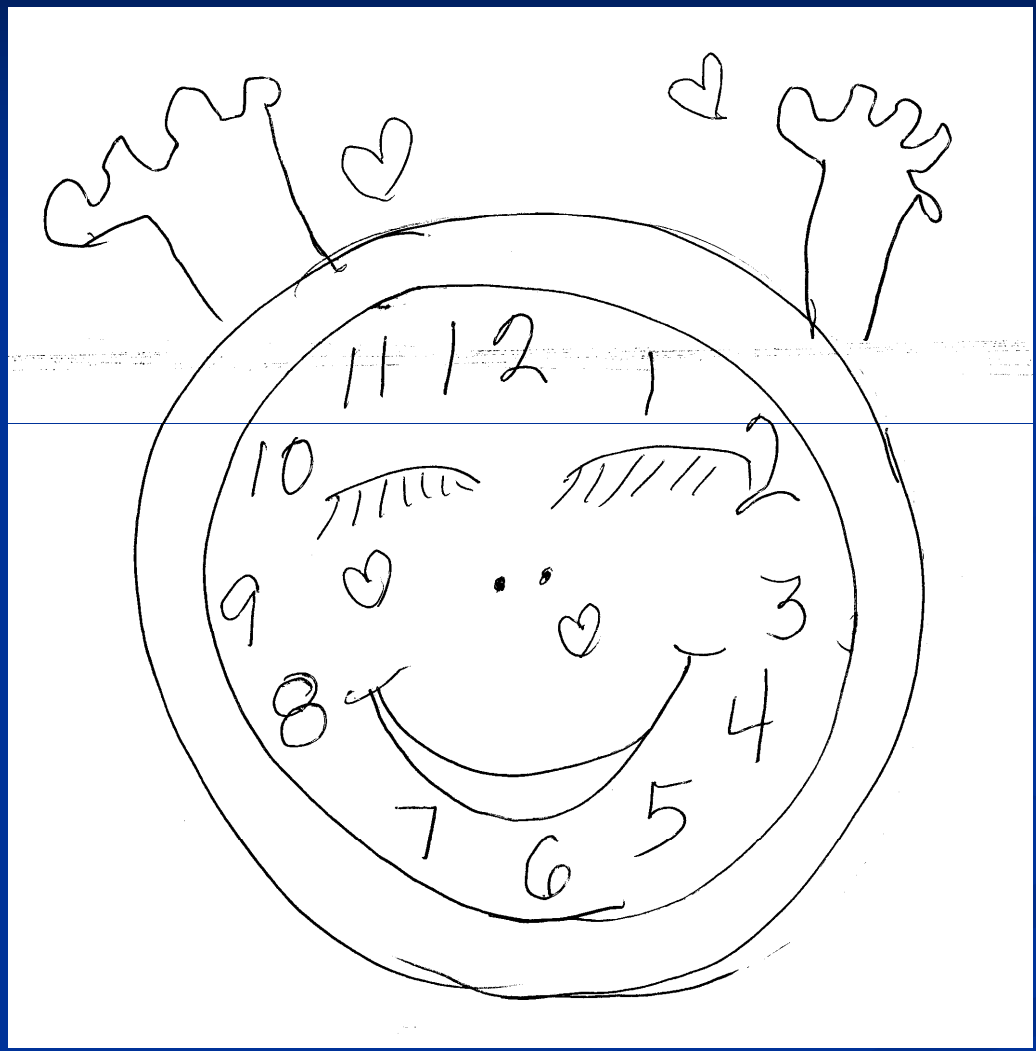
7). Any intrusion from circle?



- 61yr with HIV Dementia (pre-printed circle intrusion)



