HETEROGENEITY

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TYPES OF HETEROGENEITY

Terminology depends on research question

- Moderation, confounding, GxE

- Measured or Manifest moderator/confounder
  - Binary, Ordinal & Continuous traits
- Unmeasured or latent moderator/confounder
  - Moderation and GxE

HETEROGENEITY QUESTIONS

Univariate Analysis:

- What are the contributions of additive genetic, dominance/shared environmental and unique environmental factors to the variance?

Heterogeneity:

- Are the contributions of genetic and environmental factors equal for different groups,
- sex, race, ethnicity, SES, environmental exposure, etc.?

THE LANGUAGE OF HETEROGENEITY

Are these differences due to differences in the magnitude of the effects (quantitative)?

- e.g. Is the contribution of genetic/environmental factors greater/smaller in males than in females?

Are the differences due to differences in the source/nature of the effects (qualitative)?

- e.g. Are there different genetic/environmental factors influencing the trait in males and females?

THE LANGUAGE OF HETEROGENEITY

Sex differences = Sex limitation

1948

ON SEX LIMITATION IN HUMAN GENETICS*

By H. HARRIS, M.B., B.Chir.(Camb.)

IT is well known that in many instances of hereditary disease the condition is observed to occur more frequently in one cases, the sons never inherit the peculiarity directly from their fathers, but the daughters, and the daughters alone, transmit the latent tendency, so that the sons of the daughters

1840

L'HÉRÉDITÉ DANS LES MALADIES,

PAR P. A. PIORRY,

Docteur en médecine, Chevalier de la Légion-d'Honneur, Médecin de l'Hôpital de la Pitié, Agrégé à la Faculté de Médecine de Paris, Professeur de Clinique et de Pathologie interne, Membre de l'Académie Royale de Médecine, des Sociétés médicales de Tours, de Boulogne, de Goettingue, de l'Académie Royale de Médecine de Madrid, etc.

1861

THE

BRITISH AND FOREIGN

MEDICO-CHIRURGICAL

REVIEW

OR

QUARTERLY JOURNAL

OF

PRACTICAL MEDICINE AND SURGERY.

VOL. XXVII.

JANUARY — APRIL, 1861.

ART. III.

On Sexual Limitation in Hereditary Disease. By WILLIAM SEDGWICK.

(*Concluded from our last.*)

FROM hereditary diseases of the organ of vision, the transition is easy to those affecting the organ of hearing, for there are some defects which these organs seem, as it were, to share in common. This connexion has been already referred to by some writers, amongst whom Mr. White Cooper* states that imperfection of the two senses (of sight and hearing) not infrequently co-exist, especially in the curious class of cases we have just been considering, where the inability to distinguish colours is often associated with a corresponding inability to distinguish musical sounds. Dr. Earle relates, in his case of colour-blindness, that "the whole family, of which the chart has been exhibited, is probably no less generally characterized by a defective musical ear than an imperfect appreciation of colours. Several of the individuals comprised in it are utterly incapable of distinguishing one tune from another."†

* Cyclopædia of Anatomy and Physiology, art. "Vision," p. 1453.
† American Journal of Medical Science, vol. xxxv. p. 347. 1845.

