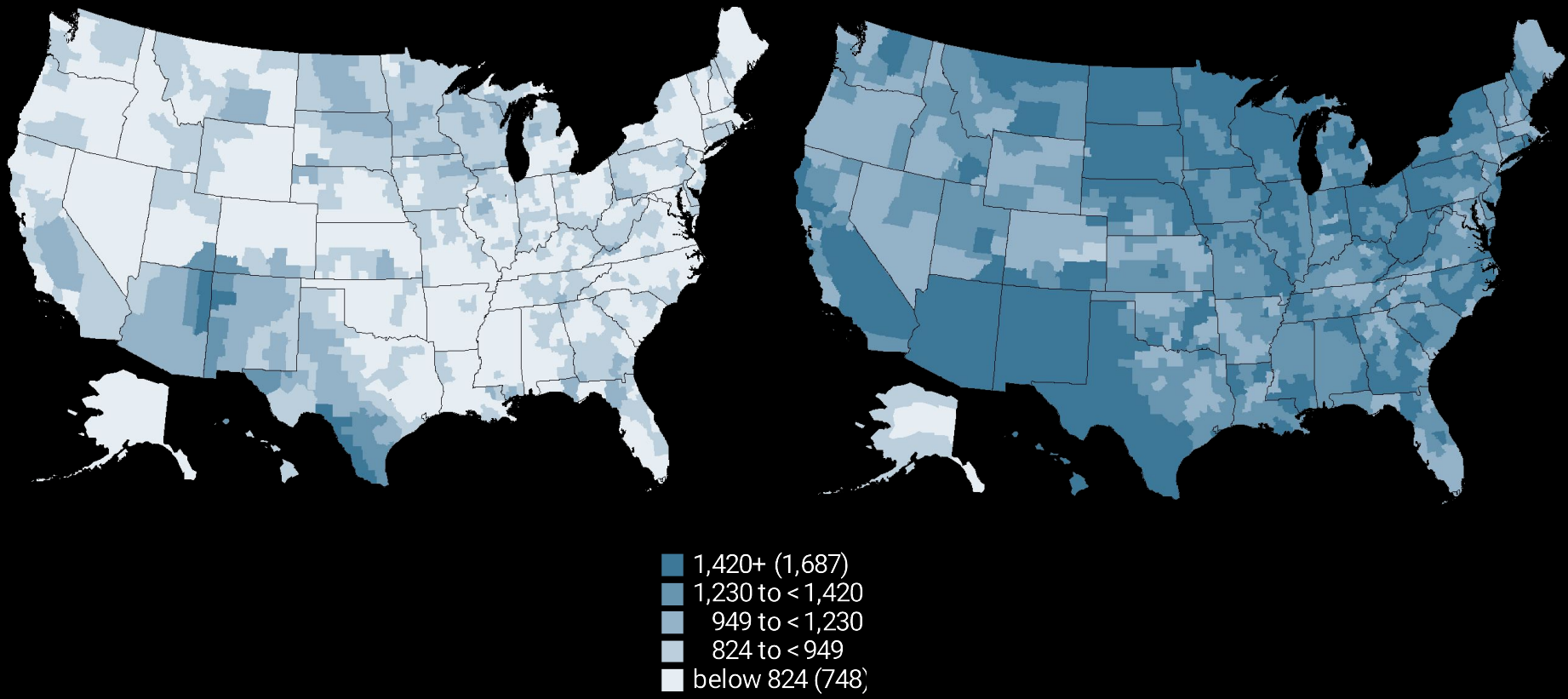
Subjective Global Assessment of Nutrition, Dialysis Quality and the Theory of Scientific Method

Lajos Zsom, M.D.

