Effect of gender and zygosity on vertical, sagittal and airway growth in a twin sample: a longitudinal study

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Introduction

- Airway dimensions
- Genetic component of airway structures
- Soft tissue role in the size of the airway

Linder-Aronson and Leighton, 1983, Guilleminault et al 1995, Schwab et al 2003.

Literature review

Upper Airway growth

- Growth direction and effect on its size
- Shape changes-from convex to concave
- Sex differences in upper airway growth

JEANS, W. D., FERNANDO, D. C., MAW, A. R. & LEIGHTON, B. C. 1981. A longitudinal study of the growth of the nasopharynx and its contents in normal children. Br J Radiol, 54, 117-21.

Literature review

- Airway components growth is proportionate to the skeletal growth
- Variability on the timeline of growth of the soft tissues of the airway

Linder-Aronson and Leighton, 1983, Park et al., 2016, Arens et al., 2002

Literature review

Twin studies

- Twin studies are an important epidemiological tool for genetic risk factor determination
- Can be used to identify heritability of traits

Aim and objectives

Aim:

- 1. To examine the influence of zygosity and gender on vertical, sagittal and airway growth in growing monozygotic (MZ) and dizygotic (DZ) twins of Boston, participants of Forsyth study.

- 2. To assess if there is any correlation between cephalometric measurements and the airway cephalometric measurements two years after peak growth in a MZ and DZ twin sample of Boston, participants of Forsyth study.

Material and Methods

- **Study design**: Cohort longitudinal study design
- **Sample:** Forsyth twin sample from 1959 to 1975, setting: Forsyth Infirmary for Children in Boston, Massachusetts (35 pairs per group)
- **Eligibility criteria**

Material and Methods

- **Selection of variables:**
- **Exposure:**

- Gender (male and female)

- Zygosity (fraternal and identical).

