# Meaningless Statements in Epidemiology

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# Happy Birthday Jean-Claude!



### My Message

•The modern theory of measurement was developed to deal with measurement in the social and behavioral sciences where scales are not as readily defined as in the physical sciences.

Utility, noise, intelligence, ...
Traditional concepts of measurement theory are not well known in the public health arena.

•They are finding interesting new applications there.

•In turn, problems of epidemiology and public health are providing new challenges for measurement theory.



measles

#### **Some Questions We Will Ask**

# •Is it meaningful to say that the malaria parasite load has doubled?





# **Some Questions We Will Ask** •Is the average cough score for one set of TB patients higher than that for another?





#### **Some Questions We Will Ask**

•For controlling the spread of HIV, which of abstinence education, universal screening, and condom distribution are more effective?



•All of these questions have something to do with measurement.

•We will discuss applications of the theory of measurement to measurement in epidemiology and public health.



# Outline

#### **1. Introduction to Measurement Theory**

- Theory of Uniqueness of Scales of Measurement/Scale Types
- 3. Meaningful Statements
- 4. Averaging Judgments of Cough Severity
- 5. Measurement of Air Pollution
- 6. Evaluation of Alternative HIV Treatments: "Merging Normalized Scores"
- 7. Optimization Problems in Epidemiology
- 8. Meaningfulness of Statistical Tests
- 9. Behavioral Responses to Health Events

•*Measurement* has something to do with numbers.



•We take the approach of the "representational theory of measurement"

•Assign numbers to "objects" being measured in such a way that certain empirical relations are "preserved."

•Important contributions of Jean-Claude to the development of this representational theory of measurement ranging from his early work on composite measurement through biorders, well graded families of relations, almost connected orders, etc.





•*Measurement* has something to do with numbers.



- •We take the approach of the "representational theory of measurement"
- •Assign numbers to "objects" being measured in such a way that certain empirical relations are "preserved."
- •Temperature, weight are key health variables.
- •In measurement of temperature, we preserve a relation "warmer than."
- •In measurement of weight, we preserve a relation "heavier than."





*A*: Set of Objects*R*: Binary relation on *A* 

 $aRb \leftrightarrow a is$  "warmer than" b  $aRb \leftrightarrow a is$  "heavier than" b

 $f: A \to \mathcal{R}$  $aRb \leftrightarrow f(a) > f(b)$ 

R could be preference. Then f is a utility function (ordinal<br/>utility function).R could be "louder than." (E.g., coughs) Then f is a<br/>measure of loudness.

*A*: Set of Objects*R*: Binary relation on *A* 

 $aRb \leftrightarrow a is$  "warmer than" b $aRb \leftrightarrow a is$  "heavier than" b

 $f: A \to \mathcal{R}$  $aRb \leftrightarrow f(a) > f(b)$ 

With *weight*, there is more going on. *There is an operation of combination of objects and weight is additive*. *aob* means *a* combined with *b*.

 $f(a \circ b) = f(a) + f(b).$ 

•This can all be generalized using a formalism called a *homomorphism*.

•It will suffice to think of a homomorphism as a way of assigning numbers to objects being measured so that certain relations and operations among objects are reflected in comparable relations among the assigned numbers.

•Even more basically: Homomorphisms will be "*acceptable*" ways to assign numbers.

•We will be particularly interested in finding ways to transform one homomorphism (acceptable way to measure) into another. 13

#### Homomorphisms: A Formalism

#### •Empirical Relational System A

Set of objects *A* and relations *R* and operations on *A*. •*Numerical Relational System B* 

Set of objects *B* where *B* is a set of real numbers, plus a relation  $R^*$  corresponding to each *R* on *A* and an operation  $\circ^*$  corresponding to each  $\circ$  on *A*. •*Homomorphism from A* into  $\mathcal{C}$ 

A function  $f:A \rightarrow B$  such that all relations and operations among elements in A are reflected in corresponding relations and operations among elements in B, e.g.,

 $aRb \leftrightarrow f(a)R^*f(b)$ 

 $f(a \circ b) = f(a) \circ f(b).$ 

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#### **The Theory of Uniqueness**

**Admissible Transformations** 

 An admissible transformation sends one homomorphism (acceptable scale) into another.
 Centigrade → Fahrenheit Kilograms → Pounds

•In most cases one can think of an admissible transformation as defined on the range of a homomorphism.

•Suppose f is a homomorphism ("acceptable scale") from  $\mathcal{A}$  into  $\mathcal{B}$ .

• $\varphi$ : $f(A) \to B$  is called an *admissible transformation of f* if  $\varphi$ of is again a homomorphism from  $\mathcal{A}$  into  $\mathcal{B}$ .

# **The Theory of Uniqueness Admissible Transformations** $\varphi$ Centigrade $\rightarrow$ Fahrenheit: $\varphi(x) = (9/5)x + 32$ Kilograms $\rightarrow$ Pounds: $\varphi(x) = 2.2x$



### **The Theory of Uniqueness**

A classification of scales is obtained by studying the class of admissible transformations associated with the scale.
This defines the *scale type*. (S.S. Stevens)



### Some Common Scale Types

| Class of Adm. Transfs.                | Scale Type | Example           |
|---------------------------------------|------------|-------------------|
| $\varphi(x) = \alpha x, \ \alpha > 0$ | ratio      | Mass              |
|                                       |            | Temp. (Kelvin)    |
|                                       |            | Time (intervals)  |
|                                       |            | Length            |
|                                       |            | Volume            |
|                                       |            | Loudness (sones)? |
|                                       |            |                   |

 $\varphi(x) = \alpha x + \beta, \alpha > 0$  *interval* Temp (F,C) Time (calendar)

### **Some Common Scale Types**

Class of Adm. Transfs.Scale TypeExample $x \ge y \leftrightarrow \varphi(x) \ge \varphi(y)$  $\varphi$  strictly increasingordinalPreference?

Preference? Hardness Grades of leather, wool, etc. Subjective

judgments:

cough, fatigue,...

 $\varphi(x) = x$ 

absolute Counting

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•In measurement theory, we speak of a statement as being *meaningful* if its truth or falsity is not an artifact of the particular scale values used.

•The following definition is due to Suppes 1959 and Suppes and Zinnes 1963.

<u>Definition</u>: A statement involving numerical scales is *meaningful* if its truth or falsity is unchanged after any (or all) of the scales is transformed (independently?) by an admissible transformation.