2013

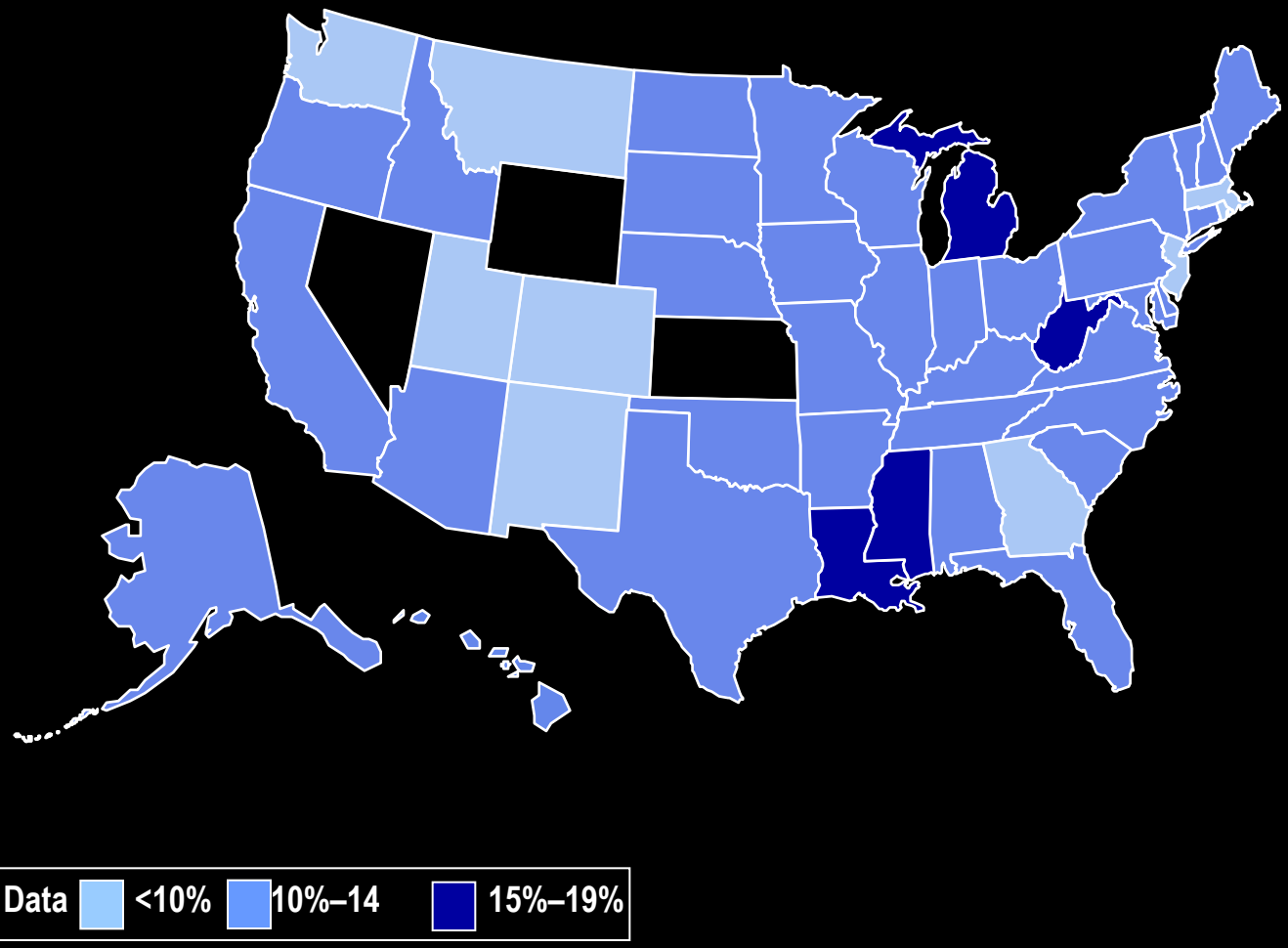
Scope of the problem: CKD is growing

Prevalence of ESRD: 1991 versus 2001 (per million population)



Obesity Trends Among U.S. Adults 1991

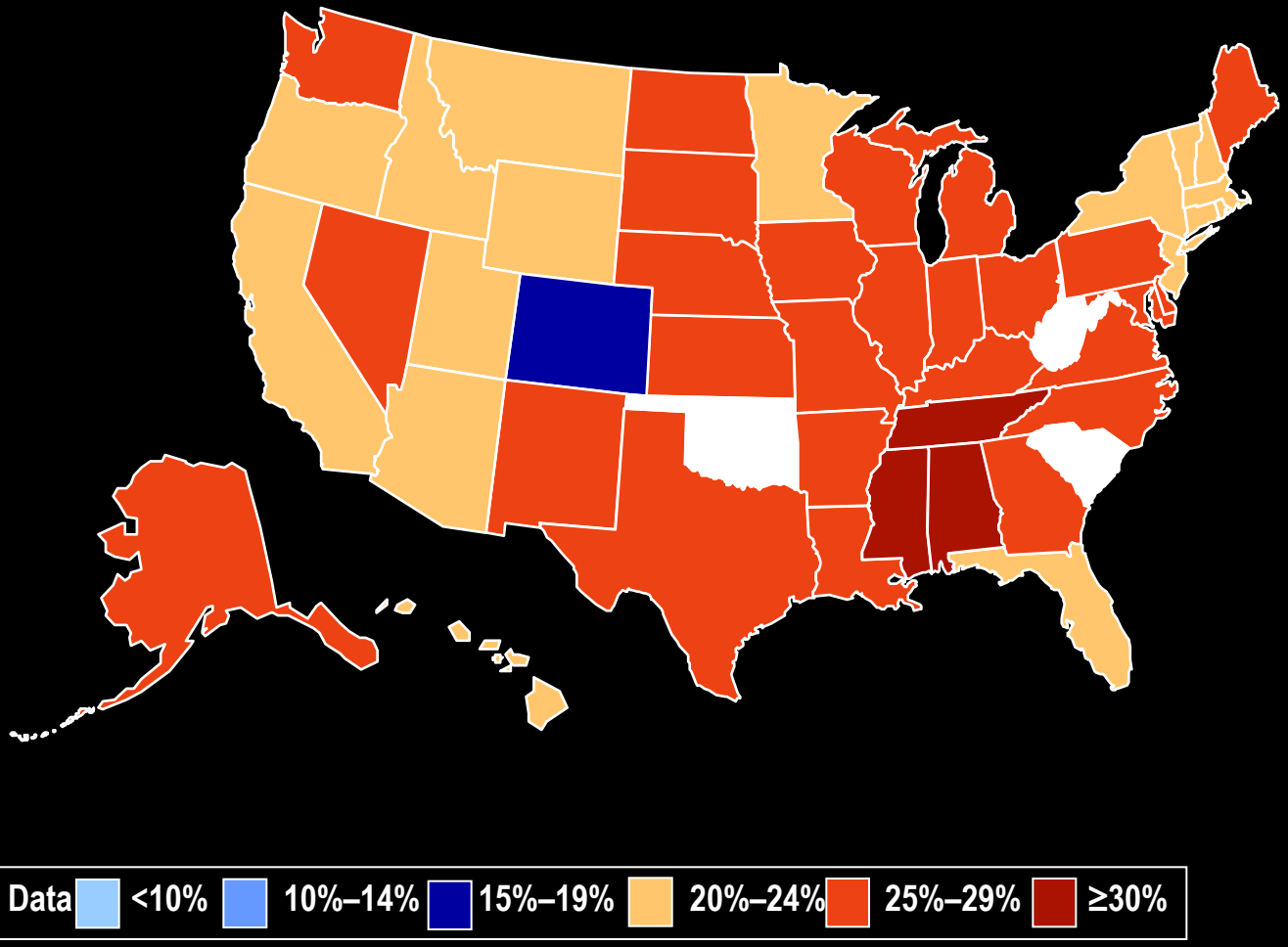
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



