An Intrinsically Valid Approach to Integrate Several Health Outcomes Into a Comprehensive Score

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CVD Risk Factors

Pt	BP	Chol	FamH	Smk
1	85	200	1	1
2	80	100	0	0

Pt 1 > Pt 2

CVD Risk Factors

Pt	BP	Chol	FamH	Smk
1	85	200	1	1
2	80	100	0	0
4	150	125	1	0
6	200	125	0	0

Sum_1 → Sum_2

Pt 4 </> Pt 6

276.0 → 375.0

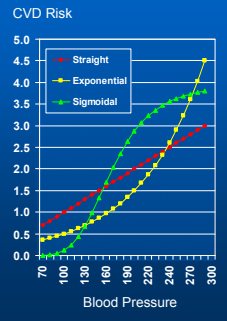
325.0 → 325.0

FamH
Smk
*100

CVD Risk Factors

Linear Model ? Rel. Importance ? Correlation ?

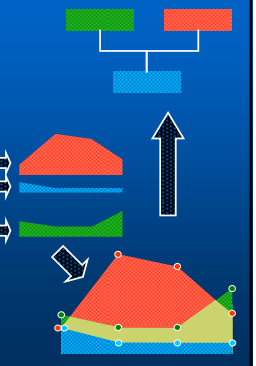
Pt	BP	Chol	FamH	Smk
1	85	200	1	1
2	80	100	0	0
4	150	125	1	0
6	200	125	0	0
5	100	520	2	1
9	75	50	0	0
8	400	510	2	1



Health Indicator Profiles

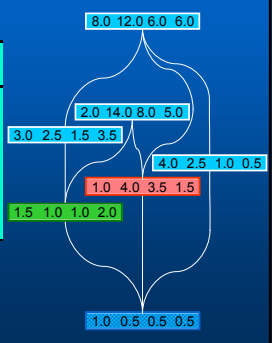
Linear Model ? Rel. Importance ? Correlation ?

Pt	Item 1	Item 2	Item 3	Item 4
1	3.0	2.5	1.5	3.5
2	4.0	2.5	1.0	0.5
4	1.0	4.0	3.5	1.5
6	1.0	0.5	0.5	0.5
5	2.0	14.0	8.0	5.0
9	1.5	1.0	1.0	2.0
8	8.0	12.0	6.0	6.0



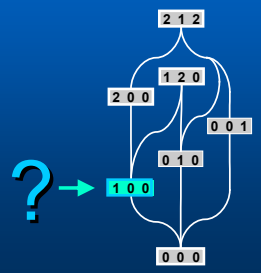
Health Indicator Profiles

Pt	Item 1	Item 2	Item 3	Item 4
1	3.0	2.5	1.5	3.5
2	4.0	2.5	1.0	0.5
4	1.0	4.0	3.5	1.5
6	1.0	0.5	0.5	0.5
5	2.0	14.0	8.0	5.0
9	1.5	1.0	1.0	2.0
8	8.0	12.0	6.0	6.0



Partial Ordering Lattice

Partial Ordering Lattice



"Propensity" Score for variables with known "orientation"

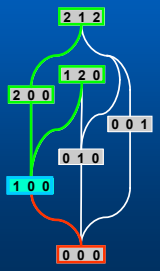
A Class of Statistics

u scores are computed as *#(lower profiles)* − *#(higher profiles)*.

unconnected profiles (ambiguous pairwise order) are ignored.

u(1 0 0) = 1−3 = −2

Partial Ordering Lattice



HOEFFDING W (1948) *AMS* 19:293

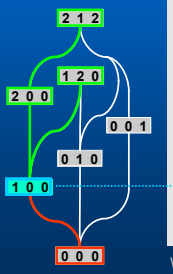
Algorithm (Deuchler, 1914):

u scores are computed as *#(lower profiles)* − *#(higher profiles)*.

unconnected profiles (ambiguous pairwise order) are ignored.

