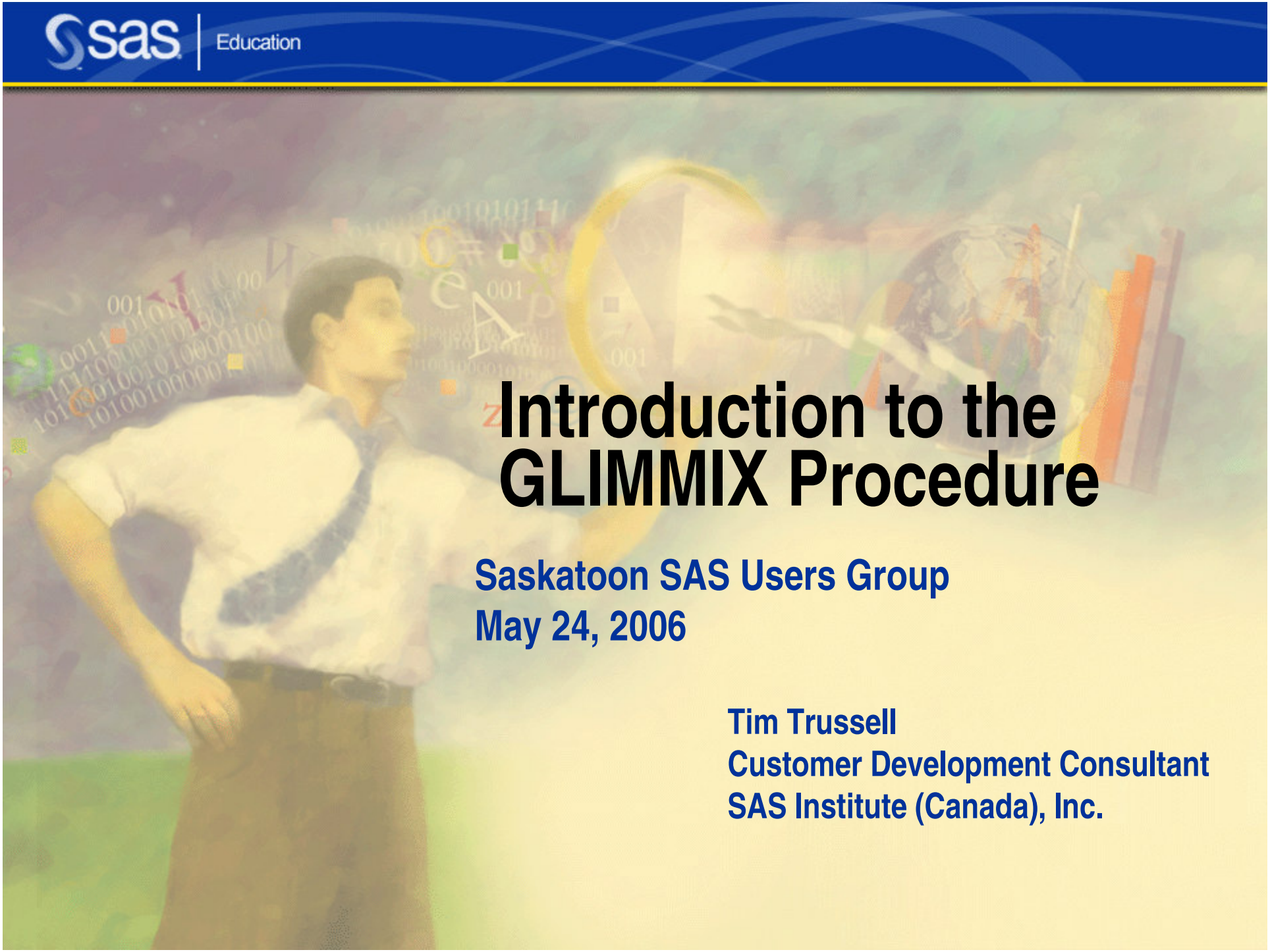

Introduction to the GLIMMIX Procedure

Saskatoon SAS Users Group
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Outline

I. Introduction to Generalized Linear Mixed Models

II. PROC GLIMMIX syntax

III. An example

Special Thanks to and Complex Questions:

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I. Introduction to Generalized Linear Mixed Models

$$g(\mu) = X\beta + Z\gamma$$

When would it be used?