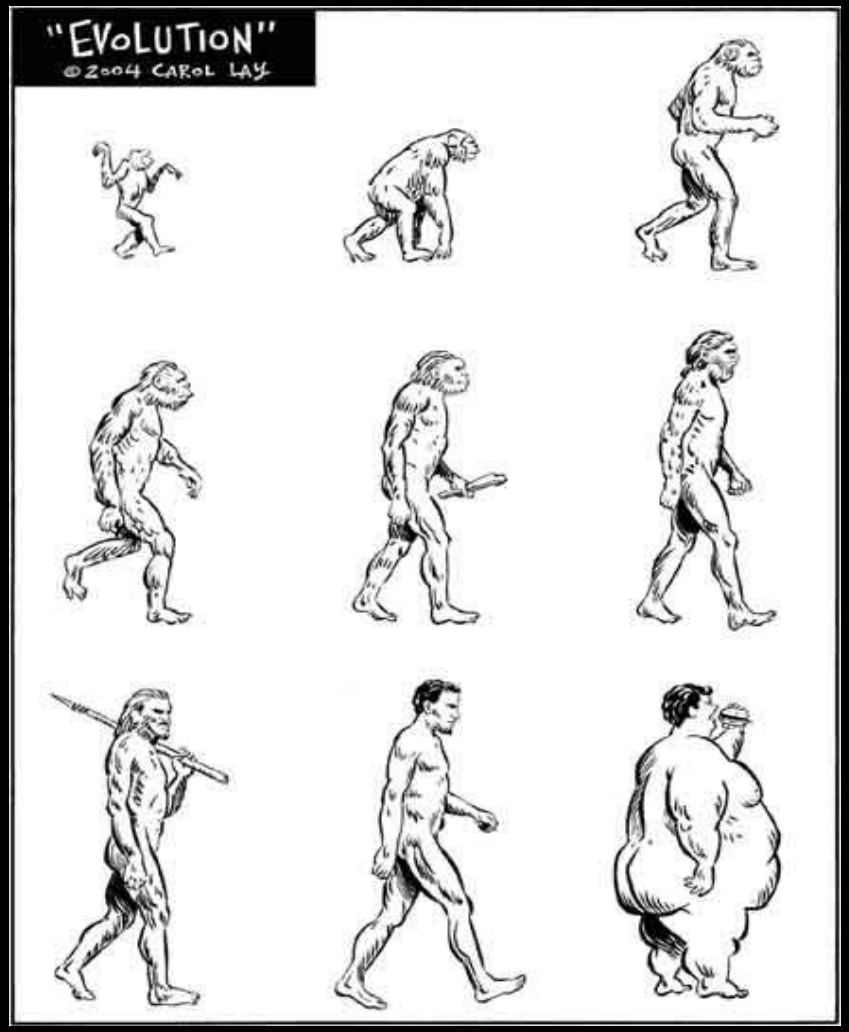
Obesity Trends Among U.S. Adults

2008

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



Evolution of *Homo Sapiens* toward *Homo Consumans*



- Hunter-gatherers (tens of thousands of years): more potassium, less salt, less animal and heavy-grain protein (acid), less fat, more exercise, less caloric intake, fiber, fresh food
  =very low blood pressure, very low cholesterol and no proteinuria
- Modern man (neolithicum, agriculture, a few millennia): diet loaded with animal-, wheat-, rice-derived protein (acid); salt, excessive calories, mass-produced sugar and industrial chemicals, congested in small urban areas
  =“normal” or high blood pressure, “normal” or high cholesterol and some proteinuria

Metabolic Syndrome and Renal Progression

Table 1. *Fructose feeding results in development of traits of the metabolic syndrome*

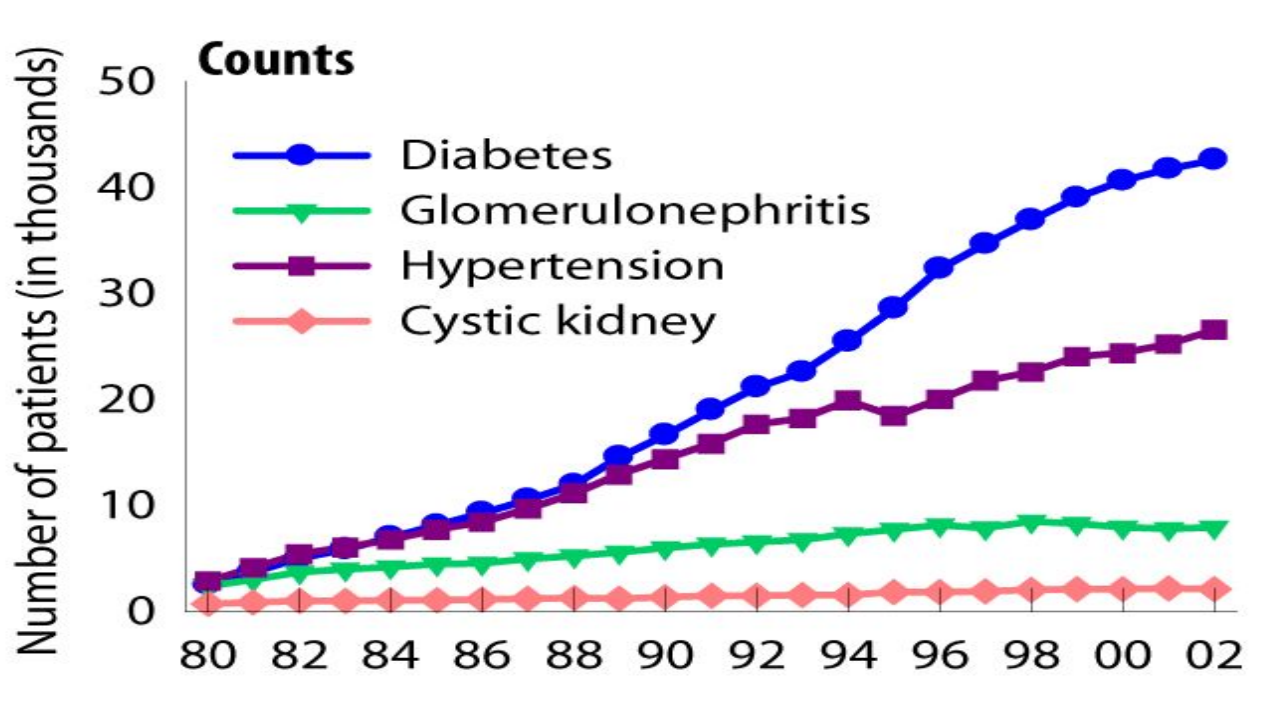
Diet	TG, mg/dl	Cholesterol, mg/dl	Uric Acid, mg/dl	Insulin, pM
Normal	161±12.5	76±3.2	1.6±0.10	3.0±0.3
Dextrose	107±8.9*	64±2.4*†	1.7±0.09	3.2±0.3
Fructose	373±38.7*	90±4.3*	1.5±0.12	4.8±0.5*