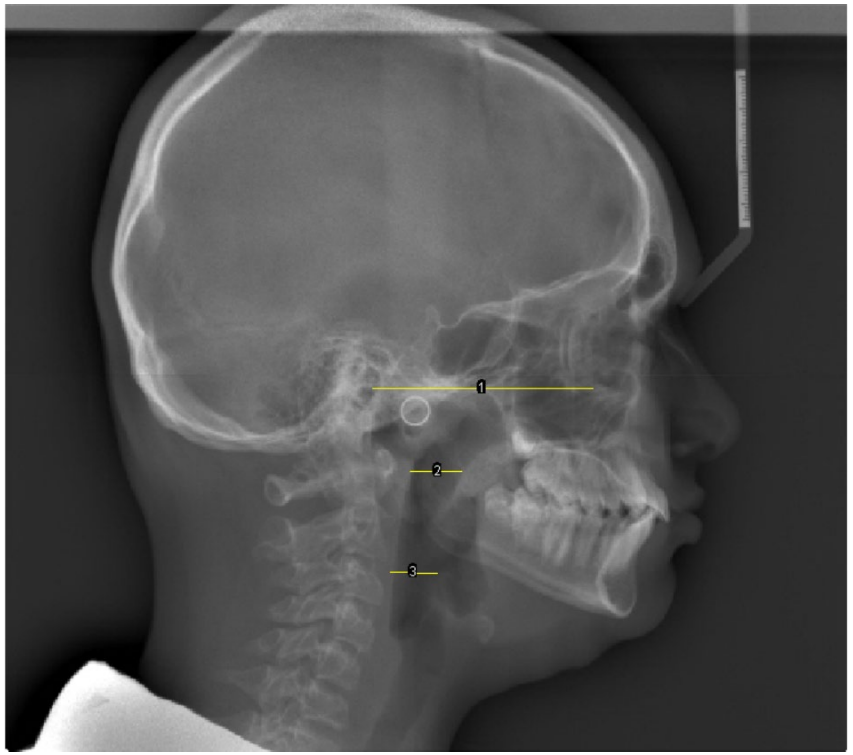
- **Confounders:**

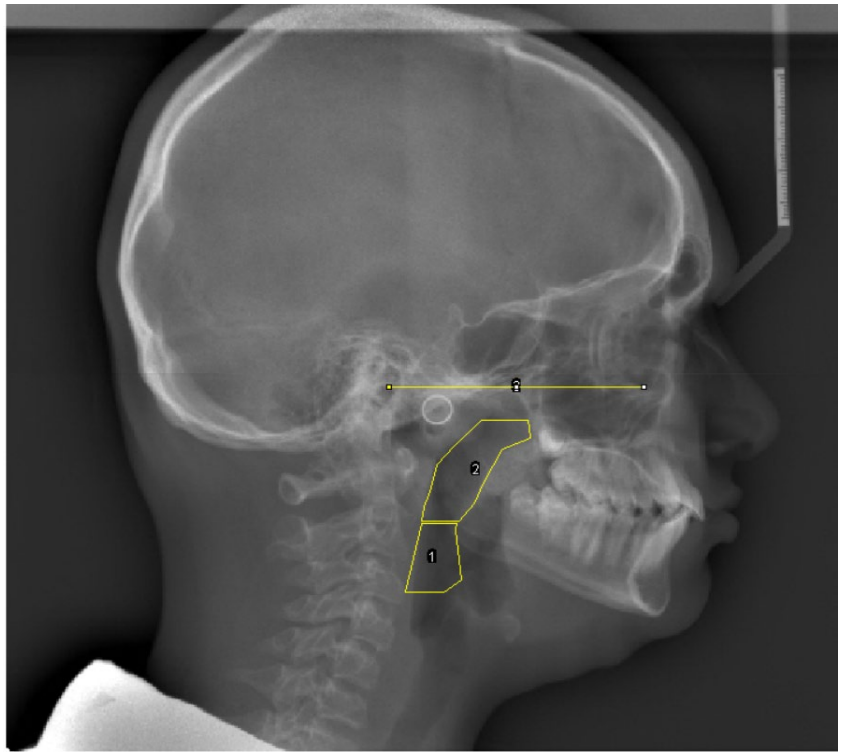
- Age, which will be measured in years.