- 35yr with Delirium/Acute Renal Failure

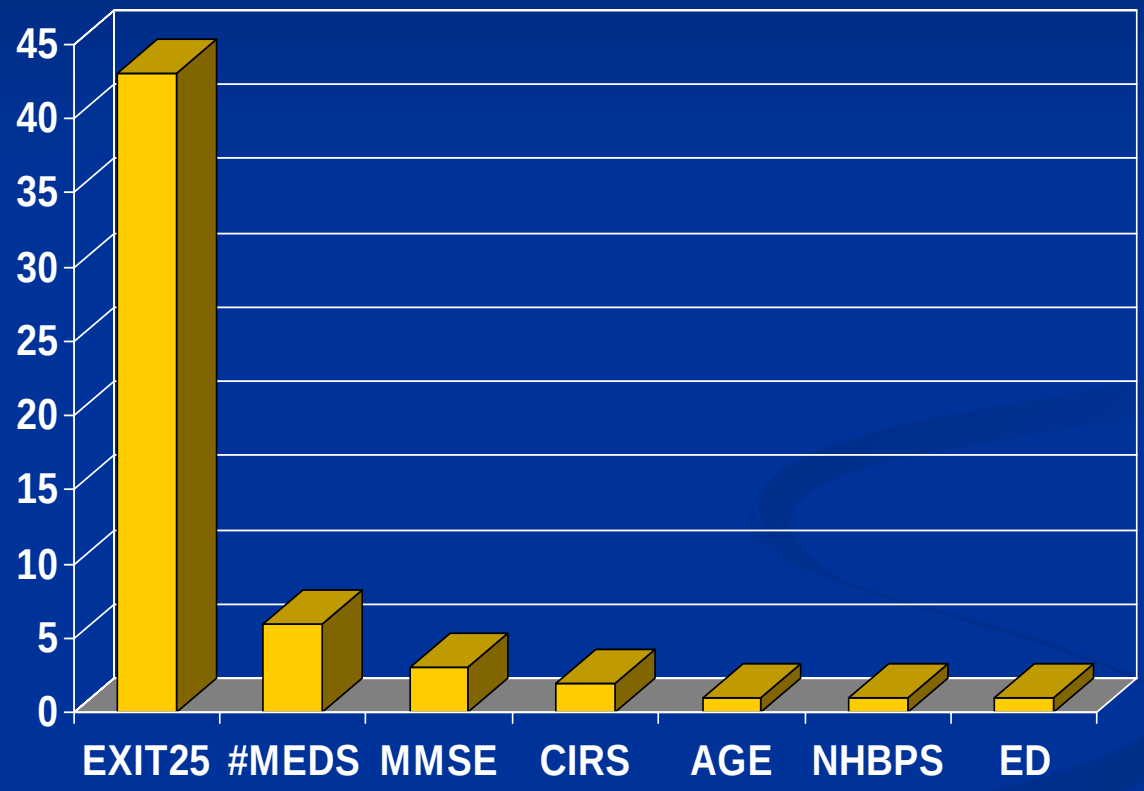


- 38yr with HIV Dementia

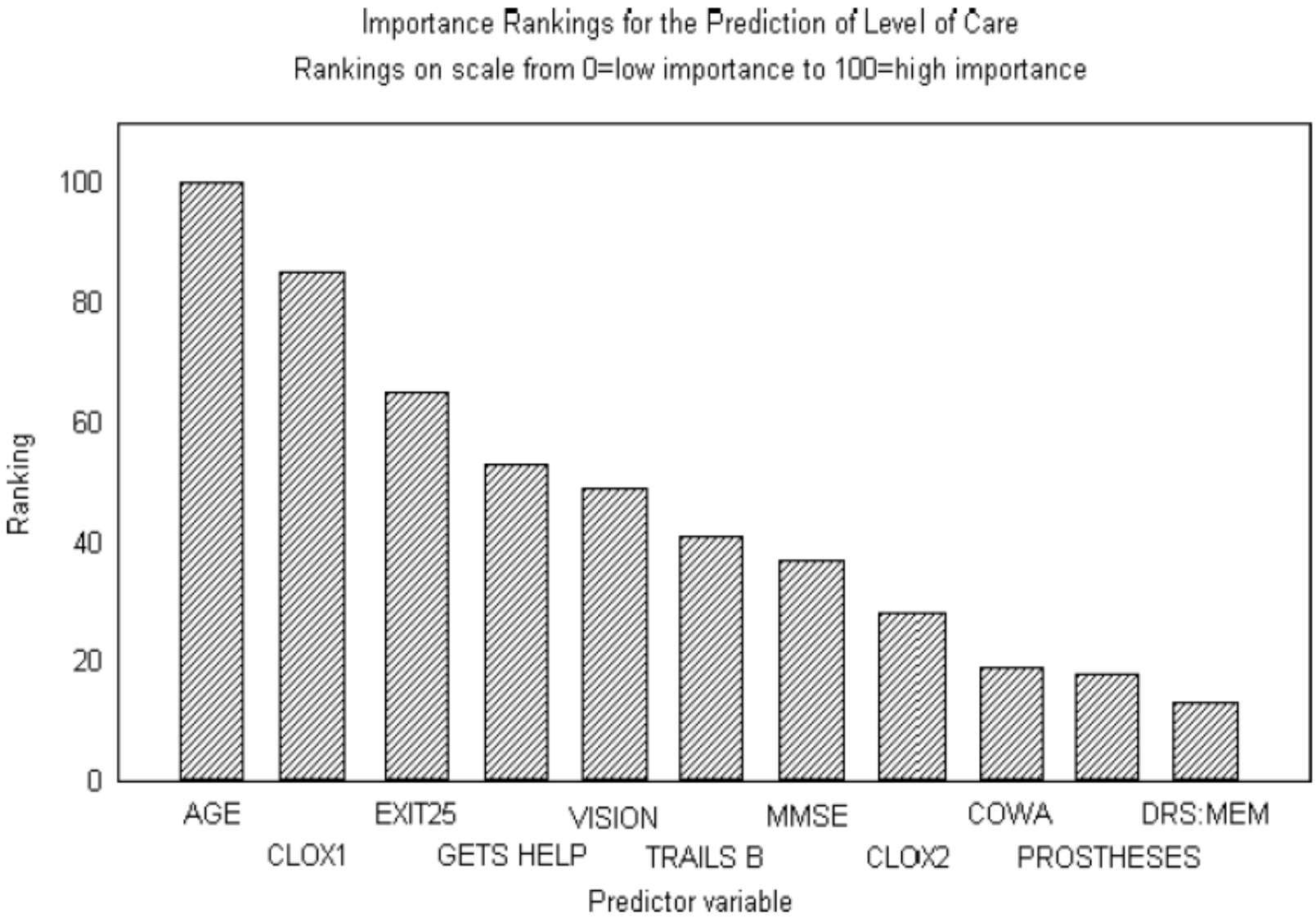
CLOX1

- ≤10/15 represents the lowest 5th percentile for young adults.
- CLOX1 correlates well with the EXIT25 (r = -0.83).
- CLOX1 is more sensitive to executive function than similar clock-drawing tasks relative to the EXIT25.

ECF Determines Level of Care



% Variance in Level of Care Among N=148 CCRC Residents (Total Model R** = 0.57)