Diet	Proteinuria, mg/dl	$C_{creatinine}$, ml/min
Normal	33±5.7	1.23±0.04
Dextrose	35±7.5	1.16±0.08
Fructose	73±15.4*	0.96±0.08*

Gersch Am J Physiol Renal Physiol 293: F1256–F126

Incident Counts & Adjusted Rates, By Primary Diagnosis

CKD as the extreme of the Metabolic Syndrome



USRDS, 2004

Metabolic Syndrome and Renal Progression

Abnormal **diet** (high fructose as an example)

- -high salt (hypertension, inflammation, mortality)
- -carbohydrates (diabetes mellitus, obesity, salt retention)
- -high protein (glomerular hypertension)
- -saturated fatty acid, cholesterol (cardiovascular events)

→metabolic syndrome including salt retention (chronic volume overload) →endothelial damage →inflammation →difficult to control hypertension (diabetes, OSA) →proteinuria →renal progression and cardiovascular disease→hypoalbuminemia/mortality

Subjective Global Assessment of Nutrition

- Definition: a semi-quantitative, semi-subjective technique to assess nutritional status
- Usually performed by dieticians
- in ESRD only used in the research setting
- Based on a score system that incorporates

-trends in weight

-subjective assessment of dietary intake

-assessment of gastrointestinal symptomatology

-estimation of functional impairment

-physical findings (muscle and subcutaneous fat loss, degree of edema)

Subjective Global Assessment-the Technique

1. Assess trends in weight- in renal patients this means dry weight so should include volume assessment
2. Subjective assessment of actual dietary intake: subjective here means interviewing the patient and find changes in dietary habits during the time period in question- this means SPENDING TIME WITH THE PATIENT
3. Assessing gastrointestinal symptoms: is there a new development (bout of gastroparesis) or medication side effect (cinacalcet, P binder, constipation due to a new antihypertensive drug)
4. Functional status-brief subjective survey (patient now is wheelchair bound so energy expenditure is down)
5. Brief physical exam assessing muscle and fat mass, edema
6. Not formally included but obvious: subjective assessment of depression (common in patients with any chronic disease and may suppress appetite)

Expectations from a Clinical Assessing Tool

- Subjective Global Assessment

should be:	it is:
-objective	-semi-objective
-specific	-global
-quantifiable	-semi-quantifiable
-reproducible	-reproducible
-verifiable	-verifiable
-relevant	-relevant

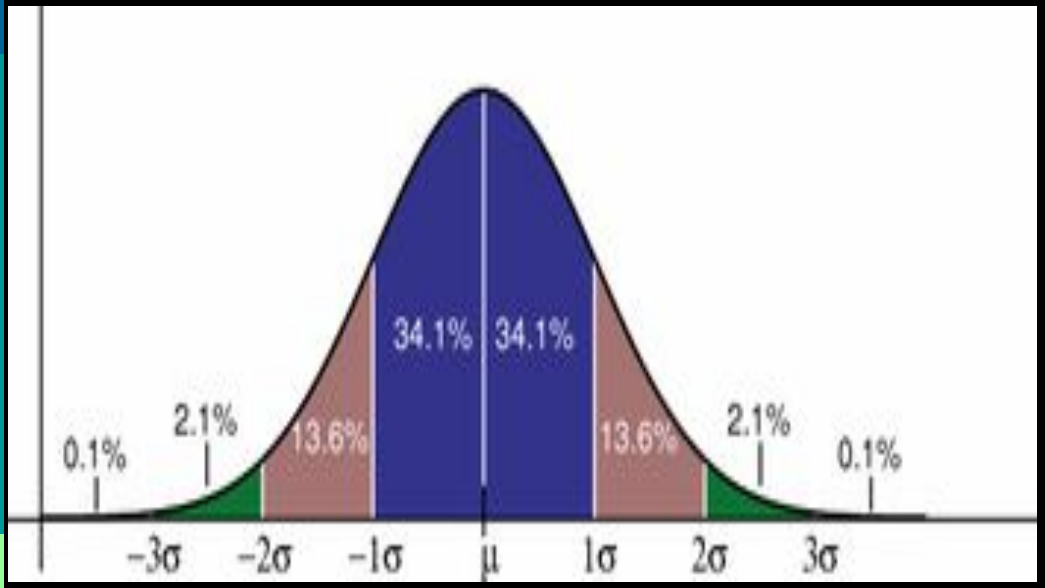
Expectations from a Clinical Assessing Tool 2.

- The Existing Alternative Measures

should be:	they are:
-objective	-objective
-specific	-specific
-quantifiable	-quantifiable
-reproducible	-reproducible
-verifiable	-verifiable
-relevant	-(....)

In addition, they are easy to use as they are *lab tests*.

Laboratory Tests versus Subjective Measures



- Laboratory medicine: population average ±2SD=normal
- Lab tests: easier to use, more convenient
- Take less time to assess
- Easier to document
- More readily standardized (for reporting to supervising agencies)

Subjective Global Assessment: an Extraordinary Claim

- Why use a *subjective* rather than an *objective* measure?
- Why use a *global* rather than a *specific* measure?
- Why use a *semi-quantitative* rather than a *quantitative* measure?
- Why is *nutritional SGA* relevant in assessing dialysis quality (is *nutrition* centrally important)?
- Can we use nutritional SGA in *clinical practice*?
- Can we extend *nutritional* SGA (currently in use) to introduce *clinical* SGA for assessing dialysis quality?