- Designed experiment with 2 drug treatment varieties and 8 random clinical sites
- Beta distribution

• PROC REG/GLM?	Normal data, fixed effects
• PROC GENMOD?	Fixed effects, beta not available
• PROC MIXED?	Normal data
• PROC NLMIXED?	More complex alternative

Generalized Linear Models (GLM)

Link function

Fixed effects

$$g(\mu) = X\beta$$

Design matrix for fixed effects

$$\mu \equiv E(y)$$

$$y \sim exponential\ family$$

$$E(y) = g^{-1}(X\beta) \quad V(y) = V(\mu)a(\phi)$$

Linear Mixed Models (LMM)

Random effects

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\boldsymbol{\gamma} + \boldsymbol{\varepsilon}$$

Design matrix for random effects

$$\boldsymbol{\gamma} \sim N(\mathbf{0}, \mathbf{G}), \quad \boldsymbol{\varepsilon} \sim N(\mathbf{0}, \mathbf{R})$$

$$E(\mathbf{y}) = \mathbf{X}\boldsymbol{\beta}, \quad Var(\mathbf{y}) = \mathbf{ZGZ'} + \mathbf{R} = \mathbf{V}$$

Generalized Linear Mixed Models (GLMM)

$$g(\mu) = X\beta + Z\gamma$$

$$\mu \equiv E(y \mid \gamma)$$

$$y \mid \gamma \sim exponential\ \ family$$

$$E(y \mid \gamma) = g^{-1}(X\beta + Z\gamma)$$

$$V(\gamma) = G \quad V(y) = A_{\mu}^{\frac{1}{2}} R A_{\mu}^{\frac{1}{2}}$$

Examples of GLMMs