Material and Methods

- **Outcome:**

1. Airway width and area

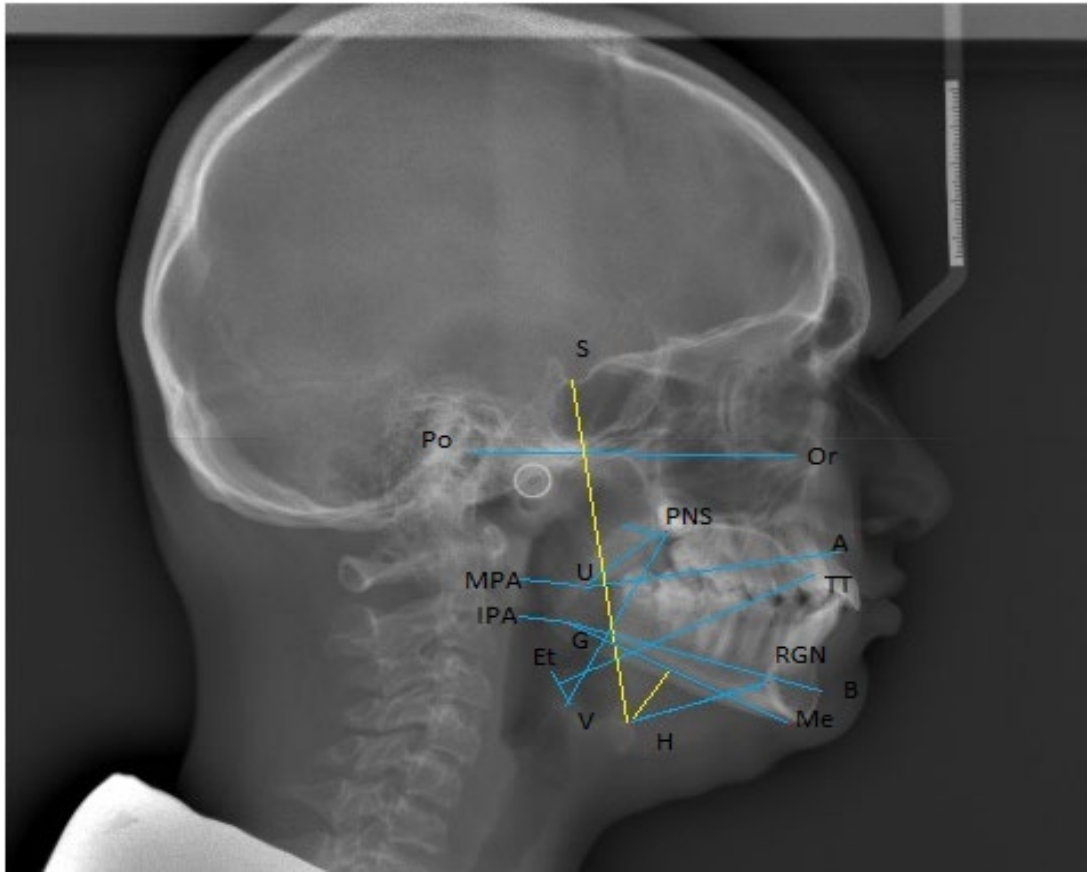




Material and Methods

2. Nasopharynx measurement
3. Oropharynx measurements
4. Hypopharynx measurements
5. Hyoid measurements
6. Skeletal measurements

(A/P and vertical)



Goncales et al., 2014, Pae et al., 2008

Statistical analysis

- All statistical analyses will be conducted using software (version 9.4; SAS, Cary, NC).
- T-test and ANOVA with post hoc Tukey will be used to quantify the differences between monozygotic and dizygotic twins.
- In addition, the estimate of heritability (h2) will be used to measure the degree of genetic vs. environmental contribution.
- Autoregressive mixed effects models will be used to estimate the changes of cephalometric measurements across gender and group, controlled by age.
- Pearson correlation coefficient will be used to investigate the correlation between cephalometric measurements and airway measurements.
- Statistical significance was evaluated at the 0.05 level.
- Method error/reliability

Results-Autoregressive model for vertical dimension

Explanatory variable	Beta estimate	95% CI	P value
Gonial Angle			
Age	-0.44	[-0.66- -0.24]	<.0001*
Gender			0.55
Male	[Ref.]	[Ref.]	
Female	-0.44	[-1.90- 1.01]	
Group			0.05*
Fraternal	1.44	[0.04 – 2.85]	
Identical	[Ref.]	[Ref.]	
SnGoGn			
Age	-0.43	[-0.59 - -0.26]	<.0001*
Gender			0.99
Male	[Ref.]	[Ref.]	
Female	-0.03	[-1.49 - 1.48]	
Group			0.12
Fraternal	1.13	[-0.32 - 2.61]	
Identical	[Ref.]	[Ref.]	

Results-Autoregressive model for sagittal dimension

Explanatory variable	Beta estimate	95% CI	P value
ANB			
Age	-0.05	[-0.11 - 0.01]	0.09
Gender			0.10
Male	[Ref.]	[Ref.]	
Female	0.43	[-0.09- 0.95]	
Group			0.02*
Fraternal	0.60	[0.09 - 1.11]	
Identical	[Ref.]	[Ref.]	
SNA			
Age	0.17	[0.04 -0.29]	0.01*
Gender			0.69
Male	[Ref.]	[Ref.]	
Female	-0.22	[-1.30 - 0.86]	
Group			0.22
Fraternal	0.65	[-0.40 - 1.70]	
Identical	[Ref.]	[Ref.]	
SNB			
Age	0.09	[-0.13-0.30]	0.42
Gender			0.57
Male	[Ref.]	[Ref.]	
Female	-0.39	[-1.75- 0.97]	
Group			0.59
Fraternal	-0.36	[-1.66 - 0.94]	
Identical	[Ref.]	[Ref.]	
U1NA			
Age	-0.09	[-0.34 - 0.15]	0.45
Gender			0.54
Male	[Ref.]	[Ref.]	
Female	-0.51	[-2.16- 1.14]	
Group			0.46
Fraternal	-0.59	[-2.18 – 0.99]	
Identical	[Ref.]	[Ref.]	
IMPA			
Age	0.12	[-0.09 - 0.33]	0.25
Gender			0.57
Male	[Ref.]	[Ref.]	
Female	0.52	[-1.28 - 2.32]	
Group			0.11
Fraternal	-1.37	[-3.13- 0.38]	
Identical	[Ref.]	[Ref.]	