THE LANGUAGE OF HETEROGENEITY

<u>Quantitative</u>

- differences in the magnitude of the effects

Models

- Scalar
- Non-scalar with/without OS twins

<u>Qualitative</u>

- differences in the source/nature of the effects

Models

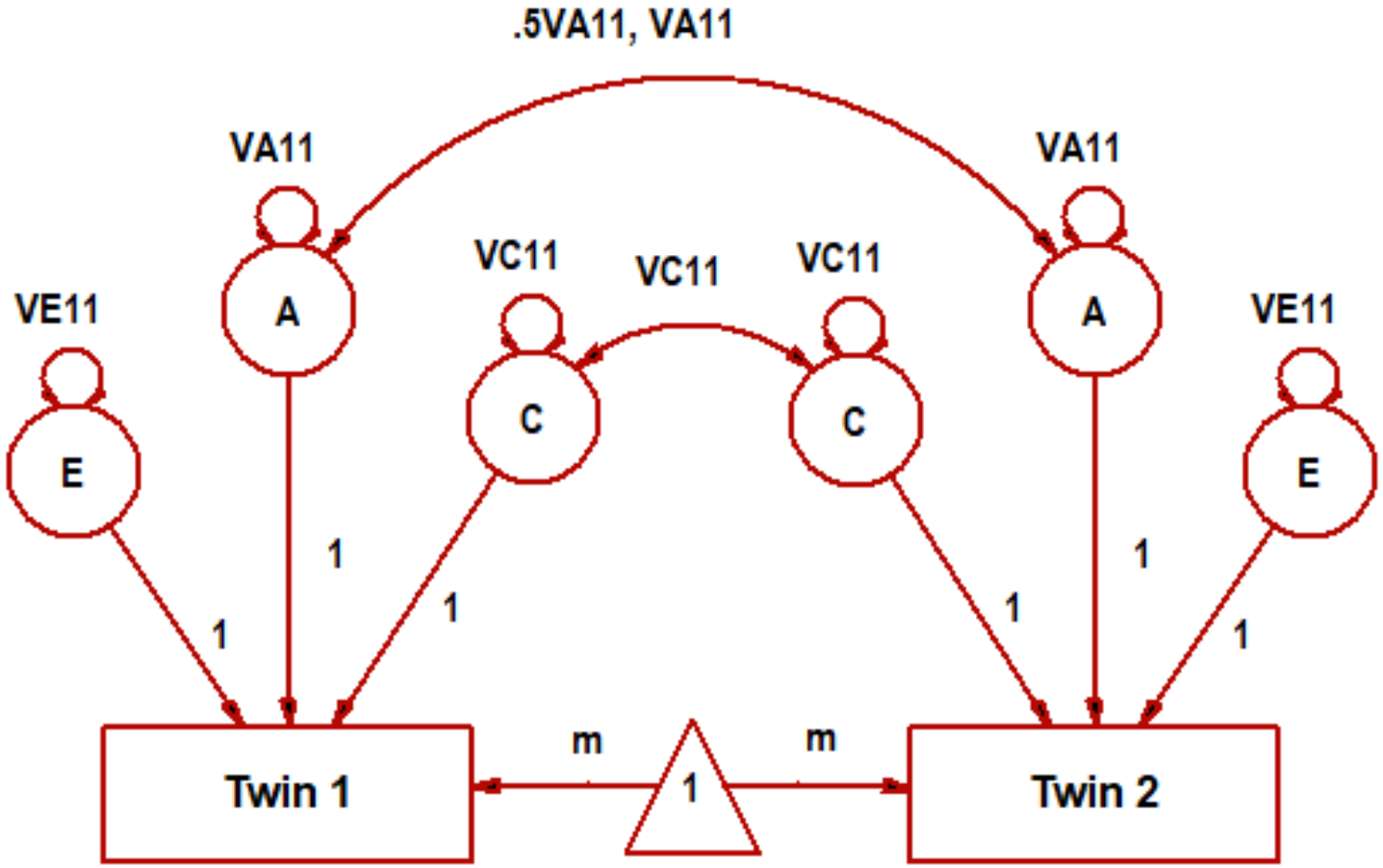
- Non-scalar with OS twins
- General Non-scalar