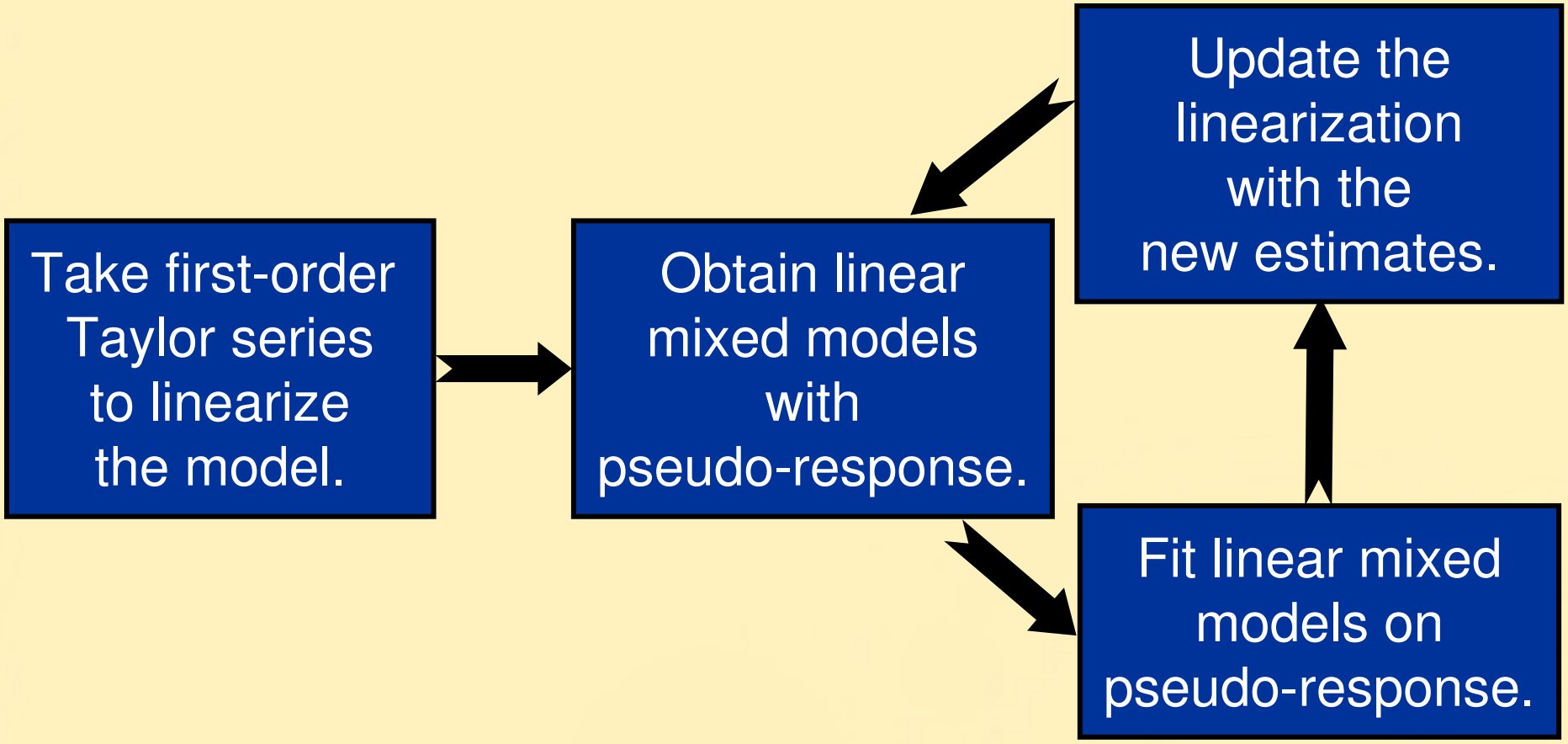
Responses	Conditional Distribution	Link	Variance	Model
Continuous	Normal	μ	σ^2	$\mu\|\gamma = X\beta+Z\gamma$
Binary	Binomial	$\log[\mu/(1-\mu)]$	$\mu(1-\mu)/n$	$\log[\mu/(1-\mu)\|\gamma] = X\beta+Z\gamma$
Count	Poisson	$\log(\mu)$	μ	$\log(\mu\|\gamma) = X\beta+Z\gamma$
Count	Negative Binomial	$\log(\mu)$	$\mu+k\mu^2$	$\log(\mu\|\gamma) = X\beta+Z\gamma$

Challenges in Fitting GLMMs

How can you obtain the marginal log-likelihood function?

- Linear mixed models:
  - Conditional distribution: $y|\gamma \sim N(X\beta+Z\gamma, R)$
  - Marginal distribution: $y \sim N(X\beta, V)$
- Generalized linear mixed models:
  - Conditional distribution: $y|\gamma \sim$ exponential family
  - Marginal distribution: *unknown*

Pseudo-Likelihood (Linearization) Method



Pseudo-Likelihood Method

- Four pseudo-likelihood estimation techniques:
  - RSPL Residual Subject-specific Pseudo-Likelihood
  - MSPL Maximum Subject-specific Pseudo-Likelihood
  - RMPL Residual Marginal Pseudo-Likelihood
  - MMPL Maximum Marginal Pseudo-Likelihood
- R*x*PL is less biased then M*x*PL because it profiles the fixed effects.
- *x*SPL models produce BLUPs.
- For linear mixed models, R*x*PL=REML and M*x*PL=ML.