•In some practical examples, for example those involving preference judgments or judgments "louder than" under the "semiorder" model, it is possible to have two scales where one can't go from one to the other by an admissible transformation, so one has to use this definition.

•A slightly more informal definition could then be used: <u>Alternate Definition:</u> A statement involving numerical scales is *meaningful* if its truth or falsity is unchanged after any (or all) of the scales is (independently?) replaced by another acceptable scale.

### Meaningful Statements: Another Point of View

•Fundamental paper by Falmagne and Narens (1983): "Scales and Meaningfulness of Quantitative Laws"

#### •Falmagne and Narens:

- This more general definition is imprecise and subject to possible misinterpretation.
- It is not clear what is meant by "involving" numerical scales
- Scales can be "involved" in a statement in more than one way
- Meaningfulness may not be a property of a single statement or relation, but of a family of relations
- This gave rise to a beautiful theory of families of numerical codes 24

#### Meaningful Statements: Another Point of View

•Falmagne and Narens:

This gave rise to a beautiful theory of families of numerical codes

•Extended in fundamental paper by Falmagne (2004): "Meaningfulness and Order-Invariance: Two Fundamental Principles for Scientific Laws"

- That paper leads to axioms based on meaningfulness that allow one to derive general form of scientific laws
- Generalizes fundamental work of Luce: "On the Possible Scientific Laws"

- •Nevertheless, the definition given is widely used in applications of the theory of measurement and in many cases can be used without ambiguity.
- •We will adopt this definition and avoid the long literature of more sophisticated approaches to meaningfulness.
- •Situations where this relatively simple-minded definition may run into trouble will be disregarded.
- •Emphasis is to be on new applications of the concept of meaningfulness.
- •But we will return to the Falmagne-Narens ideas

### **Meaningful Statements "This talk will be three times as long as the next talk."** •Is this meaningful?

**"This talk will be three times as long as the next talk."**•Is this meaningful?

#### I hope not!



**"This talk will be three times as long as the next talk."**•Is this meaningful?



Me too

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"This talk will be three times as long as the next talk."

- •Is this meaningful?
- •We have a ratio scale (time intervals).
- (1) f(a) = 3f(b).
- •This is meaningful if f is a ratio scale. For, an admissible transformation is  $\varphi(x) = \alpha x$ ,  $\alpha > 0$ . We want (1) to hold iff
- (2)  $(\varphi \circ f)(a) = 3(\varphi \circ f)(b)$
- •But (2) becomes
- (3)  $\alpha f(a) = 3\alpha f(b)$
- •(1)  $\leftrightarrow$  (3) since  $\alpha > 0$ .

"The patient's temperature at 9AM today is 2 per cent higher than it was at 9 AM yesterday."

•Is this meaningful?



"The patient's temperature at 9AM today is 2 per cent higher than it was at 9 AM yesterday."

f(a) = 1.02f(b)

•Meaningless. It could be true with Fahrenheit and false with Centigrade, or vice versa.

In general:

For ratio scales, it is meaningful to compare ratios: f(a)/f(b) > f(c)/f(d)
For interval scales, it is meaningful to compare intervals: f(a) - f(b) > f(c) - f(d)
For ordinal scales, it is meaningful to compare size: f(a) > f(b)

Malaria parasite density is still mainly obtained by reading slides under microscopes.

"The parasite density in this slide is double the parasite density in that slide."

#### •Is this meaningful?





"The parasite density in this slide is double the parasite density in that slide."

•Density is measured in number per microliter. So, if one slide has 100,000 per  $\mu$ L and another 50,000 per  $\mu$ L, is it meaningful to conclude that the first slide has twice the density of the second?

•Meaningful. Volume involves ratio scales. And counts are absolute scales.

•However: This disregards errors in measurement. A statement can be meaningful in the measurement theory sense but meaningless in a practical sense.

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Jean-Claude has done more than anyone to give a theoretical account of errors in measurement.
Extending framework of fundamental measurement to include probabilistic representations.
See papers on

- Random conjoint measurement
- Probabilistic theory of extensive measurement
- Statistical issues in measurement
- Etc.
# **Meaningful Statements**

# **"I weigh 1000 times what that elephant weighs."**•Is this meaningful?



## **Meaningful Statements**

"I weigh 1000 times what that elephant weighs."

- •Meaningful. It involves ratio scales.
- It is false no matter what the unit.

•Meaningfulness is different from truth.

•It has to do with what kinds of assertions it makes sense to make, which assertions are not accidents of the particular choice of scale (units, zero points) in use.

"The ratio of Stendhal's weight to Jane Austen's on July 3, 1914 was 1.42."
Lovely discussion in Falmagne and Narens.



# Meaningful Statements: Another Point of View

"I weigh 1000 times what that elephant weighs."

#### •Falmagne and Narens:

- A particular scale has been used to measure weight, but that scale not mentioned in the statement
- Assume initial scaling has been made with weight in pounds
- Interpretation 1: The sentence defines a numerical relation *T* such that T(a,x) iff *a* is my weight, x is the elephant's weight, and a/x = 1000.
- The sentence is meaningful since for all admissible transformations of scale *f* and all *a*, *x*:
   (a) *T*(*a*,*x*) ↔ *T*[*f*(*a*),*f*(*x*)].

# **Meaningful Statements: Another**

# **Point of View**

- "I weigh 1000 times what that elephant weighs."
- •Falmagne and Narens:
  - Interpretation 2: *Meaningfulness as a property of a family of relations.*
  - If *f* defines a particular homomorphism (scale) (e.g., pounds, grams, kilograms), then the sentence defines a family of relations  $T_f$  such that  $T_f(a,x)$  iff *a* is my weight, *x* is the elephant's weight, both measured on scale *f*, and a/x = 1000.
  - $T_f$  can be thought of as a 3-ary relation T'(f,a,x)
  - Meaningfulness can be thought of as: for all scales *f*,
     *g* and all *a*, *x*:

(b)  $T_f[f(a),f(x)] \leftrightarrow T_g[g(a),g(x)]$ 

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**Meaningful Statements: Another Point of View** "I weigh 1000 times what that elephant weighs." •Falmagne and Narens: - Since we have a ratio scale ("ratio scale family"), we get meaningfulness in both senses: (a)  $T(a,x) \leftrightarrow T[f(a),f(x)]$ . (b)  $T_f[f(a),f(x)] \leftrightarrow T_g[g(a),g(x)]$ - (a) holds since for all  $\alpha > 0$ ,  $a/x = 1000 \leftrightarrow \alpha a/\alpha x = 1000$ - (b) holds since for all  $\alpha$ ,  $\beta > 0$ ,  $\alpha a/\alpha x = 1000 \leftrightarrow \beta x/\beta y = 1000$ 

# Meaningful Statements: Another Point of View

- •However, there are examples where the two interpretations differ.
- Fix an initial scale *F* and assume we have a ratio scale.
  Then for any scale *f*, there is α so that *f*(*a*) = α*F*(*a*) for all *a*.
- •Fix *k* and for all *a*, *x*, let T(a,x) be the statement T(a,x): a = x + k
- •Interpretation 1: *T* as a statement is not meaningful since  $T(a,x) \leftrightarrow T[\alpha F(a), \alpha F(x)]$

can hold for some values of  $\alpha$  and not others.