THE LANGUAGE OF HETEROGENEITY

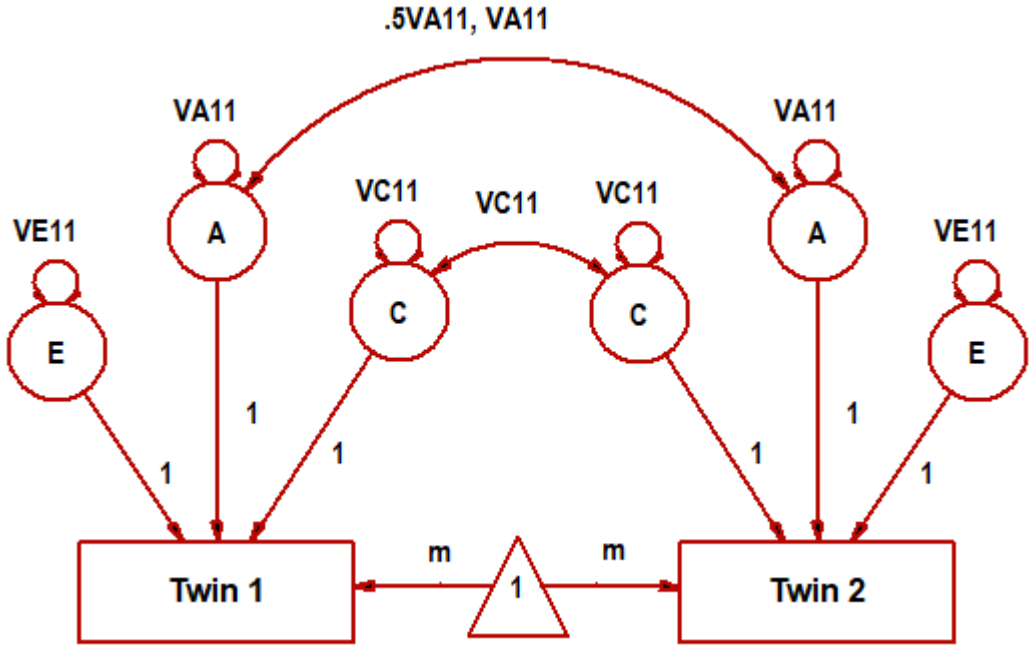
Scalar limitation (Quantitative)

- % of variance due to A,C,E are the same between groups
- The total variance is not ie:
  - $var_{Female} = k*var_{Male}$
  - $VA_{Female} = k*VA_{Male}$
  - $VC_{Female} = k*VC_{Male}$
  - $VE_{Female} = k*VE_{Male}$