Continued

UpperlipEplane			
Age	-0.30	[-0.42- -0.18]	<.0001*
Gender			0.003*
Male			
Female	[Ref.]	[Ref.]	
	-0.93	[-1.54 - -0.32]	
Group			0.40
Fraternal	0.25	[-0.33 - 0.81]	
Identical	[Ref.]	[Ref.]	

Results-Autoregressive model for airway

Explanatory variable	Beta estimate	95% CI	P value
FHUA			
Age	-0.21	[-0.37 - -0.05]	0.009*
Gender			0.10
Male	[Ref.]	[Ref.]	
Female	-0.60	[-1.32 – 0.12]	
Group			0.01*
Fraternal	-0.83	[-1.48 - 0.17]	
Identical	[Ref.]	[Ref.]	
PNSU			
Age	0.52	[0.34 - 0.70]	<.0001*
Gender			0.38
Male	[Ref.]	[Ref.]	
Female	-0.37	[-1.19 - 0.45]	
Group			0.75
Fraternal	0.12	[-0.63 – 0.88]]	
Identical	[Ref.]	[Ref.]	
PHWU			
Age	0.92	[0.71 - 1.12]	<.0001*
Gender			0.75
Male	[Ref.]	[Ref.]	
Female	0.17	[-0.87 – 1.20]	
Group			0.20
Fraternal	-0.62	[-1.58 – 0.34]	
Identical	[Ref.]	[Ref.]	
GoU			
Age	0.48	[0.31- 0.65]	<.0001*
Gender			0.36
Male	[Ref.]	[Ref.]	
Female	-0.41	[-1.29 – 0.47]	
Group			<.0001*
Fraternal	-2.73	[-3.55 - -1.90]	
Identical	[Ref.]	[Ref.]	
PHWGo			
Age	1.34	[1.08- 1.59]	<.0001*
Gender			0.97
Male	[Ref.]	[Ref.]	
Female	-0.02	[-1.20 - 1.24]	
Group			<.0001*
Fraternal	-3.14	[-4.27 - -2.01]	
Identical	[Ref.]	[Ref.]	

Continued

SegPNS			
Age	1.33	[1.01- 1.65]	<.0001*
Gender			0.42
Male	[Ref.]	[Ref.]	
Female	-0.60	[-2.09 - 0.88]	
Group			0.0008*
Fraternal	-2.35	[-3.72 - -0.99]	
Identical	[Ref.]	[Ref.]	
HyS			
Age	2.40	[1.82- 2.98]	<.0001*
Gender			0.24
Male	[Ref.]	[Ref.]	
Female	-1.63	[-4.38 - 1.12]	
Group			0.001*
Fraternal	-4.31	[-6.84 - - 1.78]	
Identical	[Ref.]	[Ref.]	
HyGT			
Age	0.70	[0.46- 0.95]	<.0001*
Gender			0.04*
Male	[Ref.]	[Ref.]	
Female	1.21	[0.07- 2.34]	
Group			0.001*
Fraternal	-2.63	[-3.66 - - 1.59]	
Identical	[Ref.]	[Ref.]	
Upper Airway Width			
Age	0.41	[0.28 - 0.53]	<.0001*
Gender			0.27
Male	[Ref.]	[Ref.]	
Female	0.33	[-0.29 - 0.95]	
Group			0.01*
Fraternal	-0.71	[-1.29 - -0.14]	
Identical	[Ref.]	[Ref.]	
Lower Airway Width			
Age	0.21	[0.11 - 0.31]	<.0001*
Gender			0.52
Male	[Ref.]	[Ref.]	
Female	-0.15	[-0.62 - 0.32]	
Group			0.02*
Fraternal	-0.50	[-0.93 - -0.07]	
Identical	[Ref.]	[Ref.]	