•Falmagne and Narens says that *T* is *meaningless in the first sense*.

#### **Another Point of View**

- Fix k and for all a, x, let T(a,x) be the statement T(a,x): a = x + k
- But perhaps the constant k really depends on the choice of scale f, i.e., k = k(f).
- Interpretation 2: Consider the meaningfulness of the family of statements  $T_f[f(a), f(b)]$
- Now consider whether

(\*)  $T_f[f(a), f(b)] \leftrightarrow T_g[g(a), g(b)]$ 

- Consider the simple case where  $k(\lambda F) = \lambda k(F)$ .
- Then if  $f = \alpha F$  and  $g = \beta F$ , (\*) becomes

 $\alpha F(a) = \alpha F(b) + \alpha k(F) \leftrightarrow \beta F(a) = \beta F(b) + \beta k(F)$ 

- This is true.
- Falmagne and Narens say that we have a family of statements *meaningful in the second sense*

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•Study two groups of patients with TB.

•*f(a)* is the cough severity of *a* as judged on one of the subjective cough severity scales (e.g., rate severity as 1 to 5)

•Data suggests that the average cough severity for patients in the first group is higher than the average cough severity of patients in the second group.

 $a_1, a_2, ..., a_n$  patients in first group  $b_1, b_2, ..., b_m$  patients in second group.

 $n \qquad m$ (1)  $\binom{1}{n} \sum f(a_i) > \binom{1}{m} \sum f(b_i)$  $i=1 \qquad i=1$ •We are comparing *arithmetic means*.



**Average Cough Severity** •Statement (1) is meaningful iff for all admissible transformations of scale  $\varphi$ , (1) holds iff n M (2)  $(1/_{n}) \Sigma (\varphi \circ f)(a_{i}) > (1/_{m}) \Sigma (\varphi \circ f)(b_{i})$ i=1i=1•If cough severity defines a ratio scale: •Then,  $\varphi(x) = \alpha x, \alpha > 0$ , so (2) becomes n M (3)  $(1/_n) \sum \alpha f(a_i) > (1/_m) \sum \alpha f(b_i)$ i=1i=1•Then  $\alpha > 0$  implies (1)  $\leftrightarrow$  (3). Hence, (1) is meaningful. •So this kind of comparison would work if we were 46 comparing weights of TB patients.

Note: (1) is still meaningful if *f* is an interval scale.
For example, we could be comparing temperatures *f(a)*.
Here, φ(x) = αx + β, α > 0. Then (2) becomes *n m*(4) (<sup>1</sup>/<sub>n</sub>) Σ αf(a<sub>i</sub>)+β > (<sup>1</sup>/<sub>m</sub>) Σ αf(b<sub>i</sub>)+β *i*=1 *i*=1

•This readily reduces to (1).

•However, (1) is meaningless if f is just an ordinal scale.

- •To show that comparison of arithmetic means can be meaningless for ordinal scales, note that we are asking experts for a subjective judgment of cough severity.
- •It seems that *f(a)* is measured on an ordinal scale, e.g., <u>5-point scale</u>: 5=extremely severe, 4=very severe, 3=severe, 2=slightly severe, 1=no cough.
- •In such a scale, the numbers may not mean anything; only their order matters.

Group 1: 5, 3, 1 average 3 Group 2: 4, 4, 2 average 3.33

•Conclude: average cough severity of group 2 patients is higher.

Suppose *f(a)* is measured on an ordinal scale, e.g., <u>5-point scale</u>: 5=extremely severe, 4=very severe, 3=severe, 2=slightly severe, 1=no cough.
In such a scale, the numbers may not mean anything; only their order matters.

Group 1: 5, 3, 1 average 3
Group 2: 4, 4, 2 average 3.33 (greater)
Admissible transformation: 5 → 100, 4 → 75, 3 → 65, 2 → 40, 1 → 30
New scale conveys the same information. New scores:
Group 1: 100, 65, 30 average 65
Group 2: 75, 75, 40 average 63.33

Conclude: average severity of group 1 patients is higher.<sup>49</sup>

•Thus, comparison of arithmetic means can be meaningless for ordinal data.

•Of course, you may argue that in the 5-point scale, at least *equal spacing* between scale values is an inherent property of the scale. In that case, the scale is *not* ordinal and this example does not apply.

•Note: Comparing *medians* is meaningful with ordinal scales: To say that one group has a higher median than another group is preserved under admissible transformations.

## **Average Fatigue**

•Fatigue is an important variable in measuring the progress of patients with serious diseases.

- •One scale widely used in measuring fatigue is the Piper Fatigue Scale.
- •It asks questions like:
  - On a scale of 1 to 10, to what degree is the fatigue you are feeling now interfering with your ability to complete your work or school activities? (1 = none, 10 = a great deal)

On a scale of 1 to 10, how would you describe the degree of intensity or severity of the fatigue which you are experiencing now? (1 = mild, 10 = severe)
 Similar analysis applies: Meaningless to compare means, meaningful to compare medians <sup>51</sup>

•Suppose each of *n* observers is asked to rate each of a collection of patients as to their relative cough severity.

•Or we rate patients on different criteria or against different benchmarks. (Similar results with performance ratings, importance ratings, etc.)

•Let  $f_i(a)$  be the rating of patient *a* by judge *i* (under criterion *i*). Is it meaningful to assert that the average rating of patient *a* is higher than the average rating of patient *b*?

•Let  $f_i(a)$  be the rating of patient *a* by judge *i* (under criterion *i*). Is it meaningful to assert that the average rating of patient *a* is higher than the average rating of patient *b*?