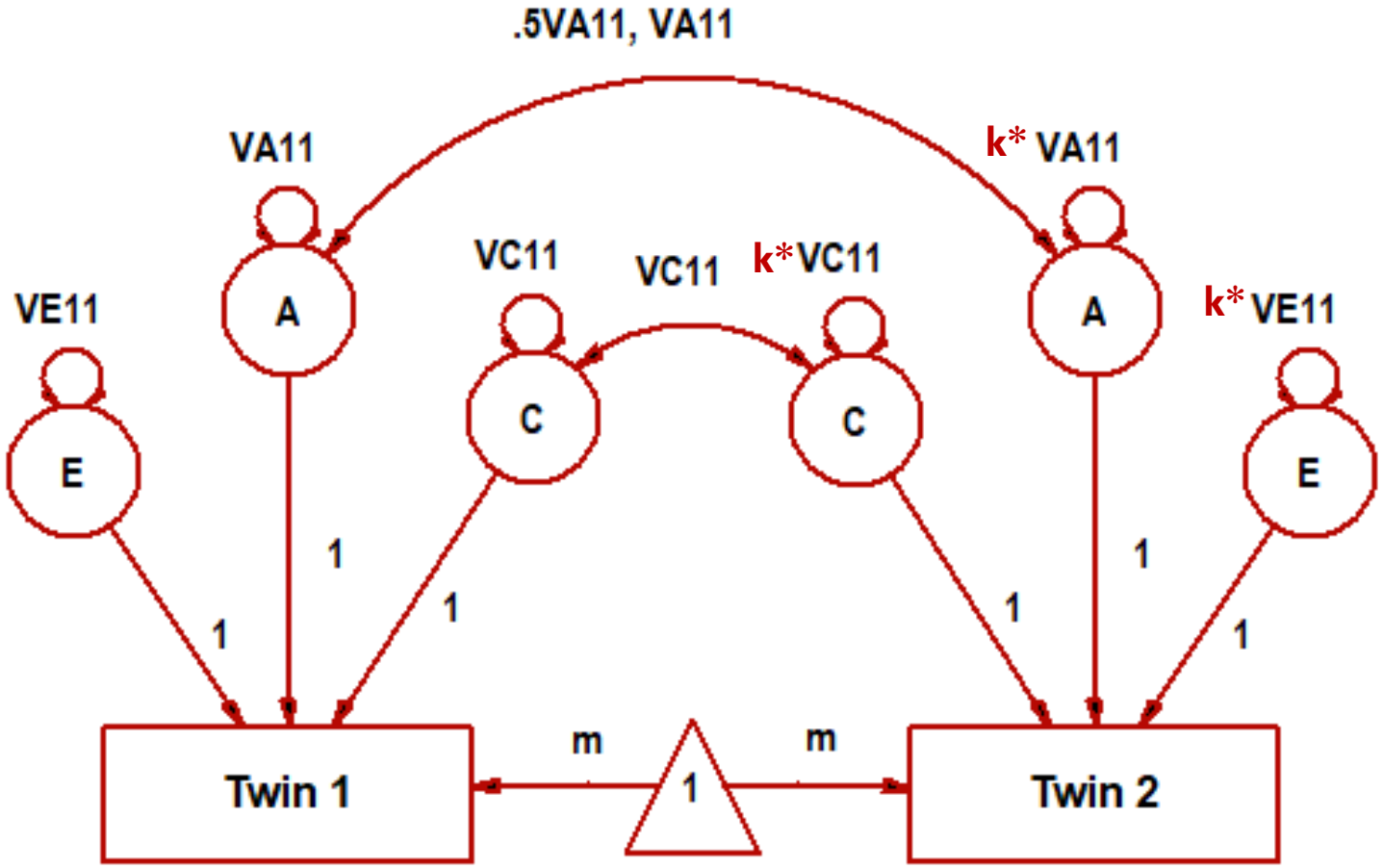
k here is the *scalar*



No Heterogeneity



MZ		DZ	
VA+VC+VE	VA+VC	VA+VC+VE	.5VA+VC
VA+VC	VA+VC+VE	.5VA+VC	VA+VC+VE



Scalar Sex-limitation
aka scalar sex-limitation of the variance

THE LANGUAGE OF HETEROGENEITY

Non-Scalar limitation

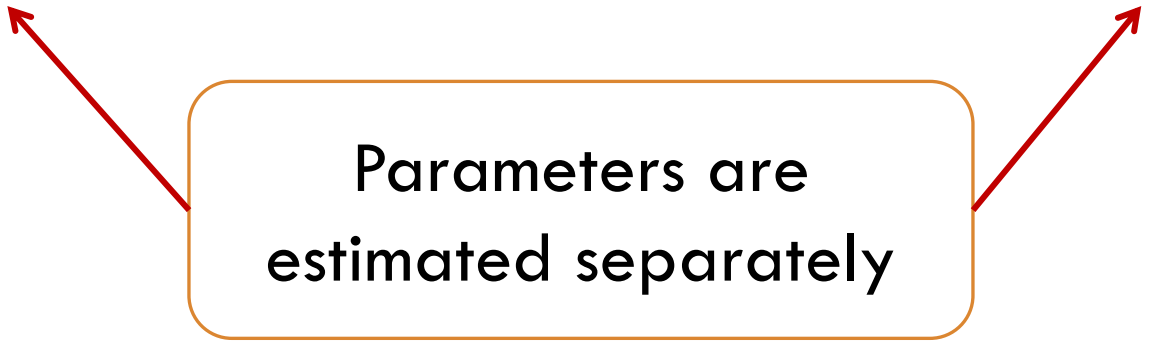
- Possible Without opposite sex twin pairs (Quantitative)
  - $var_{Female} \neq var_{Male}$
  - $VA_{Female} \neq VA_{Male}$
  - $VC_{Female} \neq VC_{Male}$
  - $VE_{Female} \neq VE_{Male}$

