

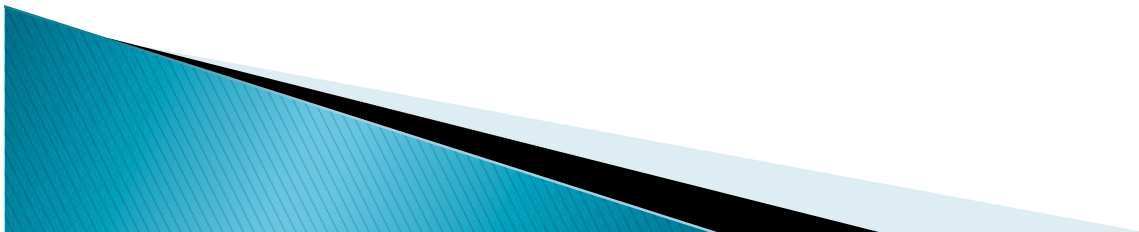
QTDT for Variance Component Estimation: Introduction

Estimating variance components with pedigrees

- ▶ QTDT Designed for family based tests of linkage disequilibrium between a marker and complex trait (= family based association mapping)
- ▶ QTDT also can be used to estimate variance components and to assess significance of components

Input Files: Same as for the Pedstat software

- ▶ Pedigree File
 - Relationships
 - Genotype data
 - Phenotype data
- ▶ Data File
 - Describes contents of pedigree file



Example Pedigree File

<contents of example.ped>

```
1 1 0 0 1 1 x 3 3 x x
1 2 0 0 2 1 x 4 4 x x
1 3 0 0 1 1 x 1 2 x x
1 4 1 2 2 1 x 4 3 x x
1 5 3 4 2 2 1.234 1 3 2 2
1 6 3 4 1 2 4.321 2 4 2 2
```

<end of example.ped>

Encodes family relationships, marker and phenotype information

Data File Field Codes

Code	Description
M	Marker Genotype
A	Affection Status.
T	Quantitative Trait.
C	Covariate.
Z	Zygoty (Twins).
S[n]	Skip n columns.

Example Data File

<contents of example.dat>

T some_trait_of_interest

M some_marker

M another_marker

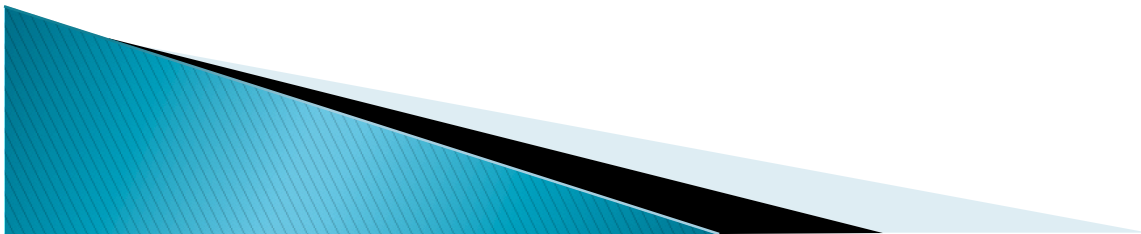
<end of example.dat>

Provides information necessary to decode
pedigree file

.dat file: If only interesting in variance components, then only need to include a single phenotype

T qpheno

E END-OF-DATA



Variance Components (QTDT)

- ▶ Allows customized variance–covariance matrices
 - Key options are `-w` and `-v`
 - Describe two alternative models for variances
- ▶ Can also build means model for association tests
 - The `-a` option
 - Using observed marker genotypes
- ▶ Can read in IBD matrix generated by other program

Common Variance Components in QTDT

Value	Description
e	Non-shared Environment. Environmental effects that are unique to each family member and measurement error.
g	Polygenic. These effects are a function of relatedness between family members and may be due to polygenes.
a	Additive Major Gene Effect. This represents the additive effect of linkage to a major gene. The pi-hat component.
t	Twin Environment. This represents the environment shared by twins, but not other types of relatives.
c	Common Environment. This represents the environment shared by all relatives.

The **-w** option specifies variances under the null. E.g. **-we** switch specifies that only environmental effects should be modeled. The **-v** switch specifies variances under the alternative. E.g. **-veg** models environmental and polygenic effects. The variance component “g” corresponds to an additive variance component

Testing Heritability With QTDT

- ▶ Disable association models
 - Use option `-a-`
- ▶ Specify two models for variances
 - Use options `-we` and `-veg`

- ▶ Typical command line:

```
qtdt -d example.dat -p example.ped -a- -we -veg
```

Typical Output: Testing Heritability

- ▶ Summary output appears on screen

The following models will be evaluated...

NULL MODEL

Means = μ

Variances = V_e

FULL MODEL

Means = μ

Variances = $V_e + V_g$

<u>Testing trait:</u>					<u>TRAIT</u>		
Allele	df(0)	-LnLk(0)	df(V)	-LnLk(V)	ChiSq	p	
N/A	403	573.67	402	544.77	57.80	3e-14	(405 probands)

- ▶ In this case the trait is highly heritable ($p < 10^{-13}$)
- ▶ Additional information, including variance component estimates output to "regress.tbl"

Files

Simulated_Trait_VAR_COMP.ped

Simulated_Trait_VAR_COMP.dat

Exercise

- Phenotype data only:
 - Use Pedstats software to estimate heritability with the various relationship types.
 - Now use QTDT to estimate additive, shared family, and unique environmental variance components, as well as heritability, using QTDT

```
qtdt -d Simulated_Trait_VAR_COMP.dat -p  
Simuated_TRAIT_VAR_COMP.ped -a- -we -veg
```

```
qtdt -d Simulated_Trait_VAR_COMP.dat -p  
Simuated_TRAIT_VAR_COMP.ped -a- -we -vegc
```