•A similar question arises in fatigue ratings, ratings of brightness of rash, etc.

 $n \qquad n$ (1)  $\binom{1}{n} \sum_{i=1}^{n} f_i(a) > \binom{1}{n} \sum_{i=1}^{n} f_i(b)$ 

•If each  $f_i$  is a ratio scale, then we consider for  $\alpha > 0$ , n n  $(2) \quad \binom{1}{n} \sum \alpha f_i(\alpha) > \binom{1}{n} \sum \alpha f_i(b)$ i=1 i=1•Clearly,  $(1) \leftrightarrow (2)$ , so (1) is meaningful.

•Problem:  $f_1, f_2, ..., f_n$  might have *independent units*. In this case, we want to allow independent admissible transformations of the  $f_i$ . Thus, we must consider

N

n

(3)  $\binom{1}{n} \sum \alpha_{i} f_{i}(a) > \binom{1}{n} \sum \alpha_{i} f_{i}(b)$  i=1 i=1• It is easy to see that there are  $\alpha_{i}$  so that (1) holds and (3) fails. Thus, (1) is meaningless. <sup>54</sup>

Motivation for considering different  $\alpha_i$ :

n = 2,  $f_1(a) =$  weight of a,  $f_2(a) =$  height of a. Then (1) says that the average of a's weight and height is greater than the average of b's weight and height. This could be true with one combination of weight and height scales and false with another.





Compare the Falmagne-Narens discussion of families of relations depending on several scales.
They consider statements like

 $\overline{T_{f_1f_2\dots f_n}[a_1,a_2,\dots,a_n]} \leftrightarrow \overline{T_{f_1f_2\dots f_n}[g_1(a_1),g_2(a_2),\dots,g_n(a_n)]}$ 





Motivation for considering different  $\alpha_i$ :

n = 2,  $f_1(a) =$  weight of a,  $f_2(a) =$  height of a. Then (1) says that the average of a's weight and height is greater than the average of b's weight and height. This could be true with one combination of weight and height scales and false with another.



•In this context, it is safer to compare *geometric means* (Dalkey).

 $\frac{n}{\sqrt{\prod f_i(a)}} > \frac{n}{\sqrt{\prod f_i(b)}} \longleftrightarrow \frac{n}{\sqrt{\prod \alpha_i f_i(a)}} > \frac{n}{\sqrt{\prod \alpha_i f_i(b)}}$ 

all  $\alpha_i > 0$ .

• Thus, if each  $f_i$  is a ratio scale, if individuals can change cough severity rating scales (performance rating scales, importance rating scales) independently, then *comparison* of geometric means is meaningful while comparison of arithmetic means is not.

# **Application of this Idea**

## Role of Air Pollution in Health.



In a study of air pollution and related energy use in San Diego, a panel of experts each estimated the relative importance of variables relevant to air pollution using the *magnitude estimation procedure*. Roberts (1972, 1973). *Magnitude estimation*: Most important gets score of 100. If half as important, score of 50. And so on.
If magnitude estimation leads to a ratio scale -- Stevens presumes this -- then comparison of geometric mean importance ratings is meaningful.

•However, comparison of arithmetic means may not be. Geometric means were used.



<u>Magnitude Estimation by One Expert of Relative</u> <u>Importance for Air Pollution of Variables Related to</u> <u>Commuter Bus Transportation in a Given Region</u>

| Variable                           | Rel. Import. Rating |
|------------------------------------|---------------------|
| 1. No. bus passenger mi. annually  | 80                  |
| 2. No. trips annually              | 100                 |
| 3. No. miles of bus routes         | 50                  |
| 4. No. miles special bus lanes     | 50                  |
| 5. Average time home to office     | 70                  |
| 6. Average distance home to office | 65                  |
| 7. Average speed                   | 10                  |
| 8. Average no. passengers per bus  | 20                  |
| 9. Distance to bus stop from home  | 50                  |
| 10. No. buses in the region        | 20                  |
| 11. No. stops, home to office      | 20 60               |

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- •Close relationship between pollution and health
- •Various pollutants are present in the air:
- •Carbon monoxide (CO), hydrocarbons (HC), nitrogen oxides (NOX), sulfur oxides (SOX), particulate matter (PM).
- •Also damaging: Products of chemical reactions among pollutants. E.g.: Oxidants such as ozone produced by HC and NOX reacting in presence of sunlight.
- •Some pollutants are more serious in presence of others, e.g., SOX are more harmful in presence of PM.
- •Can we measure pollution with one overall measure? <sub>63</sub>

To compare pollution control policies, need to compare effects of different pollutants. We might allow increase of some pollutants in order to achieve decrease of others.
One single measure could give indication of how bad pollution level is and might help us determine if we have made progress.

**Combining Weight of Pollutants:** 

•Measure total weight of emissions of pollutant i over fixed period of time and sum over i.

e(i,t,k) = total weight of emissions of pollutant *i* (per cubic meter) over *t*th time period and due to *k*th source or measured in *k*th location.

n  $A(t,k) = \sum_{i=1}^{n} e(i,t,k)$ 

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• Early uses of this simple index *A* in the early 1970s led to the conclusions:

(A) Transportation is the largest source of air pollution, with stationary fuel combustion (especially by electric power plants) second largest.
(B) Transportation accounts for over 50% of all air pollution.
(C) CO accounts for over half of all emitted air pollution.

•Are these meaningful conclusions?

• Early uses of this simple index *A* in the early 1970s led to the conclusions:

(A) Transportation is the largest source of air pollution, with stationary fuel combustion (especially by electric power plants) second largest.

•Are these meaningful conclusions?

A(t,k) > A(t,k')



• Early uses of this simple index A in the early 1970s led to the conclusions:

(B) Transportation accounts for over 50% of all air pollution.

• Are these meaningful conclusions?

 $\underline{A(t,k_r)} > \Sigma A(t,\overline{k})$   $\underline{k \neq k_r}$ 



•Early uses of this simple index *A* in the early 1970s led to the conclusions:

(C) CO accounts for over half of all emitted air pollution.

•Are these meaningful conclusions?