THE LANGUAGE OF HETEROGENEITY

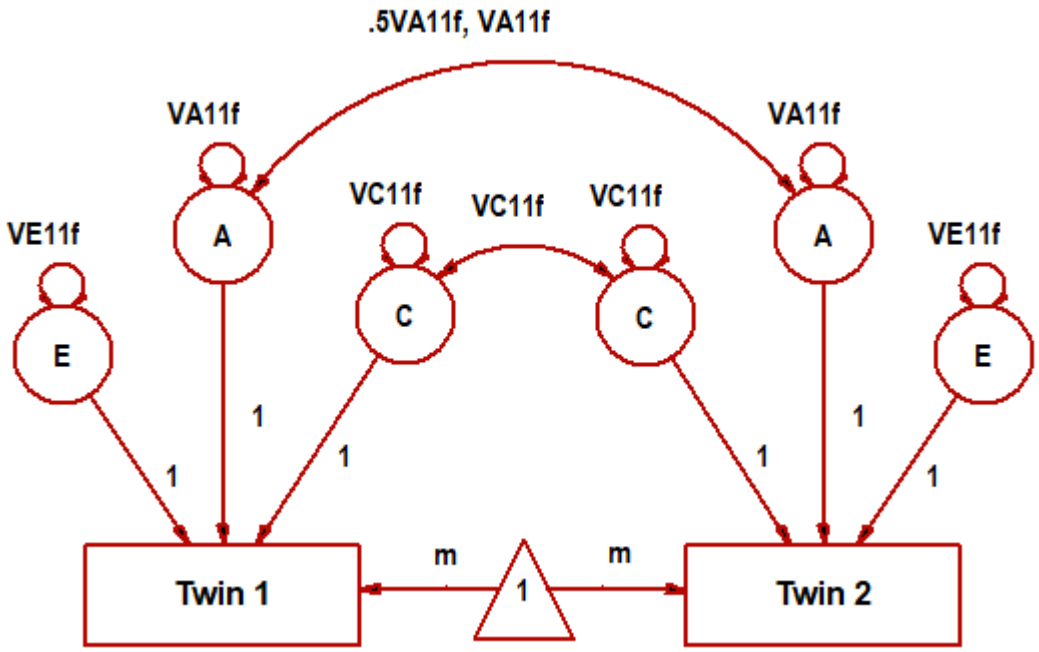
Non-Scalar limitation

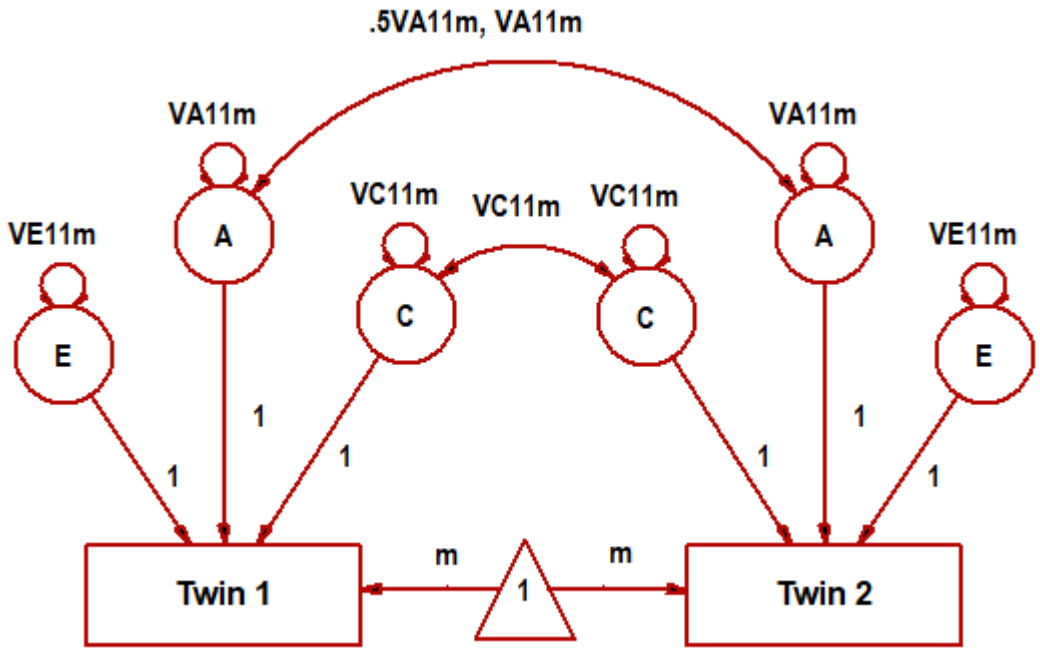
- Without opposite sex twin pairs (Quantitative)

- Male Parameters
  - $means_M$
  - VA_M VC_M *and* VE_M
- Female Parameters
  - $mean_F$
  - VA_F VC_F *and* VE_F



Male ACE model





Female ACE model

THE LANGUAGE OF HETEROGENEITY

Non-Scalar limitation aka Common-effects sex limitation model

- With opposite sex twin pairs (Quantitative)