II. PROC GLIMMIX Syntax

PROC GLIMMIX *options* **;**

…*programming statements…;*

CLASS *variables***;**

MODEL *response=fixed-effects / dist= link= options***;**

RANDOM *random-effects / options;*

RANDOM *_residual_ / options;*

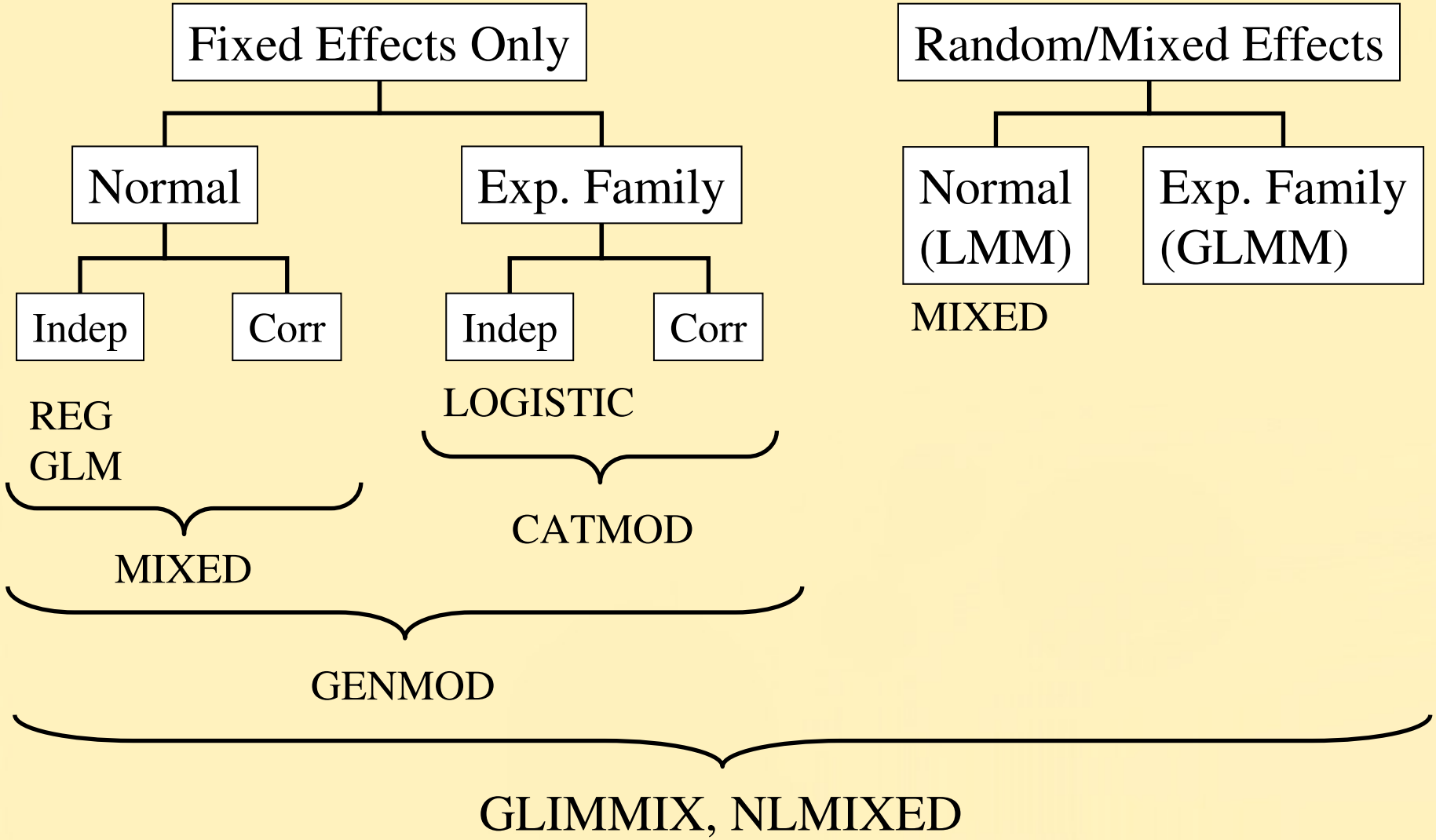
RUN;

The GLIMMIX Procedure

The GLIMMIX procedure is

- a new procedure in SAS/STAT for estimation and inference in generalized linear mixed models
- an add-on to SAS 9.1 for Windows only
- available by download from support.sas.com.