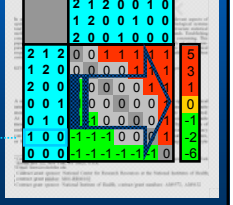
u(1 0 0) = 1−3 = −2

Partial Ordering Lattice



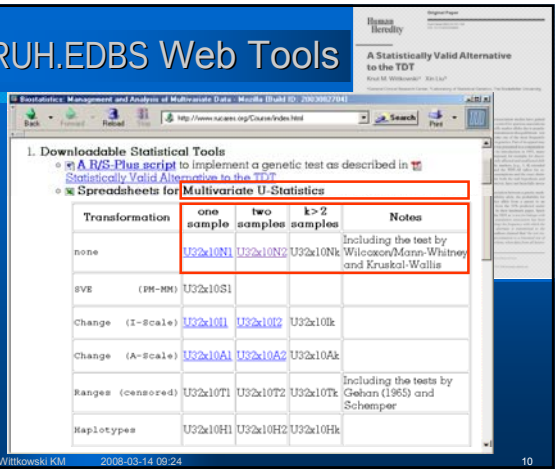
Pairwise Orderings

u Scores

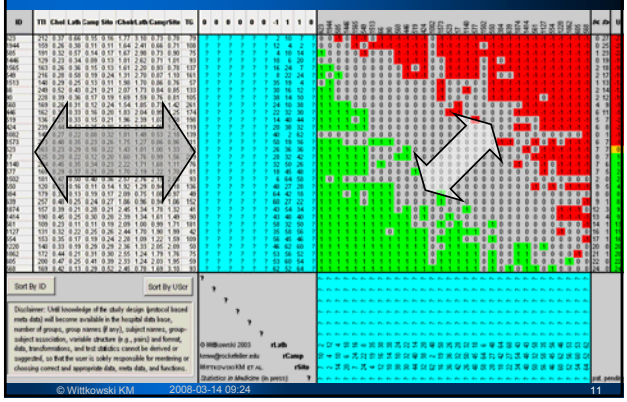


WITTKOWSKI KM (2004) *Stat Med* 23

RUH.EDBS Web Tools



More Variables: Less Information Content



S/R Functions

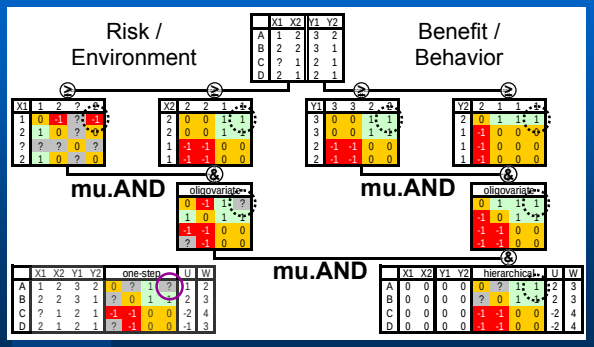
CRAN cran.r-project.org

CSAN csan.insightful.com

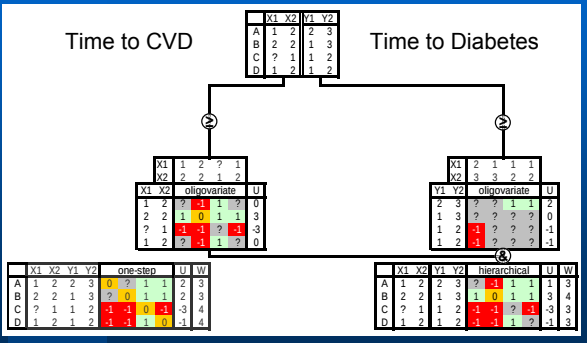
"muStat"

- ≥ **mu.GE**
  pairwise comparison
- & **mu.AND**
  combine pairwise comparisons allowing for hierarchical formula
- Σ **mu.Sums (mu.scores/mu.weight)**
  generate scores and weights from (combination of) pairwise comparisons

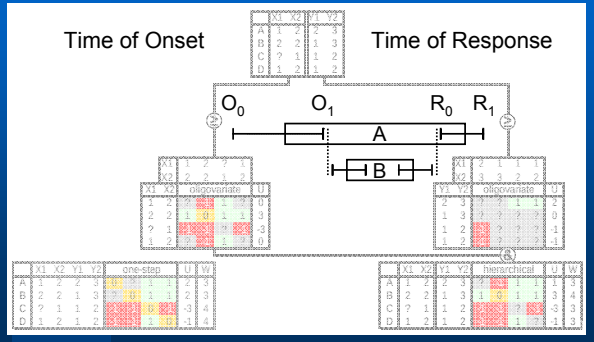
Hierarchical Variables



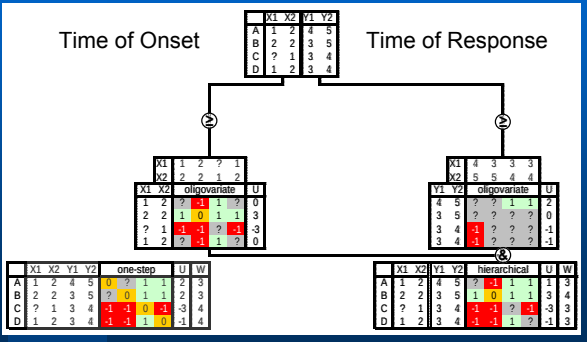
Censored Data



Doubly Censored Data



Doubly Censored Data



U Statistics: Special Cases

U statistics (univariate data: = rank tests)
are well established and widely used:

- Binary data, exact
- Binary data, inexact
- Univariate data
- Censored data (“log-rank”)

McNemar 1947 *Psychometrica*
Dixon Massey 1951 *An Intro ...*
Dixon Mood 1946 *JASA*
Wittkowski 1989 *Statistician*
Wittkowski 1998 *Biometrics*
Rayner Best 1999 *Biometrics*
Randles 2001 *The Am Stat*
Friedman 1937 *JASA*
Wilcoxon 1945 *Biometrics*
Mann Whitney 1946 *JASA*
Kruskal Wallis 1952 *JASA*
Wittkowski 1988 *JASA*
Gehan 1965 *Biometrika*
Schemper 1983 *Statist Neerland*

U-Statistics for Biological Data

Advantage over methods based on linear models:

Do not assume that all differences of the same magnitude have the same relevance.