- Male Parameters
  - $means_M$
  - VA_M VC_M and VE_M

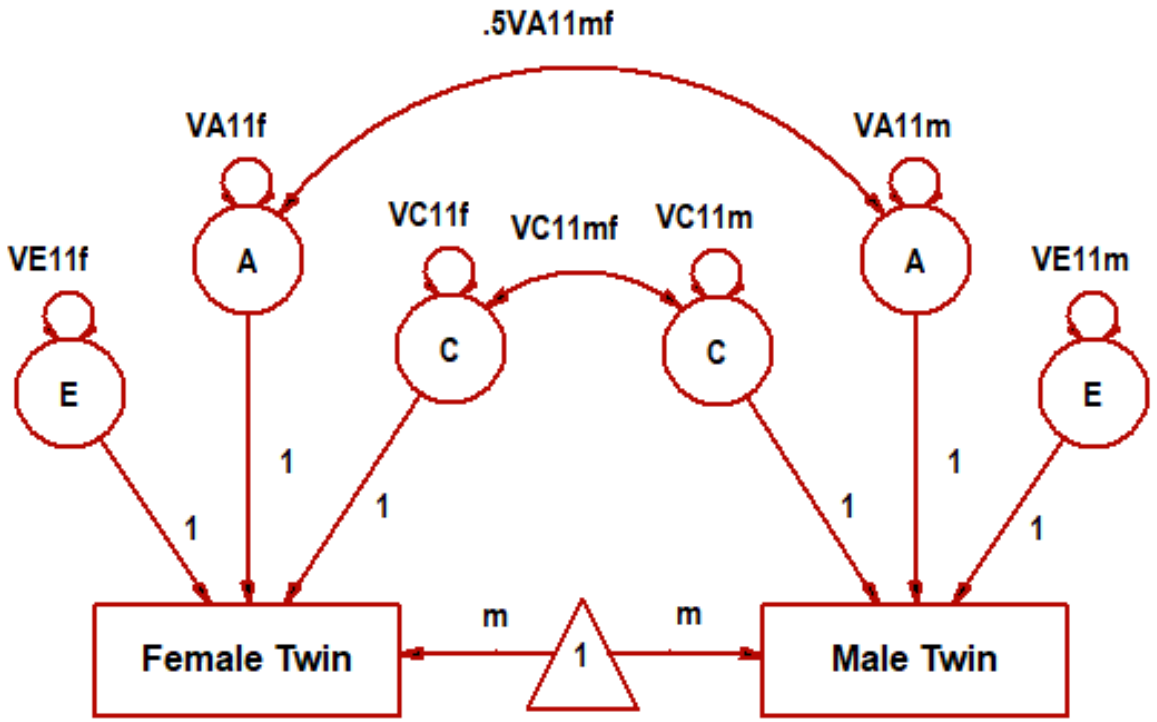
- Female Parameters
  - $mean_F$
  - VA_F VC_F and VE_F