SAS Procedure Hierarchy for Linear Models



Generalized Linear Mixed Models (GLMM)

LINK= option

RANDOM statement

$$g(\mu) = X\beta + Z\gamma$$

MODEL statement

DIST= option

$$y \mid \gamma \sim exponential\ \ family$$

RANDOM statement TYPE= option

RANDOM _RESIDUAL_ statement

$$V(\gamma) = G \quad V(y) = A_{\mu}^{\frac{1}{2}} R A_{\mu}^{\frac{1}{2}}$$

GLIMMIX Procedure

```
PROC GLIMMIX <options>;
      CLASS variables;
      CONTRAST 'label' contrast-specification </options>;
      ESTIMATE 'label' contrast-specification </options>;
      LSMEANS fixed-effects </options>;
      LSMESTIMATE fixed-effect <'label'> values </options>;
      MODEL response<(response options)>=<fixed-effects>
                  </options>;
      NLOPTIONS <options>;
      OUTPUT <OUT=SAS-data-set><keyword<(keyword-options) >
                        <=name>>.. </ options>;
      PARMS (value-list)…</options>;
      RANDOM random-effects </options>;
      WEIGHT variable;
RUN;
```

GLIMMIX Procedure

```
PROC GLIMMIX <options>;
    CLASS variables;
    CONTRAST 'label' contrast-specification </options>;
    ESTIMATE 'label' contrast-specification </options>;
    MODEL response = fixed-effects / DIST=
                                     LINK= ;
    NLOPTIONS <options>;
    OUTPUT <OUT=SAS-data-set><keyword<(keyword-options) >
                <=name>>.. </ options>;
    PARMS (value-list)…</options>;
    RANDOM random-effects </options>;
    WEIGHT variable;
RUN;
```

Distributions Supported by PROC GLIMMIX

Discrete Response	Continuous Response
Binary	Beta
Binomial	Normal
Poisson	“Lognormal”
Geometric	Gamma
Negative Binomial	Exponential
Multinomial (nominal and ordinal)	Inverse Gaussian
+ combinations	Shifted T
	+ combinations

Link Functions in PROC GLIMMIX

- Cumulative Complementary log-log
- Cumulative logit
- Cumulative log-log
- Cumulative probit
- Complementary log-log
- Generalized logit
- Identity
- Log
- Logit
- Log-log
- Probit
- Power with exponent
- Power with exponent -2
- Reciprocal

GLIMMIX Procedure

```
PROC GLIMMIX <options>;
    CLASS variables;
    CONTRAST 'label' contrast-specification </options>;
    ESTIMATE 'label' contrast-spe                    s>;
    LSMEANS fixed-effects </optio
    OUTPUT <OUT=SAS-data-set><k          word<(keyword-options) >
                <=nam                              ;
    PARMS (value-list)…</options>;
    RANDOM random-effects </options>;
    WEIGHT variable;
RUN;
```

G-side

RANDOM *random-effects* / TYPE = ;

RANDOM _RESIDUAL_ / TYPE = ;

R-side

Selected COV Structures in PROC GLIMMIX

- Variance Components
- Compound Symmetry
- Unstructured
- First-Order Autoregressive
- Toeplitz
- Spatial Power
- Spatial Exponential
- Spatial Gaussian
- First-Order Factor Analytic
- Radial Smoother