Royall et al., J Gerontol A: Med Sci 2005; 60:1059–1064

Transition to 24-hour Care

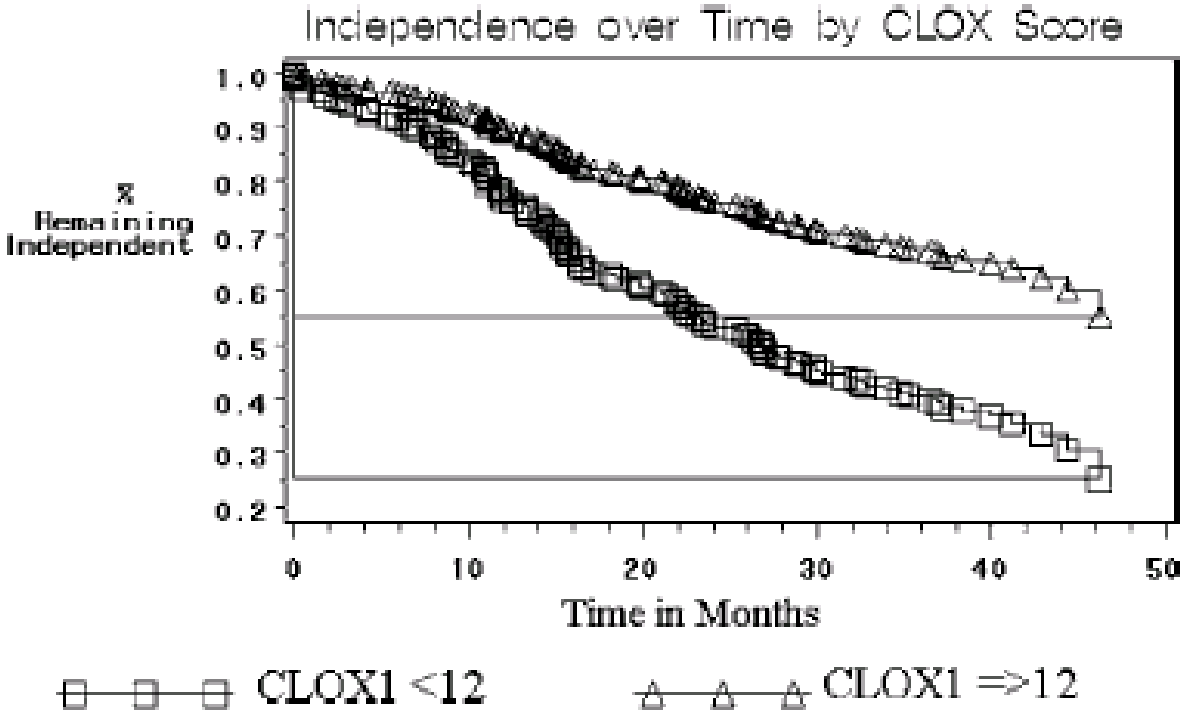


Figure 1. Survival curve analysis of maintenance of independence in residents with CLOX1 scores ≥12 and CLOX1 scores <12.

Lavery LL, Starenchak SM, Flynn WB, *et al*. The clock drawing test is an independent predictor of incident use of 24-hour care in a retirement community. *J Gerontol A Biol Sci Med Sci* 2005; 60: 928-932.

Transition to 24-hour Care

Table 1. Multivariate Analysis of Cognitive Tests With Incident Use of 24-Hour Care

	Hazard Ratio (95% Confidence Interval)			
Variable	Model 1*	Model 2*	Model 3†	Model 4‡
CLOX1				
score (<12)	2.1 (1.4–3.1)	—	2.0 (1.4–3.0)	2.2 (1.5–3.4)
Age, y	1.0 (1.0–1.1)	1.0 (1.0–1.1)	1.0 (1.0–1.1)	NS
Sex (male)	0.9 (0.6–1.5)	0.9 (0.6–1.4)	1.0 (0.7–1.5)	NS
MMSE				
score (<26)	—	1.6 (0.9–1.1)	1.2 (0.7–2.2)	NS

Note: *Adjusted for age and sex.

†Adjusted for CLOX1, age, sex, and MMSE.

‡Adjusted for CLOX1, age, sex, MMSE, comorbidity, Geriatric Depression Scale score, Tinetti Gait and Balance score, and number of medications.

MMSE = Mini-Mental State Examination; NS = not significant.

Lavery LL, Starenchak SM, Flynn WB, *et al.* The clock drawing test is an independent predictor of incident use of 24-hour care in a retirement community. *J Gerontol A Biol Sci Med Sci* 2005; 60: 928-932.

ECF and Capacity to Consent to a Minimally Invasive Research Protocol

Methods:

1. N = 21 subjects were administered the MacCAT modified to assess decision-making capacity to participate in a minimally invasive research protocol.

2. Subjects were administered the EXIT25, CLOX1, CLOX2, and the MMSE

3. A subject was considered to have failed the MacCAT if they failed one or more of the following categories with the following cut-points: understanding ($\leq$4), reasoning ($\leq$3), appreciation of disorder and treatment benefit (0 for each).

Results

Table 1. Demographic and cognitive test means in patients passing and failing the MacCAT-T (standard deviation in parentheses).

Variable	Pass MacCAT (n=11)	Fail MacCAT (n=10)	Significance
Age	61.3 (5.7)	68.6 (10.7)	$p = 0.03$
Education	13.9 (2.5)	11.7 (2.2)	$p = 0.02$
EXIT25	11.5 (4.1)	15.5 (5.0)	$p = 0.03$
CLOX1	11.5 (2.3)	10.4 (2.6)	$p = 0.15$
CLOX2	13.1 (1.3)	13.4 (0.7)	$p = 0.26$
MMSE	28.8 (1.5)	27.9 (1.6)	$p = 0.10$

Results

TABLE 1. Spearman Correlation Coefficients for Modified MacCAT-T Performance

Variable	Capacity Domain		
	Understanding	Appreciation	Reasoning
Age	−0.43	−0.19	−0.44
Education	0.64[a]	0.09	0.77[a]
EXIT25	−0.64[a]	−0.44[b]	−0.54[b]
CLOX1	0.25	−0.03	0.43
CLOX2	−0.12	0.06	0.12
MMSE	0.45[b]	−0.02	0.54[b]