 $\begin{array}{c|c} \overline{\Sigma \ e(i,t,k)} > \Sigma & \overline{\Sigma \ e(j,t,k)} \\ t,k & t,k & j \neq i \end{array}$ 



A(t,k) > A(t,k')

 $A(t,k_r) > \sum A(t,k)$  $k \neq k_r$ 

 $\sum_{\substack{t,k \\ t,k \\ t,k \\ t,k \\ t,k \\ t,k \\ t,k \\ j \neq i}} \sum_{\substack{t,k \\ t,k \\ t \neq i}} \sum_{\substack{t,k \\ t \neq i}} e(j,t,k)$ 

All these conclusions are meaningful if we measure all e(i,t,k) in same units of mass (e.g., milligrams per cubic meter) and so admissible transformation means multiply e(i,t,k) by same constant.

- •These comparisons are meaningful in the technical sense.
- •But: Are they meaningful comparisons of pollution level in a practical sense?
- •A unit of mass of CO is far less harmful than a unit of mass of NOX. EPA standards based on health effects for 24 hour period allow 7800 units of CO to 330 units of NOX.
- These are *Minimum acute toxicity effluent tolerance factors* (MATE criteria).

*Tolerance factor* is level at which adverse effects are known. Let *τ(i)* be tolerance factor for *i*th pollutant. *Severity factor*: *τ*(CO)/*τ(i)* or 1/*τ(i)*

•One idea (Babcock and Nagda, Walther, Caretto and Sawyer): Weight the emission levels (in mass) by severity factor and get a weighted sum. This amounts to using the indices

**Degree of hazard**:  $1/\tau(i) * e(i,t,k)$ and the combined index

 $\begin{array}{c}n\\Pindex: B(t,k) = \sum \left[1/\tau(i) * e(i,t,k)\right]\\i=1\end{array}$ 

•Under pindex, transportation is still the largest source of pollutants, but now accounts for less than 50%. Stationary sources fall to fourth place. CO drops to bottom of list of pollutants, accounting for just over 2% of the total. <sup>71</sup>

- These conclusions are again meaningful if all emission weights are measured in the same units. For an admissible transformation multiplies  $\tau$  and e by the same constant and thus leaves the degree of hazard unchanged and pindex unchanged.
- •Pindex was introduced in the San Francisco Bay Area in the 1960s.



•But, are comparisons using pindex meaningful in the practical sense?
#### **MEASUREMENT OF AIR POLLUTION**

• Pindex amounts to: For a given pollutant, take the percentage of a given harmful level of emissions that is reached in a given period of time, and add up these percentages over all pollutants. (Sum can be greater than 100% as a result.)

•If 100% of the CO tolerance level is reached, this is known to have some damaging effects. Pindex implies that the effects are equally severe if levels of five major pollutants are relatively low, say 20% of their known harmful levels.

## **MEASUREMENT OF AIR POLLUTION**

- •*Severity tonnage* of pollutant *i* due to a given source is actual tonnage times the severity factor  $1/\tau(i)$ .
- •In early air pollution measurement literature, severity tonnage was considered a measure of how severe pollution due to a source was.
- •Data from Walther 1972 suggests the following.
- •Interesting exercise to decide which of these conclusions are meaningful.



**MEASUREMENT OF AIR POLLUTION** 

1. HC emissions are more severe (have greater severity tonnage) than NOX emissions.

2. Effects of HC emissions from transportation are more severe than those of HC emissions from industry. (Same for NOX.).

3. Effects of HC emissions from transportation are more severe than those of CO emissions from industry.

4. Effects of HC emissions from transportation are more than 20 times as severe as effects of CO emissions from transportation.

5. The total effect of HC emissions due to all sources is more than 8 times as severe as total effect of NOX emissions due to all sources.<sup>75</sup>

## Outline

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- 8. Meaningfulness of Statistical Tests
- 9. Behavioral Responses to Health Events

## **Evaluation of Alternative HIV Treatments**

- •How do we evaluate alternative possible treatment plans or interventions for a given disease?
- One common procedure: A number of treatments are compared on different criteria/benchmarks.
- •Their scores on each criterion are normalized relative to the score of one of the treatments.
- •The normalized scores of a treatment are combined by some averaging procedure and normalized scores are compared.



AIDS orphans

## **Evaluation of Alternative HIV Treatments**

- •The normalized scores of a treatment are combined by some averaging procedure.
- •If the averaging is the arithmetic mean, then the statement "one treatment has a higher arithmetic mean normalized score than another system" is meaningless:
- •The treatment to which scores are normalized can determine which has the higher arithmetic mean.



AIDS street kids

## **Evaluation of HIV Treatments**

•Similar methods are used in comparing performance of alternative computer systems or other types of machinery.

•Consider a number of treatments/interventions:

Universal screening
Free condom distribution
Abstinence education
Male circumcision



Consider a number of criteria/outcomes:
✓ CD4 count
✓ Days without symptoms of ...
✓ Number days hospitalized ...

## Treatment Evaluation Evaluation of HIV Treatments CRITERION

|             |   | E   | F  | G   | H      | Ι   |
|-------------|---|-----|----|-----|--------|-----|
| T<br>R<br>E | R | 417 | 83 | 66  | 39,449 | 772 |
| A<br>T<br>M | Μ | 244 | 70 | 153 | 33,527 | 368 |
| E<br>N<br>T | Z | 134 | 70 | 135 | 66,000 | 369 |

## Normalize Relative to Treatment R CRITERION

|        |   | E    | F    | G    | H      | Ι    |
|--------|---|------|------|------|--------|------|
| Τ      |   | 417  | 83   | 66   | 39,449 | 772  |
| R      | R | 1.00 | 1.00 | 1.00 | 1.00   | 1.00 |
| E      |   |      |      |      |        |      |
| A      |   | 244  | 70   | 153  | 33,527 | 368  |
| T      | Μ | .59  | .84  | 2.32 | .85    | .48  |
| M      |   |      |      |      |        |      |
| E      |   | 134  | 70   | 135  | 66,000 | 369  |
| N<br>T | Z | .32  | .85  | 2.05 | 1.67   | .45  |
|        |   |      |      |      |        |      |