- **Insure** that statistical results are biologically meaningful
- Are **robust** to the effect of outliers
- Do **not require** data to be transformed prior to statistical analysis

U-statistics lack of a unifying theory:

- **Hodgepodge** of methods
- Restricted to **special cases**

Tests for μ-Scores

The new function '**prentice.test**' integrates / extends (at twice the speed) several well-known tests:

"muStat"

	Conditions	Granularity	Replications	Blocks
mcnemar.test	2	2	≥2	1
SMN.pvalue	2	2	≥2	3
wilcox.test	2	≥2	≥2	1
kruskal.test	≥2	≥2	≥2	1
friedman.test	≥2	≥2	1	≥2
prentice.test	**≥2**	**≥2**	**≥0**	**≥2**

CRAN **CSAN**
cran.r-project.org
csan.insightful.com

Propensity / mu-Scores

prentice.test()

```
prentice.test <- function(
    y,                      # data   (NA allowed)
    groups,                 # groups (un/balanced)
    blocks  = NULL,         # blocks (unequal size)
    score   = "rank",       # NULL: y already scored
    blkwght = "prentice",   # block weights
                            # Wittkowski (1988) JASA

    alternative = "two.sided",      # wilcox only
    mu          = 0,                # wilcox only
    paired      = FALSE,            # wilcox only
    exact       = NULL,             # wilcox only
    correct     = NULL              # wilcox only
)
```


Signal Tandmobiel® Study

Does fluoride-intake at a young age protect permanent teeth from caries?

- Flemish schoolchidren (2315 boys, 2153 girls)
- First molars:
  maxillary "16"/"26", exchangable
  mandibular "36"/"46", exchangable
- Time of onset: Emergence of tooth
- Time of effect: Caries detected
- Grouping: Fluoride spots on permanent teeth (y/n)

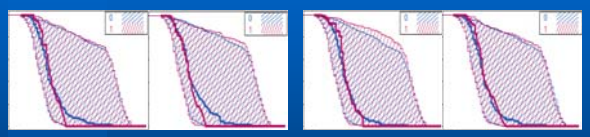
KOMAREK 2005 *Biostatistics*

The French Tooth Numbering System

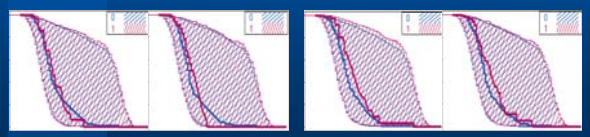
UPPER RIGHT								UPPER LEFT							
3rd Molar (Wisdom Tooth)	2nd Molar	1st Molar	2nd Pre-Molar	1st Pre-Molar	Canine	Lateral Incisor	Central Incisor	Central Incisor	Lateral Incisor	Canine	1st Pre-Molar	2nd Pre-Molar	1st Molar	2nd Molar	3rd Molar (Wisdom Tooth)
18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
LOWER RIGHT								LOWER LEFT							
3rd Molar (Wisdom Tooth)	2nd Molar	1st Molar	2nd Pre-Molar	1st Pre-Molar	Canine	Lateral Incisor	Central Incisor	Central Incisor	Lateral Incisor	Canine	1st Pre-Molar	2nd Pre-Molar	1st Molar	2nd Molar	3rd Molar (Wisdom Tooth)
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Age of Caries Onset by Sex and Tooth