Continued

Upper Airway Area			
Age	22.82	[18.56- 27.09]	<.0001*
Gender			0.62
Male	[Ref.]	[Ref.]	
Female	-6.65	[-32.224- 18.93]	
Group			0.0004*
Fraternal	-44.76	[-69.09 - -20.42]	
Identical	[Ref.]	[Ref.]	
Lower Airway Area			
Age	11.97	[8.64- 15.30]	<.0001*
Gender			0.40
Male	[Ref.]	[Ref.]	
Female	-7.09	[-23.70 – 9.51]	
Group			0.0002*
Fraternal	-29.36	[-44.78 - -13.94]	
Identical	[Ref.]	[Ref.]	

Results-Correlation of cephalometric to airway measurements for males/females

Explanatory variables	FHUA	PNSU	PHWU	GoU	PHWGo	SegPNS	HyS	HyGT	Upper Airway Width	Lower Airway Width	Upper airway Area	Lower Airway Area
	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)
GonialAngle	-0.13 (0.29)	-0.03 (0.78)	-0.07 (0.57)	-0.30 (0.01)	-0.13 (0.29)	0.08 (0.49)	-0.16 (0.18)	-0.18 (0.14)	-0.07 (0.56)	-0.05 (0.67)	-0.11 (0.35)	0.10 (0.39)
SnGoGn	0.07 (0.56)	0.20 (0.10)	-0.10 (0.40)	-0.14 (0.24)	-0.07 (0.54)	0.31 (0.01)	0.12 (0.34)	-0.10 (0.39)	-0.22 (0.07)	-0.06 (0.62)	-0.32 (0.006)	-0.10 (0.42)
ANB	-0.03 (0.78)	0.24 (0.04)	0.07 (0.53)	-0.03 (0.81)	0.02 (0.85)	0.20 (0.10)	0.07 (0.55)	0.005 (0.96)	0.07 (0.58)	0.13 (0.27)	0.07 (0.58)	0.02 (0.85)
SNA	-0.26 (0.03)	0.03 (0.79)	-0.02 (0.89)	-0.04 (0.73)	-0.15 (0.22)	-0.09 (0.44)	-0.02 (0.88)	0.14 (0.24)	0.13 (0.30)	-0.003 (0.98)	0.03 (0.77)	-0.02 (0.83)
SNB	-0.17 (0.16)	0.06 (0.63)	-0.13 (0.28)	-0.04 (0.73)	-0.19 (0.12)	-0.04 (0.74)	0.03 (0.80)	-0.02 (0.86)	-0.008 (0.94)	-0.15 (0.22)	-0.04 0.72	-0.18 (0.13)
U1NA	-0.07 (0.54)	-0.18 (0.13)	0.10 (0.41)	-0.06 (0.59)	0.01614 0.8953	-0.008 (0.94)	-0.15 (0.22)	0.14 (0.25)	0.27 (0.04)	0.09 (0.45)	0.10 (0.39)	0.03 (0.78)
IMPA	0.01 (0.90)	0.11 (0.34)	0.10 (0.42)	0.20 (0.10)	0.17 (0.16)	0.02 (0.85)	0.04 (0.71)	0.17 (0.15)	0.35 (0.003)	0.32 (0.01)	0.14 (0.23)	0.08 (0.49)
UpperlipEplane	-0.19 (0.11)	0.05 (0.67)	0.07 (0.58)	-0.12 0.32	0.07 (0.57)	-0.08 (0.50)	-0.16 (0.17)	-0.11 (0.38)	0.16 (0.18)	0.03 (0.79)	-0.06 (0.63)	-0.01 (0.91)