Parameters are estimated jointly – linked via the opposite sex correlations

$r(VA_{Female}, VA_{male}) = .5$

$r(VC_{Female} \neq VC_{Male}) = 1$

$r(VE_{Female} \neq VE_{Male}) = 0$



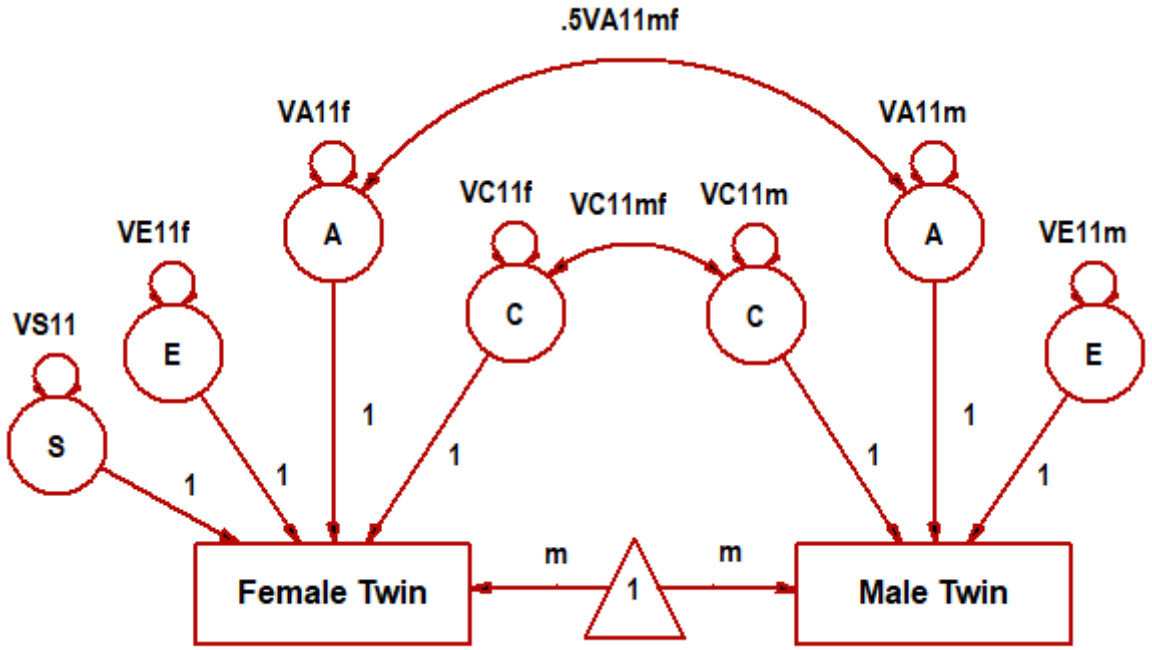
Non-scalar Sex-limitation
aka common-effects sex limitation

THE LANGUAGE OF HETEROGENEITY

General Non-Scalar limitation

- With opposite sex twin pairs (Quantitative/Qualitative)
  - Male Parameters
    - $means_M$
    - VA_M VC_M VE_M
  - Female Parameters
    - $mean_F$
    - VA_F VC_F VE_F and $VA_{Specific}$
    - Extra genetic/ environmental effects

Parameters are estimated jointly – linked via the opposite sex correlations



General Non-scalar Sex-limitation
aka general sex limitation

THE LANGUAGE OF HETEROGENEITY

General Non-Scalar limitation via r_G

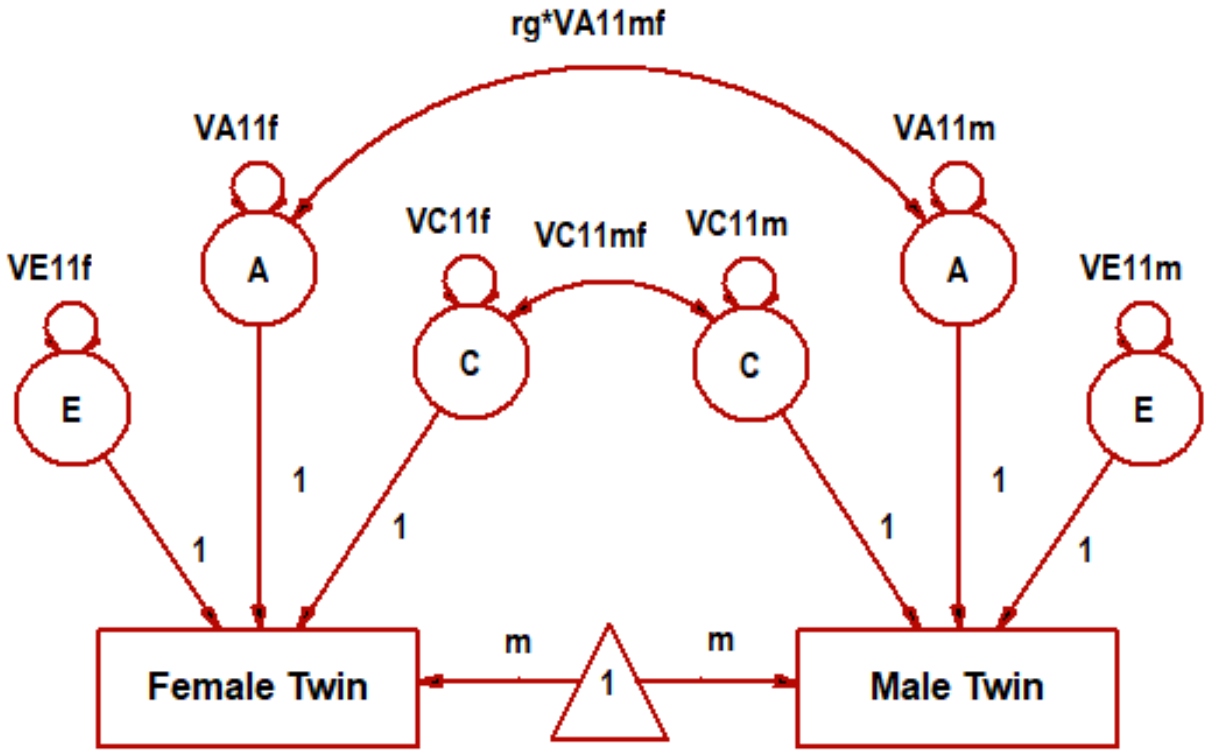
- With opposite sex twin pairs (Quantitative/Qualitative)
  - Male Parameters
    - $means_M$
    - VA_M VC_M VE_M
  - Female Parameters
    - $mean_F$
    - VA_F VC_F *and* VE_F