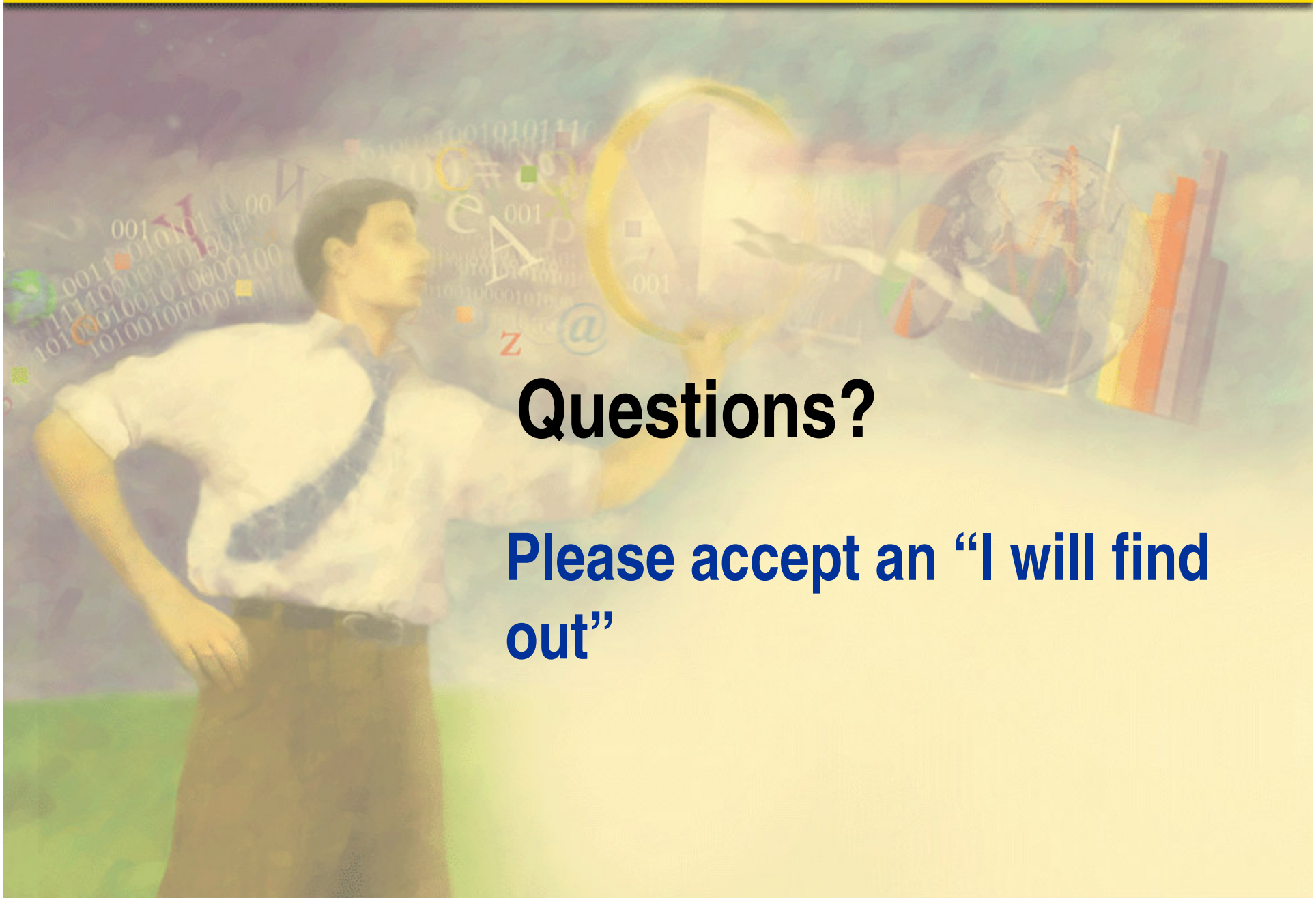
GLIMMIX Procedure

```
PROC GLIMMIX <options>;
    CLASS variables;
    CONTRAST 'label' contrast-specification </options>;
    ESTIMATE 'label' contrast-specification </options>;
    LSMESTIMATE fixed-effect 'label' values / options ;
                </options>;
    NLOPTIONS <options>;
    OUTPUT <OUT=SAS-data-set><keyword<(keyword-options) >
                <=name>>.. </ options>;
    PARMS (value-list)…</options>;
    RANDOM random-effects </options>;
    WEIGHT variable;
RUN;
```

III. An Example: Binomial Data in a Multi-center Clinical Trail

- 2 treatment methods, 8 clinic locations
- Predict probability of a favorable response.
- Clinics sampled from population and are thus random effects

• PROC REG/GLM?	Binary Distribution, non fixed
• PROC GENMOD?	Designed for fixed effects only
• PROC MIXED?	Binary Distribution
• PROC NLMIXED?	Possible alternative



Questions?

Please accept an “I will find out”