Explanatory variables	FHUA	PNSU	PHWU	GoU	PHWGo	SegPNS	HyS	HyGT	Upper Airway Width	Lower Airway Width	Upper airway Area	Lower Airway Area
	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)
GonialAngle	0.02 (0.89)	-0.18 (0.13)	-0.26 (0.03)	-0.31 (0.01)	-0.35 (0.002)	-0.003 (0.98)	0.01 0.92	-0.10 (0.42)	0.05 (0.70)	0.02 (0.84)	0.19 (0.11)	0.04 (0.71)
SnGoGn	0.004 (0.97)	-0.03 (0.81)	-0.26 (0.03)	-0.09 (0.47)	-0.20 (0.10)	0.07 (0.57)	0.13 (0.28)	0.02 (0.83)	0.007 (0.95)	0.05 (0.66)	-0.03 (0.77)	0.005 (0.97)
ANB	0.01 (0.90)	0.12 (0.31)	-0.16 (0.18)	0.08 (0.52)	-0.08 (0.50)	-0.03 (0.80)	0.08 (0.50)	-0.14 (0.23)	-0.19 (0.10)	0.04 (0.74)	-0.08 (0.50)	0.007 (0.95)
SNA	0.06 (0.63)	-0.23 (0.05)	-0.08 (0.51)	0.15 (0.21)	0.002 (0.99)	-0.18 (0.13)	-0.05 (0.70)	-0.11 (0.35)	0.04 (0.73)	-0.10 (0.40)	0.13 (0.27)	-0.08 (0.50)
SNB	0.05 (0.65)	-0.27 (0.02)	-0.003 (0.98)	0.11 (0.37)	0.04 (0.76)	-0.15 (0.20)	-0.07 (0.53)	-0.04 (0.76)	0.13 (0.27)	-0.11 (0.36)	0.16 (0.17)	-0.07 (0.54)
U1NA	0.20 (0.09)	-0.24 (0.05)	0.04 (0.72)	-0.06 (0.62)	-0.05 (0.70)	-0.14 (0.23)	-0.18 (0.12)	-0.13 (0.27)	0.07 (0.58)	-0.10 (0.40)	-0.04 (0.72)	0.07 (0.57)
IMPA	0.05 (0.70)	0.15 (0.21)	0.16 (0.17)	0.21 (0.07)	0.27 (0.02)	0.08 (0.49)	0.006 (0.96)	-0.005 (0.97)	0.05 (0.67)	0.05 (0.69)	0.02 (0.86)	0.03 (0.80)
UpperlipEplane	0.08 (0.52)	-0.14 (0.24)	-0.10 (0.39)	0.03 (0.82)	-0.13 (0.29)	-0.21 (0.07)	-0.24 (0.05)	-0.23 0.05	-0.07 (0.58)	-0.07 (0.54)	-0.06 (0.59)	-0.03 (0.77)

Results-Correlation of cephalometric to airway measurements for fraternal/identical group

Explanatory variables	FHUA	PNSU	PHWU	GoU	PHWGo	SegPNS	HyS	HyGT	Upper Airway Width	Lower Airway Width	Upper airway Area	Lower Airway Area
	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)
GonialAngle	-0.07 (0.55)	-0.14 (0.25)	-0.21 (0.08)	-0.39 (0.0009)	-0.31 (0.009)	0.14 (0.24)	-0.08 (0.51)	-0.18 (0.14)	0.07 (0.57)	0.14 (0.25)	0.21 (0.08)	0.18 (0.14)
SnGoGn	0.13 (0.26)	0.08 (0.49)	-0.21 (0.07)	-0.05 (0.65)	-0.09 (0.47)	0.40 (0.0005)	0.17 (0.15)	-0.05 (0.66)	-0.08 (0.49)	0.09 (0.45)	-0.13 (0.28)	0.05 (0.60)
ANB	-0.07 (0.54)	0.09 (0.48)	-0.06 (0.64)	-0.03 (0.79)	-0.04 (0.73)	-0.04 (0.71)	-0.09 (0.43)	-0.18 (0.13)	0.04 (0.71)	0.10 (0.40)	0.19 (0.11)	0.10 (0.42)
SNA	-0.27 (0.02)	-0.07 (0.56)	-0.05 (0.66)	0.09 (0.47)	-0.14 (0.25)	-0.26 (0.03)	-0.002 (0.98)	0.02 (0.85)	0.16 (0.18)	0.01 (0.91)	0.10 (0.39)	0.02 (0.86)
SNB	-0.18 (0.14)	0.02 (0.88)	-0.20 (0.09)	-0.08 (0.51)	-0.32 (0.01)	-0.12 (0.31)	0.003 (0.98)	-0.09 (0.44)	-0.02 (0.83)	-0.20 (0.10)	-0.11 (0.36)	-0.27 (0.02)
U1NA	-0.12 (0.32)	-0.176 (0.16)	0.08 (0.51)	-0.31 (0.01)	-0.17 (0.15	-0.11 (0.35)	-0.22 (0.06)	-0.10 (0.39)	0.21 (0.08)	0.11 (0.39)	0.22 (0.07)	0.09 (0.45)
IMPA	-0.09 (0.47)	0.13 (0.28)	0.01 (0.91)	0.16 (0.20)	0.10 (0.40)	-0.06 (0.61)	-0.05 (0.68)	0.03 (0.81)	0.16 (0.19)	0.09 (0.47)	0.04 (0.72)	-0.01 (0.93)
UpperlipEplane	-0.16 (0.18)	0.05 (0.70)	-0.23 (0.05)	0.05 (0.70)	-0.05 (0.66)	-0.09 (0.48)	-0.07 (0.56)	-0.17 (0.15)	0.06 (0.60)	0.10 (0.39)	-0.03 (0.79)	0.12 (0.32)