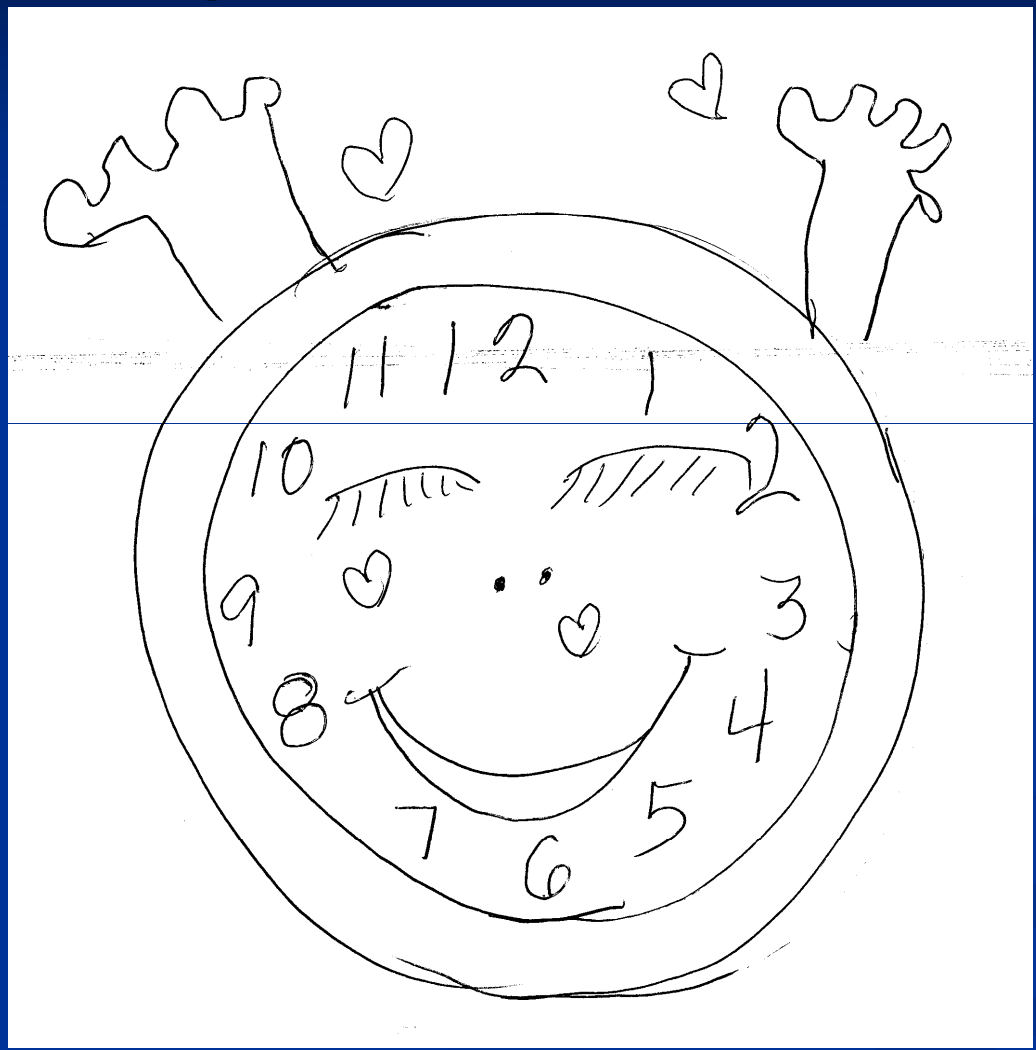
[a]$p < 0.01$. [b]$p < 0.05$. $Age_n = 19$; $Education_n = 20$; EXIT25, CLOX1, CLOX2, and $MMSE_n = 21$. EXIT25: Executive Interview; CLOX: Executive Clock Drawing Task; MMSE: Mini-Mental State Examination.

Schillerstrom JE. Rickenbacker D. Joshi KG. Royall DR. Executive function and capacity to consent to a noninvasive research protocol. American Journal of Geriatric Psychiatry. 15(2):159-62, 2007

Allen et al. *Age & Aging*, 2003

- EXIT25 failure (at 15 /50) was 100% accurate in predicting the capacity of elder COPD patients to learn to use an inhaler.

Questions???



- 38yr with HIV Dementia