Extraordinary Evidence: Induction and Dialysis Clearance

Induction:

-scientific experiment under controlled circumstances establishes relationships between parameters ("natural laws")

-inference: extrapolating results with the expectation that "under similar circumstances" "everything being equal" relationships will hold true

- Example: dialysis clearance as objective, quantifiable, reproducible measure of "dialysis dose" based on extrapolation of the clearance concept (originally used to describe *renal excretory function*) to describe the *effects of renal replacement therapy*

The Fateful Inference: Renal Clearance to Dialysis Clearance

- CP=UV

where

-P is the plasma concentration of an ideal filtration marker

-U is the urinary concentration of an ideal filtration marker

-V is *urinary flow rate* (or urine volume for 24 h clearance)

- UV: urinary removal of a substance over time
- C: P-independent virtual term representing virtual volume cleared (assumption: even distribution of ideal marker in total body water and instant refill to plasma from extra-vascular space, an assumption

Inference: Renal Clearance to Dialysis Clearance 2.

- Renal clearance as defined for quantification of renal excretory function (continuous filtration by natural membrane plus multiple level of regulation by both filtration and tubular secretion/reabsorption

can be applied (by analogy) to

- Dialysis, a discontinuous filtration by an artificial membrane with different filtration characteristics not supported by multiple level of regulation and subject to characteristics of regional blood flow patterns

  that has hemodynamic (and other) side effects hindering equilibration of marker from tissues to plasma and from plasma to the dialyzate

Dialysis Clearance: Definition

- Measure of urea removal ($K_{urea}t$) by a *single dialysis* session irrespective of

-dialysis membrane quality

-speed of dialysis

-modality of dialysis (peritoneal, home, platforms)

-composition of the dialyzate

Normalized by a hypothetical urea distribution volume (V) extrapolated to represent 12-13 dialysis sessions per month irrespective of hemodynamic or other toleration of sessions.

- Gotch 1984: it does not seem to matter *how* urea is removed *so far as we achieve a* $K_{urea}t/V$ *of 0.8*, dialysis can be considered as adequate

The Fateful Assumption

alias

"Let us start the battle and then we shall see!"

(Napoléon)

- **Change in urea concentration during dialysis can approximate "dialysis dose"**
- Sargent & Gotch 1975: concentration change during dialysis equals generation during dialysis minus removal during dialysis
- As concentration of urea changes from C_0 to C_t during dialysis from time t_0 to t_d then:

$$\int_{Co}^{Ct} VdC/ [G - (K_d+K_r)C] = \int_{to}^{td} dt$$

where V = distribution volume of urea

Co= pre BUN

Ct = post BUN

G = urea generation during dialysis

Kd= dialyzer clearance

Kr= residual renal function during dialysis

t = time from beginning to end of dialysis

Pay Attention Here!

$$Ct = Co\, e^{-(Kd+Kr)\, td\, /V} + G/\,(K_d+K_r)\,(1- e^{-(Kd+Kr)\, td\, /V})$$

$$Co = Ct\, e^{-Kr\, tid\, /V} + G/\,K_r\,(1- e^{-Kr\, tid\, /V})$$

- **These equations implicitly assume the *equivalence of 2 different clearing processes Kd and Kr!!!!***

- **There are too many unknowns!**

  We know these:

  Ct, Co, Kr, td, tid

  (although: Ct and Co may not be constant, Kr may be variable, td may not be as we assume, tid likewise)

  We do not know these:

  Kd, G, V

Dialysis clearance- Why is it misleading?

- The concept of stdKt/V critically omits the dependence of dialysis quality and dialysis tolerance on time exposure (the choice of urea as a marker merely exacerbates this problem) and the qualitative difference between residual renal clearance and dialysis clearance

$$K\uparrow t\downarrow = K\downarrow t\uparrow$$

And

$$Kd = Kr$$

Mathematical Product-How does it work?

- 5x6=30 and 10x3=30
- Apply to Ca=5 and P=6 versus Ca=10 and P=3
- Both yield a CaP product of 30 but what a difference!
- Kt/V may be 1.3 by low K high t or high K low t
- Both yield equivalent Kt/V- is there a difference?

Treatment time vs. Clinical outcomes

-If

t~mortality or albumin

independent of Kt/V and therefore Kt

- then even if Kt/V~mortality or albumin

Proves:

K↑t↓ ≠ K↓t↑

Eliminating the reason of using the Kt product

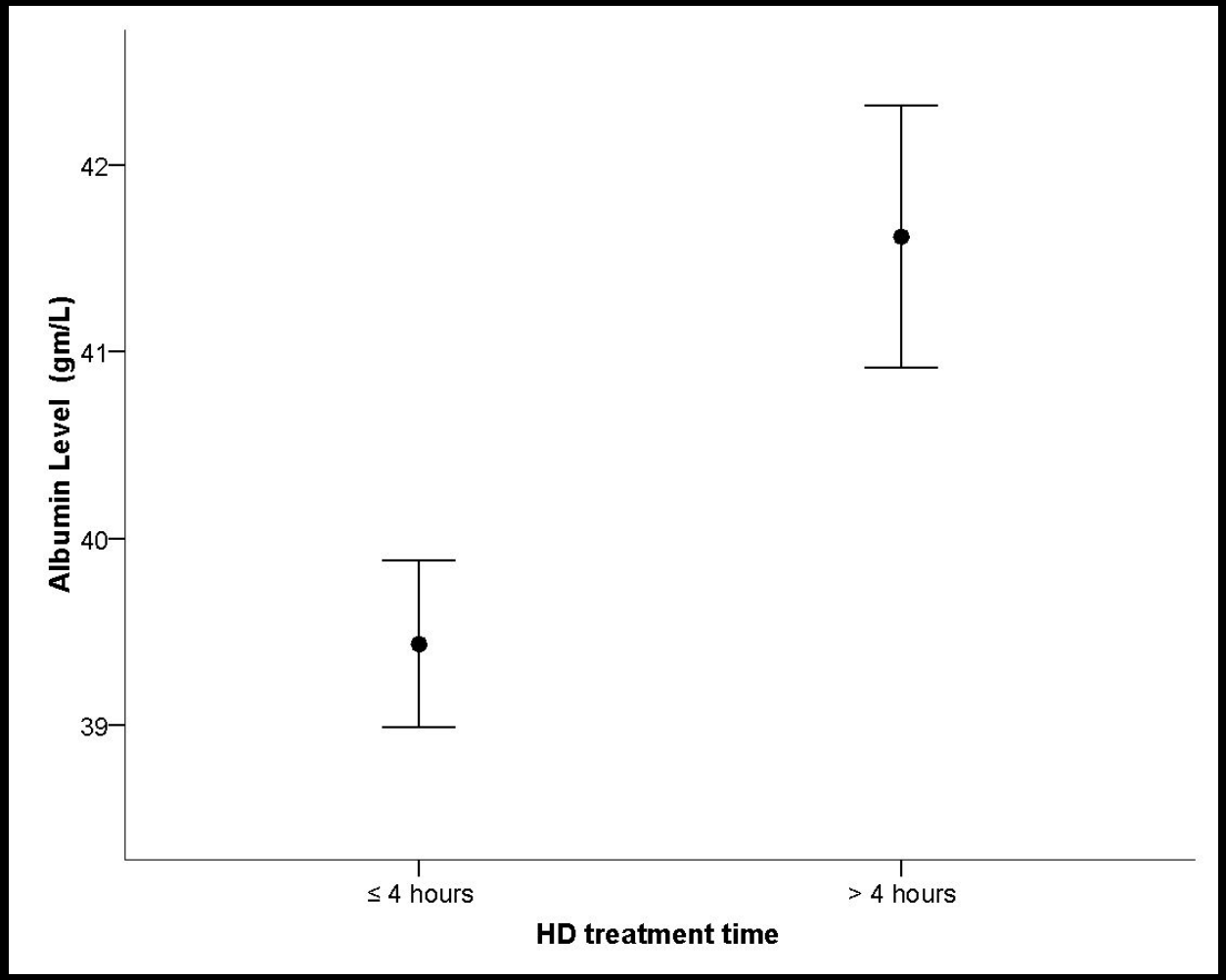
Logistic Regression: Treatment Time vs. Serum albumin