| Take Arithmetic Mean of Normalized Scores |           |      |      |      |        |      |      |  |  |
|---|-----------|------|------|------|--------|------|------|--|--|
|   | CRITERION |      |      |      |        |      |      |  |  |
|   |           | E    | F    | G    | H      | Ι    | Mean |  |  |
| Τ   |           | 417  | 83   | 66   | 39,449 | 772  | 1.00 |  |  |
| R   | R         | 1.00 | 1.00 | 1.00 | 1.00   | 1.00 | 1.00 |  |  |
| E   |           |      |      |      |        |      |      |  |  |
| A   |           | 244  | 70   | 153  | 33,527 | 368  | 1.01 |  |  |
| T   | M         | .59  | .84  | 2.32 | .85    | .48  |      |  |  |
| M   |           |      |      |      |        |      | -    |  |  |
| E   |           | 134  | 70   | 135  | 66,000 | 369  | 1.07 |  |  |
|   | Z         | .32  | .85  | 2.05 | 1.67   | .45  | 1.07 |  |  |
| I   |           |      |      |      |        |      | 82   |  |  |

| Take Arithmetic Mean of Normalized Scores |           |       |          |        |                   |      |      |  |  |
|---|-----------|-------|----------|--------|-------------------|------|------|--|--|
|   | CRITERION |       |          |        |                   |      |      |  |  |
|   |           | E     | F        | G      | Η                 | Ι    | Mean |  |  |
| Τ   |           | 417   | 83       | 66     | 39,449            | 772  | 1.00 |  |  |
| R<br>E                                    | R         | 1.00  | 1.00     | 1.00   | 1.00              | 1.00 | 1.00 |  |  |
| A   |           | 244   | 70       | 153    | 33,527            | 368  | 1.01 |  |  |
| I<br>M                                    | M         | .59   | .84      | 2.32   | .85               | .48  |      |  |  |
| E<br>N                                    |           | 134   | 70       | 135    | 66,000            | 369  | 1.07 |  |  |
| T   | Z         | .32   | .85      | 2.05   | 1.67              | .45  | 1.07 |  |  |
|   |           | Concl | ude that | treatm | ent <b>7</b> is h | est  | 83   |  |  |

## Now Normalize Relative to Treatment M CRITERION

|         |   | E    | F    | G    | H      | Ι    |
|---------|---|------|------|------|--------|------|
| Τ       |   | 417  | 83   | 66   | 39,449 | 772  |
| R       | R | 1.71 | 1.19 | .43  | 1.18   | 2.10 |
| E       |   |      |      |      |        |      |
| A       |   | 244  | 70   | 153  | 33,527 | 368  |
| T       | M | 1.00 | 1.00 | 1.00 | 1.00   | 1.00 |
|         |   |      |      |      |        |      |
| E       |   | 134  | 70   | 135  | 66,000 | 369  |
| IN<br>T | Ζ | .55  | 1.00 | .88  | 1.97   | 1.00 |
| L       |   |      |      |      |        |      |

#### **Take Arithmetic Mean of Normalized Scores** Arithmetic **CRITERION** Mean E F G H Π T 772 39,449 417 83 66 1.32 R R 1.18 1.71 1.19 2.10 .43 E A 33,527 244 70 153 368 1.00 T Μ 1.00 1.00 1.00 1.00 1.00 Μ E 66,000 134 70 135 369 N 1.08 Ζ .55 1.97 1.00 1.00 .88 Т 85

#### **Take Arithmetic Mean of Normalized Scores** Arithmetic **CRITERION** Mean E F G H Ι T 417 39,449 772 83 66 1.32 R R 1.71 1.19 1.18 2.10 .43 E A 33,527 244 70 153 368 1.00 T Μ 1.00 1.00 1.00 1.00 1.00 Μ E 66,000 134 70 135 369 1.08 N Ζ .55 1.97 1.00 .88 1.00 T 86

**Conclude that treatment R is best** 

- So, the conclusion that a given treatment is best by taking arithmetic mean of normalized scores is meaningless in this case.
- Above example from Fleming and Wallace (1986), data from Heath (1984) (in a computing machine application)
- Sometimes, geometric mean is helpful.
- Geometric mean is

$$\sqrt[n]{\prod_i \mathbf{s}(x_i)}$$

| Treatment Evaluation              |   |      |      |       |        |      |           |  |  |
|-----------------------------------|---|------|------|-------|--------|------|-----------|--|--|
| Normalize Relative to Treatment R |   |      |      |       |        |      |           |  |  |
|                                   |   |      | C    | RITER | ION    |      | Geometric |  |  |
|                                   |   | E    | F    | G     | H      | Ι    | Mean      |  |  |
| Τ                                 |   | 417  | 83   | 66    | 39,449 | 772  |           |  |  |
| R                                 | R | 1.00 | 1.00 | 1.00  | 1.00   | 1.00 | 1.00      |  |  |
| E                                 |   |      |      |       |        |      |           |  |  |
| A                                 |   | 244  | 70   | 153   | 33,527 | 368  | .86       |  |  |
| T                                 | M | .59  | .84  | 2.32  | .85    | .48  |           |  |  |
|                                   |   |      |      |       |        |      |           |  |  |
|                                   | 7 | 134  | 70   | 135   | 66,000 | 369  | <u>84</u> |  |  |
| T                                 |   | .32  | .85  | 2.05  | 1.67   | .45  | .04       |  |  |
| -                                 |   |      |      |       |        |      | 88        |  |  |

Conclude that treatment R is best

#### Now Normalize Relative to Treatment M

CDITEDION

Geometric

|   |   | E      | F    | G    | H      | Ι    | Mean |
|---|---|--------|------|------|--------|------|------|
| Τ |   | 417    | 83   | 66   | 39,449 | 772  |      |
| R | R | 1.71   | 1.19 | .43  | 1.18   | 2.10 | 1.17 |
| E |   |        |      |      |        |      |      |
| A |   | 244    | 70   | 153  | 33,527 | 368  |      |
| T | M | 1.00   | 1.00 | 1.00 | 1.00   | 1.00 | 1.00 |
| M |   |        |      |      |        |      |      |
| E |   | 134    | 70   | 135  | 66,000 | 369  | 00   |
|   | Z | .55    | 1.00 | .88  | 1.97   | 1.00 | .99  |
|   |   | C 4 11 |      |      |        |      | 89   |
|   |   |        |      |      |        |      |      |

Still conclude that treatment **R** is best

- In this situation, it is easy to show that *the conclusion that a given treatment has highest geometric mean normalized score is a meaningful conclusion.*
- Even meaningful: A given treatment has geometric mean normalized score 20% higher than another treatment.
- Fleming and Wallace give general conditions under which comparing geometric means of normalized scores is meaningful.
- Research area: what averaging procedures make sense in what situations? Large literature.

Message from measurement theory:



Do not perform arithmetic operations on data without paying attention to whether the conclusions you get are meaningful.