Female

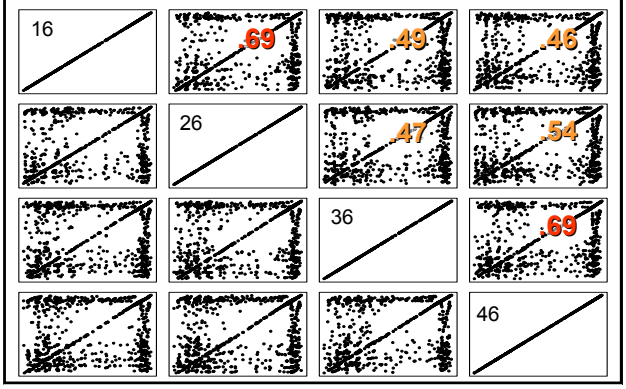


Male

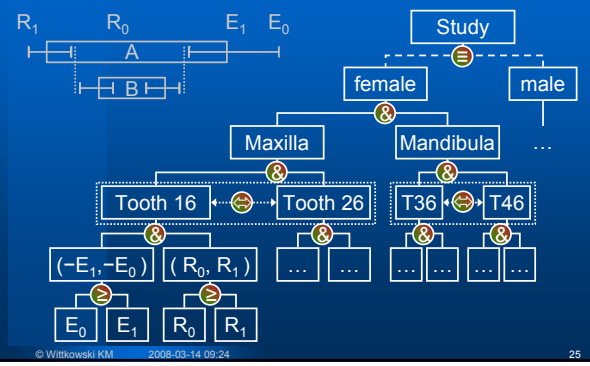


Tooth 16 Tooth 26 Tooth 36 Tooth 46

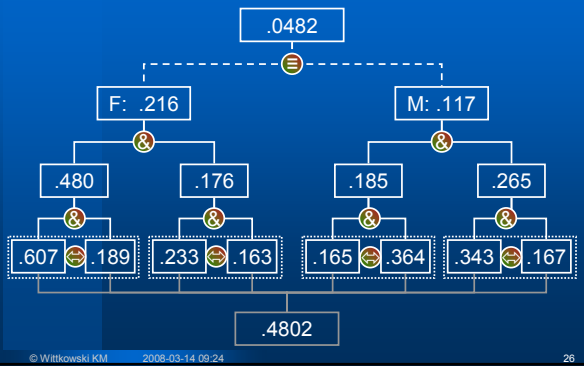
muScore Correlations



Analysis Strategy



Structural Info Improves P-Values



A Bayesian analysis of multivariate doubly-interval-censored dental data

ARNOŠT KOMÁREK*
EMMANUEL LESAFFRE

Biostatistics (2005), **6**, 1, *pp.* 145–155

Our approach is computationally demanding. Our analysis will be limited to the first molars. Case-control subsampling was done do reduce computation time.

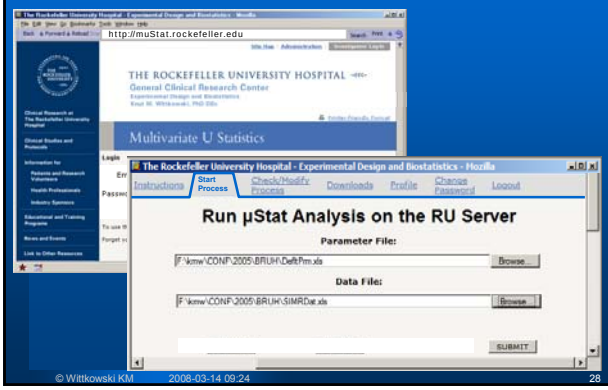
[Still,] on a Pentium IV 2 GHz PC with 512 MB RAM, one run took about 5 days to converge.

Our analysis shows no convincing effect of fluoride-intake on caries development.

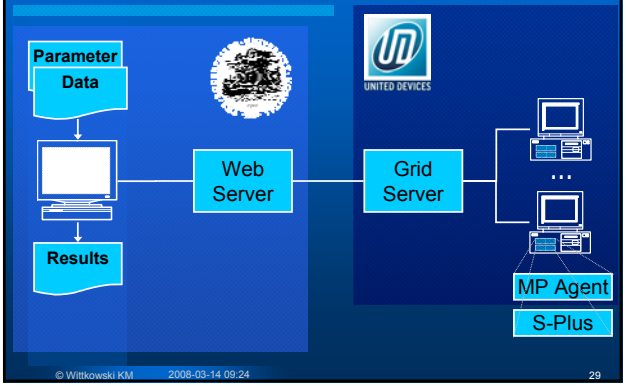
	Flemish data only	
Group	Poster. mean	95% CI
Boys, maxilla	0.651	(0.463, 0.960)
Boys, mandible	0.549	(0.386, 0.779)
Girls, maxilla	1.002	(0.698, 1.333)
Girls, mandible	0.844	(0.602, 1.135)

This agrees with current guidelines where only *topical* application is considered essential.

µStat: Uploading Files



µStat: Grid Architecture



Conclusions

µ-scores have many properties important to health policy statistics. µ-scores ...

- ... integrate interval, ordinal, and binary data
- ... are objective and intrinsically valid
- ... can reflect various design characteristics (hierarchical, exchangable, interval-censored data)
- ... are computational efficient (<1 min : 5 d for Bayes)
- ... can be used as risk/benefit or “propensity” scores

Tools are provided at mustat.rockefeller.edu

- R / S scripts and packages (also on CRAN / CSAN)
- MS Excel spreadsheets for teaching
- Grid server for (genetic/genomic) screening