Failing to reach serum albumin target (≥4 g/dl) for treatment time>240 min:

Odds ratio (95% CI): 0.397 (0.235-0.672)
p<0.001

***Correlation of Treatment Time and Ultrafiltration Rate with Serum Albumin and C-reactive Protein Levels in Patients with End Stage Kidney Disease Receiving Chronic Maintenance Hemodialysis: A Cross-Sectional Study**
Lajos Zsom, Marianna Zsom, Tibor Fülöp, Catherine Wells, Michael F Flessner, József Eller, Charlotta Wollheim, Jörgen Hegbrant, Giovanni FM Strippoli
Blood Purification (accepted) 2010

Mean ±SD serum albumin levels in the short and long dialysis groups



The Idea came from…

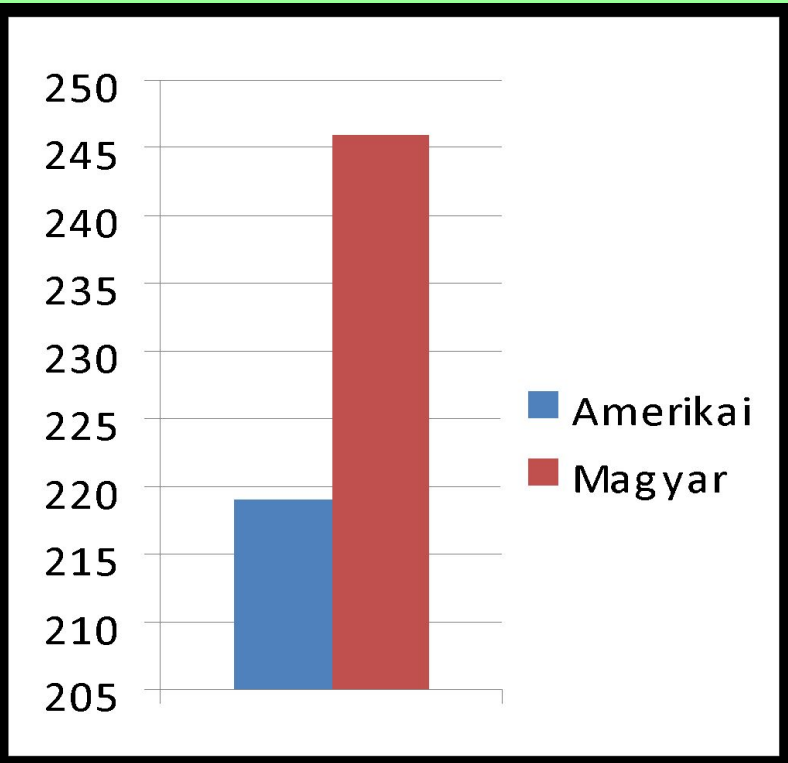
Zsom Lajos, Zsom Marianna

Debrecen Renal Week
2007

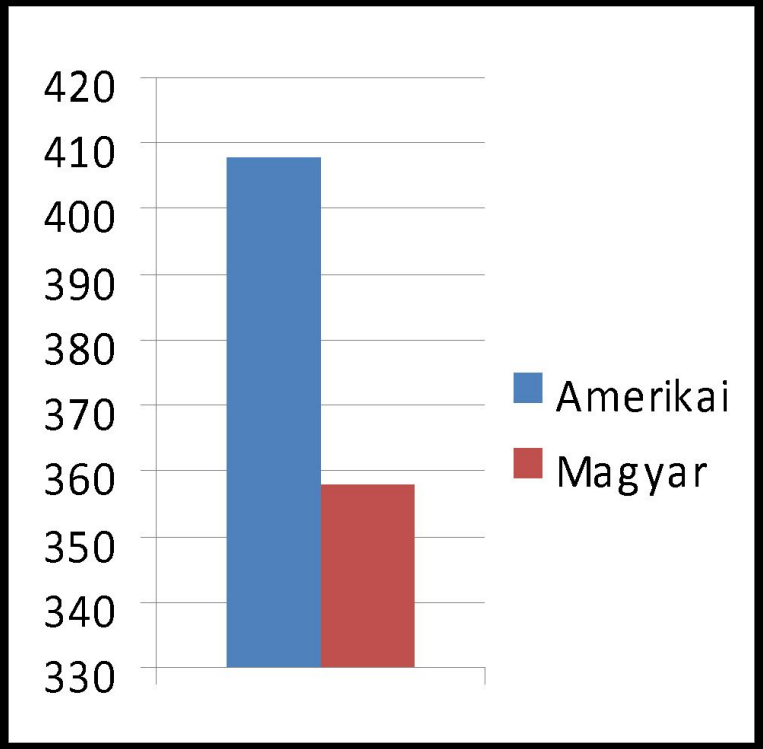
Comparison of Clinical Outcomes in an American and a Hungarian Hemodialysis Unit