- We have seen that in some situations, comparing arithmetic means is not a good idea and comparing geometric means is.
- There are situations where the reverse is true.
- Can we lay down some guidelines as to when to use what averaging procedure?
- Some results of Aczél, Roberts and Rosenbaum following on work of Luce on the possible psychophysical laws.

•Aczél, Roberts, Rosenbaum: •Suppose the averaging function F is defined based on scales  $a_1, a_2, ..., a_n$ . •Suppose the following statements are meaningful:  $F(a_1, a_2, \dots, a_n) = kF(b_1, b_2, \dots, b_n)$ •Suppose  $a_1, a_2, ..., a_n$  are independent ratio scales •Suppose F is reflexive: F(a,a,...,a) = a•Suppose *F* is symmetric:  $F(a_1, a_2, \dots, a_n) = F(a_{\pi(1)}, a_{\pi(2)}, \dots, a_{\pi(n)})$ for all permutations  $\pi$  of  $\{1, 2, ..., n\}$ 

•Then F is the geometric mean.

Aczél, Roberts, Rosenbaum
Suppose the averaging function *F* is defined based on scales *a*<sub>1</sub>, *a*<sub>2</sub>, ..., *a*<sub>n</sub>.
Suppose the following statements are meaningful: *F*(*a*<sub>1</sub>,*a*<sub>2</sub>, ..., *a<sub>n</sub>*) - *F*(*b*<sub>1</sub>,*b*<sub>2</sub>, ..., *b<sub>n</sub>*) = *k*[*F*(*c*<sub>1</sub>,*c*<sub>2</sub>, ..., *c<sub>n</sub>*) - *F*(*d*<sub>1</sub>,*d*<sub>2</sub>, ..., *d<sub>n</sub>*)]

F(a<sub>1</sub>,a<sub>2</sub>,..., a<sub>n</sub>) > F(b<sub>1</sub>,b<sub>2</sub>,..., b<sub>n</sub>)
Suppose a<sub>1</sub>, a<sub>2</sub>, ..., a<sub>n</sub> are interval scales with the same unit and independent zero points
Suppose F is reflexive and symmetric
Then F is the arithmetic mean.

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## **DIMACS** Initiative on Climate and Health

•Spurred by concerns about global warming. •Resulting impact on health -Of people -Of animals Earth's temperature has risen about 1 degree Fahrenheit in the last century. The past Greenhouse gases are 50 years of warming ions that rise into the -Of plants has been here and trap the attributed to energy, keeping hea Most Burning fuels such as human of the world's coal, natural gas and activity emissions are oil produces green-The United States attributed to the house gases in United States' excessive was responsible -Of ecosystems large-scale use for 20 percent of amounts of fuels in the global vehicles and greenhouse gases

#### **Global warming: Causes and effects**



## **Climate and Health**

•Special emphasis on extreme heat events, e.g.,: -1995 extreme heat event in Chicago >514 heat-related deaths > 3300 excess emergency admissions -2003 heat wave in Europe **Oppressive heat settles in Europe** >35,000 deaths 60 F Temperature, Wednesday.



Officials warned citizens, especially the elderly, to stay indoors and drink plenty of water during the summer's second major heat wave.



## **DIMACS Project: Extreme Heat Events**



- Result in increased incidence of heat stroke, dehydration, cardiac stress, respiratory distress
- Hyperthermia in elderly patients can lead to cardiac arrest.
- Effects not independent: Individuals under stress due to climate may be more susceptible to infectious diseases

## **Extreme Heat Events: Evacuation**

•One response to such events: evacuation of most vulnerable individuals to climate controlled environments.

- •Modeling challenges:
  - –Where to locate the evacuation centers?
  - –Whom to send where?



-Goals include minimizing travel time, keeping facilities to their maximum capacity, etc.

-Relevance of mathematical tools of operations research – location theory, assignment problems, etc.

**One Approach to Evacuation: Find the Shortest Route from Home to Evacuation Center** 





## Optimization Problems in Epidemiology: Shortest Path Problem



Numbers = some sort of weights or lengths

*Problem: Find the shortest path from x to z in the network.*Widely applied problem.
✓ US Dept. of Transportation alone uses it billions of times a year.



The shortest path from x to z is the path x to y to z.
Is this conclusion meaningful?

- •It is if the numbers define a ratio scale.
- •The numbers define a ratio scale if they are distances, as in the DIMACS Climate and Health project.



However, what if the numbers define an interval scale?
For example, the numbers could be costs in terms of utility (or disutility) assigned to a route, and these might only define an interval scale.



#### •Consider the admissible transformation $\varphi(x) = 3x + 100$ .



Consider the admissible transformation φ(x) = 3x + 100.
Now we get the above numbers on the edges.

• Now the shortest path is to go directly from x to z.

• The original conclusion was meaningless.

## **Linear Programming**

- The shortest path problem can be formulated as a linear programming problem.
- Thus: The conclusion that A is the solution to a linear programming problem can be meaningless if cost parameters are measured on an interval scale.
- How many people realize that?
- Note that linear programming is widely used in public health, for example to solve problems like:
  - ✓ Optimal inventories of medicines
  - Assignment of patients or doctors to clinics
  - ✓ Optimization of size of a treatment facility
  - ✓ Amount to invest in preventive treatments

# **Related Example: Minimum Spanning Tree Problem**



• A spanning tree is a tree using the edges of the graph and containing all of the vertices.

• It is minimum if the sum of the numbers on the edges used is as small as possible.

# **Related Example: Minimum Spanning Tree Problem**



Red edges define a minimum spanning tree.
Is it meaningful to conclude that this is a minimum spanning tree?
- Minimum spanning trees arise in many applications.
- One example: Given a road network, find usable roads that allow you to go from any vertex to any other vertex, minimizing the lengths of the roads used.
- This problem arises in another DIMACS Climate and Health project: Find a usable road network for emergency vehicles in case extreme events leave flooded roads.







•Consider the admissible transformation  $\varphi(x) = 3x + 100$ .



Consider the admissible transformation φ(x) = 3x + 100.
We now get the above numbers on edges.



• The minimum spanning tree is the same.



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• Is this an accident?

• No: By Kruskal' s algorithm for finding the minimum spanning tree, even an ordinal transformation will leave the minimum spanning tree unchanged.