Parameters are estimated jointly – linked via the opposite sex correlations

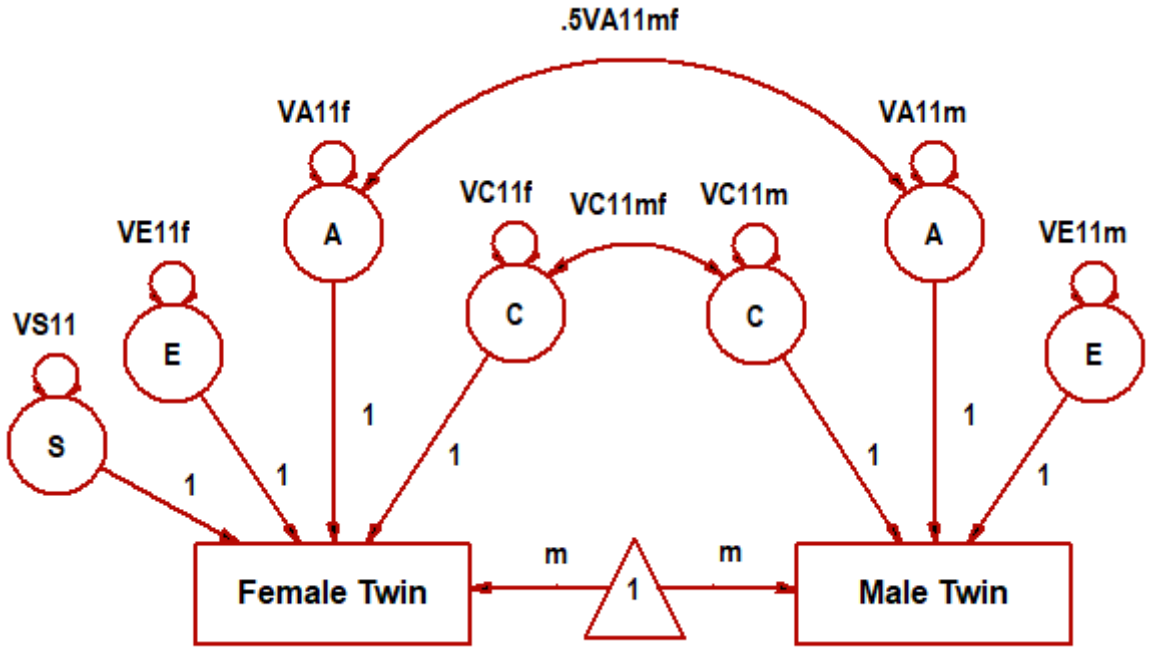
$$r(A_{Female}, A_{male}) = ? \text{ (estimated)}$$

$$r(C_{Female} \neq C_{Male}) = 1$$

$$r(E_{Female} \neq E_{Male}) = 0$$



General Non-scalar Sex-limitation
aka general sex limitation



General Non-scalar Sex-limitation
aka general sex limitation