Kezelési paraméterek

Kezelési idő (perc/HD):



Vérátfolyás (ml/perc):



Amerikai állomás

1. **Kezelési idő:** 219±25,5 SD (165-285)
2. **QB:** 408±51 SD (300-500)
3. **High Flux:** 100%
4. **QD:** A1,5 (80%) vagy A2,0 (20%)

Magyar állomás

1. **Kezelési idő:** 246±23,6 SD (210-300)
2. **QB:** 358±43,8 SD (250-450)
3. **High Flux:** 17%
4. **QD:** 500 (84%) vagy 700 (16%)

Memento Tassin!
(*The Tale of Two Kinds of Bread*)

- ***French baguette***
- Slow inefficient dialysis (8h)
- Ancient technology (low flux)
- Low-normal blood pressure
- No blood pressure medicines
- No LVH
- Low mortality (few diabetics)

- ***English toast***
- Fast, high-efficiency dialysis
- Top-notch technology
- High blood pressure for long interdialytic periods
- Several blood pressure medicines
- LVH
- Very high mortality!!!!!!!

Misinterpretation of Clinical trials on Dialysis Clearance Corrected in…30 years

- NCDS: study population, fixed BUN study design, short follow up, insufficient power
- HEMO: as treatment arms were not separated by time "this study demonstrated that merely optimizing effective dialyzer urea clearance (K) without increasing treatment time (t) is not associated with survival benefit"

Treatment Time, Chronic Inflammation, and Hemodynamic Stability: The Overlooked Parameters in Hemodialysis Quantification

Lajos Zsom, Marianna Zsom, Tibor Fulop, Michael F. Flessner

Seminars in Dialysis 2008

- NCDS: "underpowered to examine mortality as an endpoint, in part due to early termination at the time of interim analysis"
- HEMO: subjects in the study were not randomized to various levels of session length…

  does not constitute

  a true randomized trial of session length

Shorter dialysis times are associated with higher mortality among incident hemodialysis patients

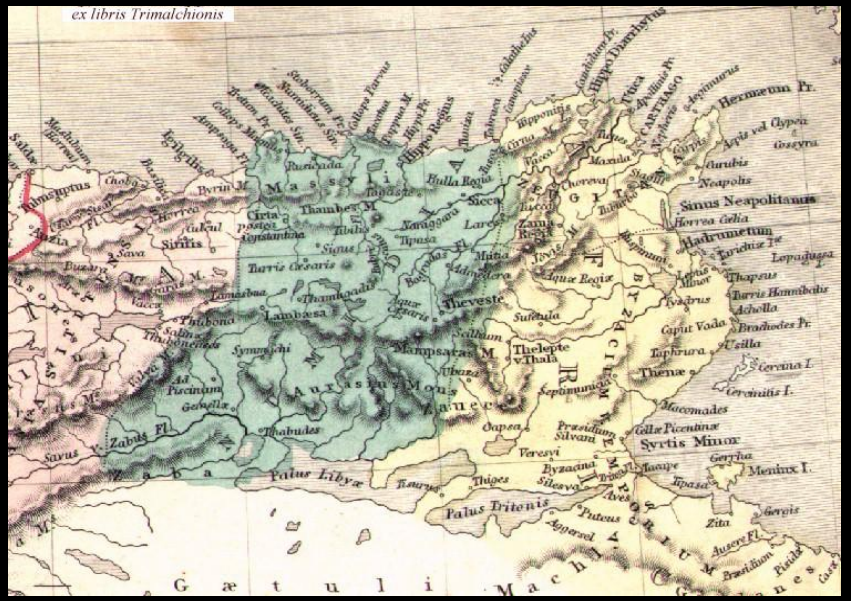
Steven M. Brunelli, Glenn M. Chertow, Elizabeth D. Ankers, Edmund G. Lowrie and Ravi Thadhani

Kidney International 2010

Our conclusion so far is…..

- Ludovicus Giomus Cato

“Ceterum censeo Cathepervinem delendam esse!”



Does SGA correlate with outcomes?

- Large cohort studies of dialysis patients in North America and in Europe aiming to establish predicting value of different dialysis quality measures in PD and HD
- Main findings:

  -Residual Renal Function is important

  -Treatment time on HD is important

  -Kt/V is not important or only important in anuric patients

  -the strongest predictor is...

SGA: Forward to the Past

- "Clinical nutrition scores are superior for the prognosis of haemodialysis patients compared to lab markers and bioelectrical impedance" Nephrol Dial Transplant. 2009 Jul 15.

  Roman Fiedler, Peter M. Jehle, Bernd Osten, Otgontogoo Dorligschaw, Matthias Girndt

  Nephrol Dial Transplant (2009) 24: 3812–3817
- 90 HD patients with 3 years of follow up
- Hazard ratio for mortality by Cox regression analysis corrected for: age, gender, dialysis vintage and diabetes status

SGA versus Blood Work: Evidence versus Delusion

- Hypoalbuminemia, NPCR: Are these good markers of a state of malnutrition or of protein intake?
- Problem: **Hypoalbuminemia is a composite outcome** of several influences such as systemic inflammation, hypervolemia and poor dialysis
- Does albumin correlate with protein intake in well dialyzed and non-inflamed normovolemic patients?
- Clue: serum albumin decreases only with severe Anorexia Nervosa and extreme malnutrition in healthy subjects experimentally undergoing fasting
- Study: dialysis patients with normal CRP identified as having good versus poor nutritional status with SGA