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•Kruskal' s algorithm:

- $\checkmark$  Order edges by weight.
- ✓ At each step, pick least-weight edge that does not create a cycle with previously chosen edges.

Many practical decision making problems involve the search for an optimal solution as in Shortest Path and Minimum Spanning Tree. *Little attention is paid to the possibility that conclusion that a particular solution is optimal may be an accident of the way things are measured.*

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#### **Meaningfulness of Statistical Tests**

(joint work with Helen Marcus-Roberts)

- •Biostatistics a key component of epidemiological research.
- •However, biostatisticians know virtually nothing about measurement theory.
- •Most have never heard about the theory of meaningfulness or limitations that meaningfulness places on conclusions from statistical tests.

#### **Meaningfulness of Statistical Tests**

(joint work with Helen Marcus-Roberts)

- For > 50 years: considerable disagreement on limitations scales of measurement impose on statistical procedures we may apply.
  Controversy stems from Stevens (1946, 1951, 1959, ...):
  - ✓ Foundational work
  - ✓ Developed the classification of scales of measurement

Provided rules for the use of statistical procedures: certain statistics are inappropriate at certain levels of measurement.

#### **Meaningfulness of Statistical Tests**

The application of Stevens' ideas to *descriptive statistics* has been widely accepted
Application to *inferential statistics* has been

labeled by some a *misconception*.

- •*P* = population whose distribution we would like to describe
- •Capture properties of *P* by finding a descriptive statistic for *P* or taking a sample *S* from *P* and finding a descriptive statistic for *S*.
- Our examples suggest: certain descriptive statistics appropriate only for certain measurement situations.
  This idea originally due to Stevens
  Popularized by Siegel in his well-known book *Nonparametric Statistics* (1956). 120

- •Our examples suggest the principle: Arithmetic means are "appropriate" statistics for interval scales, medians for ordinal scales.
- •Other side of the coin: It is argued that it is *always* appropriate to calculate means, medians, and other descriptive statistics, no matter what the scale of measurement.

<u>Frederic Lord</u>: Famous football player example. "The numbers don't remember where they came from."

I agree: It is *always* appropriate to *calculate* means, medians, ...
But: Is it appropriate to make certain statements using these descriptive statistics?

- •My position: It is usually appropriate to make a statement using descriptive statistics iff the statement is meaningful.
- •A statement that is true but meaningless gives information that is an accident of the scale of measurement used, not information that describes the population in some fundamental way.
- •So, it is appropriate to calculate the mean of ordinal data
- •It is just not appropriate to say that the mean of one group is higher than the mean of another group.

•Stevens' ideas have come to be applied to inferential statistics -- inferences about an unknown population P.

•They have led to such principles as the following:

(1). Classical <u>parametric tests</u> (e.g., t-test, Pearson correlation, analysis of variance) are inappropriate for ordinal data. They should be applied only to data that define an interval or ratio scale.

(2). For ordinal scales, non-parametric tests (e.g., Mann-Whitney U, Kruskal-Wallis, Kendall's tau) can be used.

Not everyone agrees. Thus: <u>Controversy</u>

My View:

•The validity of a statistical test depends on a *statistical model* 

 This includes information about the distribution of the population and about the sampling procedure.

• The validity of the test does not depend on a *measurement model* 

✓ This is concerned with the admissible transformations and scale type.

• The scale type enters in deciding whether the hypothesis is worth testing at all -- is it a meaningful hypothesis?

• The issue is: If we perform admissible transformations of scale, is the truth or falsity of the hypothesis unchanged?

•Example: Ordinal data. Hypothesis: Mean is 0. Conclusion: This is a meaningless hypothesis.

Can we test meaningless hypotheses?
Sure. But I question what information we get outside of information about the population as measured.

More details: Testing  $H_0$  about P: 1). Draw a *random sample* S from P. 2). Calculate a *test statistic* based on S. 3). Calculate probability that the test statistic is what was observed given  $H_0$  is true. 4). Accept or reject  $H_0$  on the basis of the test.

•Calculation of probability depends on a *statistical model*, which includes information about the distribution of *P* and about the sampling procedure.

•But, validity of the test depends only on the statistical model, not on the measurement model.

- Thus, you can apply parametric tests to ordinal data, provided the statistical model is satisfied.
- Model satisfied if the data is normally distributed.
- Where does the scale type enter?
- In determining if the hypothesis is worth testing at all. i.e., if it is meaningful.

Meaningfulness of Statistical Tests: Inferential Statistics • For instance, consider ordinal data and H<sub>0</sub>: mean is 0

The hypothesis is meaningless.
But, if the data meets certain distributional requirements such as normality, we can apply a parametric test, such as the t-test, to check if the mean is 0.

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•Governments are making detailed plans for how to respond to future health "events" such as pandemic influenza, a bioterrorist attack with the smallpox virus, etc.



smallpox

- A major unknown in planning for future disease outbreaks is how people will respond.
- Behavioral responses to health events form a key issue in Economic Epidemiology.

Will they follow instructions to stay home?
Will critical personnel report to work or take care of their families?

≻Will instructions for immunization be followed?



- •Mathematical models are increasingly used to help plan for health events or to develop responses to them.
- •Especially important in planning responses to such events as:
  - Foot and Mouth Disease in Britain
    SARS
    Swine Flu





•Models in epidemiology typically omit behavioral responses.

 $\succ$ Hard to quantify.

 $\succ$ Hard to measure.

•Leads to challenges for behavioral scientists.

•Leads to challenges for mathematical sciences.

- We can learn some things from the study of responses to various disasters:
  - Earthquakes
    Hurricanes
    Fires
    Etc.



Turkey earthquake 1999



New Orleans hurricane 2005

**Behavioral Responses to Health Events** Some Behavioral Responses that Need to be Addressed:

Compliance:
Quarantine
Resistance
Willingness to seek/receive treatment
Credibility of government
Trust of decision makers

**Behavioral Responses to Health Events** Some Behavioral Responses that Need to be Addressed:

•Movement •Rumor •Perception of risk •Person to person interactions SARS Response Motivation • Social stigmata (discrimination against social groups) •Panic •Peer pressure



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**Behavioral Responses to Health Events** The Challenge to Measurement Theory:

How do we measure some of these factors?
How do we bring them into mathematical models?
What statements using the new scales of measurement are meaningful?

There is much more analysis of a similar nature in the field of epidemiology that can be done with the principles of measurement theory. There are important challenges for researchers.

### Happy Birthday Jean-Claude!