Sudden Cardiac Death and the Weekend

Characteristics of sudden death in hemodialysis patients

AJ Bleyer[1], J Hartman[1], PC Brannon[2], A Reeves-Daniel[1], SG Satko[1] and G Russell[2]

[1]Section on Nephrology, Department of Internal Medicine, Wake Forest University School of Medicine, Winston Salem, North Carolina, USA and [2]Section on Biostatistics, Department of Public Health Sciences, Wake Forest University School of Medicine, Winston Salem, North Carolina, USA

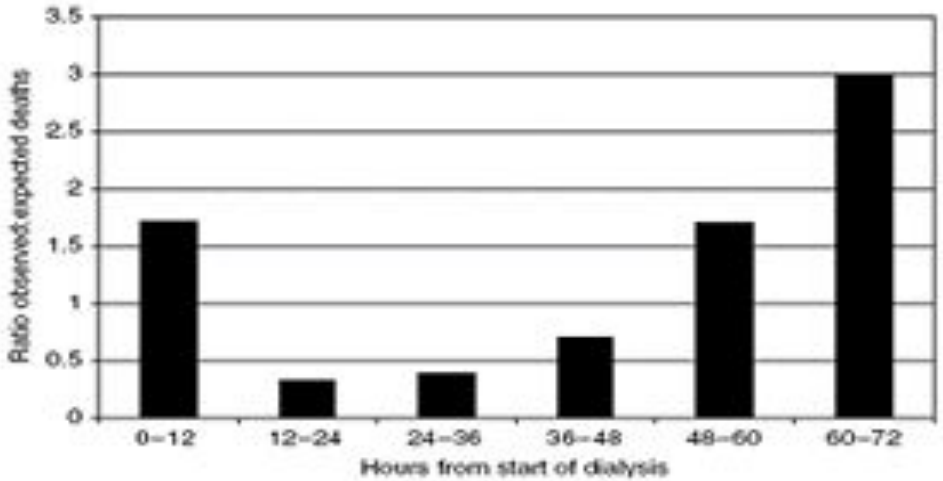


Figure 2 | Ratio of actual to expected number of occurrences of sudden death for each 12 h interval beginning with the start of HD.

Bleyer et al KI 2006

Sudden Cardiac Death and SGA

- Most dialysis patients have cardiac fibrosis predisposing them for arrhythmia
- Most dialysis patient deaths are due to sudden cardiac death
- They tend to occur either immediately after dialysis (rapid electrolyte shifts, acute phase reaction) or after weekends (hypervolemia, hyperkalemia etc)
- So: short of increasing dialysis time and frequency dietary restrictions of Na, K, acid may help
- Ideal dialysis: small differences in electrolyte concentrations due to slow and continuous removal

Fluctuations…..and SGA

- Italian patient with a strong preference for tomato dialyzed MWF: K levels before and after dialysis: Monday 6.5→3.4, Wednesday 5.6→3.2, Friday 5.4 →3.1 dialyzed for 3.5h on a 1 K bath
- Non-Italian patient with no preference for tomato dialyzed MWF: K levels before and after dialysis: Monday 5.5→3.8, Wednesday 5.6→3.9, Friday 5.4 →3.7 dialyzed for 4h on a 3 K bath
- Who is likely to survive longer **with the same pre K level on Wednesday**? How would you modify dialysis in the Italian patient based on subjective assessment of dietary intake/preferences?

Plasma Refill Rates

- Plasma refill rates in stable patients:

-Nephrotic syndrome 19.9 ml/min

-CKD 16.5 ml/min

-CHF 12.7 ml/min

- In acute decompensation may be much lower

Subjective Global Assessment: a Different kind of Inference

- If Subjective Global Assessment of *nutritional status*

  assessed *by a dietician* works
- Then by analogy perhaps Subjective Global Assessment of

  clinical status

  assessed *by a doctor* may also work

Subjective Global Assessment: a *Global* Concept 1.

- Mathematical equations such as

$$Ct = Co\, e^{-(Kd+Kr)\, td/V} + G/(K_d+K_r)\,(1 - e^{-(Kd+Kr)\, td/V})$$

May seem complex (and therefore impressive) but

-often describe simple linear or exponential relationships (as above)

-tend to operate with a limited number of parameters (here: C: concentration of urea, t: time, K: dialyzer clearance, V: volume of distribution, G: urea generation, e=constant, the base of natural logarithm)

-usually describe parameters that are fully quantifiable

Integrating SGA into Interdisciplinary Teamwork 2

Lab: Patient B's monthly status is reviewed by an interdisciplinary team. The physician notes that the phosphorus that had been ranging 5.7-6.1 over several months now is 4.7. The patient's albumin has remained 3.8-3.9, blood pressure is better controlled. Residual renal function is unknown and there does not seem to be any inflammatory signs present. Kt/V is 1.8.

The physician is very happy.

Clinical SGA: The social worker then informs him that the patient is more withdrawn and seems depressed. Apparently, there was a death in the family. The dietician adds that there is a dramatic worsening of appetite and a major decline in protein intake. The physician then recalls that he cut the patient's dry weight several time during the month. The patient had several low blood pressure episodes. Physical examination shows a slight increase in edema and a decline in muscle mass, subcutaneous fat and poor exercise tolerance.

The physician is now not so happy (and more importantly neither is the patient).

Educational/social assistance options are now considered to improve the patient's nutritional status and dialysis is intensified by increasing treatment time in an attempt to increase appetite and decrease ultrafiltration rate.

Subjective Global Assessment: Conclusions

- Accept that a semi-objective, semi-quantitative score system may work better than objective, easy to use but largely irrelevant lab tests.
- Abandon the concept of quantifying dialysis quality ("dialysis adequacy") by the degree of removal ("dialysis clearance") of a single marker.
- Assess risk profile of dialysis patients (nutrition, inflammation, catabolism, fluid status).
- Assess patient needs and expected toleration of dialysis treatment sessions by focusing on the concept of electrolyte/osmolar/toxin *balances* and on current hemodynamic status.
- Adjust treatment time and other modifiable prescription parameters by risk profile and expected dialysis tolerance.
- Use interdisciplinary teamwork to apply these principles in dialysis practice.