Explanatory variables	FHUA	PNSU	PHWU	GoU	PHWGo	SegPNS	HyS	HyGT	Upper Airway Width	Lower Airway Width	Upper airway Area	Lower Airway Area
	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)
GonialAngle	-0.01 (0.96)	-0.08 (0.50)	-0.06 (0.[illegible])	-0.16 (0.17)	-0.05 (0.67)	0.03 (0.80)	-0.01 (0.[illegible])	-0.01 (0.91)	-0.01 (0.92)	-0.11 (0.35)	-0.12 (0.34)	0.05 (0.68)
SnGoGn	-0.06 (0.64)	0.07 (0.56)	-0.12 (0.31)	-0.15 (0.21)	-0.12 (0.33)	0.11 (0.38)	0.07 (0.57)	0.06 (0.63)	-0.10 (0.42)	-0.11 (0.36)	-0.31 (0.01)	-0.16 (0.17)
ANB	0.09 (0.47)	0.19 (0.12)	0.01 (0.93)	0.11 (0.34)	0.06 (0.61)	0.20 (0.09)	0.15 (0.11)	0.11 (0.37)	-0.06 (0.59)	0.12 (0.34)	-0.16 (0.20)	-0.06 (0.62)
SNA	0.11 (0.37)	-0.09 (0.46)	0.004 (0.97)	0.06 (0.60)	0.01 (0.95)	-0.01 (0.95)	-0.01 (0.95)	0.02 (0.85)	0.04 (0.71)	-0.08 (0.53)	0.09 (0.45)	-0.07 (0.57)
SNB	0.06 (0.63)	-0.17 (0.16)	0.01 (0.94)	0.003 (0.98)	-0.02 (0.85)	-0.10 (0.40)	-0.09 (0.43)	-0.02 (0.84)	0.08 (0.53)	-0.12 (0.31)	0.16 (0.18)	-0.03 (0.81)
U1NA	0.19 (0.12)	-0.21 (0.08)	0.08 (0.51)	0.08 (0.49)	0.09 (0.45)	-0.04 (0.71)	-0.12 (0.32)	0.04 (0.77)	0.13 (0.28)	-0.08 (0.49)	-0.07 (0.55)	0.02 (0.88)
IMPA	0.15 (0.22)	0.12 (0.30)	0.19 (0.11)	0.21 (0.08)	0.25 (0.03)	0.08 (0.48)	0.05 (0.65)	0.06 (0.64)	0.21 (0.07)	0.27 (0.02)	0.10 (0.42)	0.07 (0.56)
UpperlipEplane	0.06 (0.60)	-0.09 (0.44)	-0.22 (0.07)	-0.08 (0.50)	0.09 (0.47)	-0.15 (0.22)	-0.21 (0.04)	-0.19 (0.12)	0.04 (0.74)	-0.11 (0.38)	-0.02 (0.84)	-0.10 (0.43)

Heritability of airway to skeletal measurements

Explanatory variables	FHUA	PNSU	PHWU	GoU	PHWGo	SegPNS	HyS	HyGT	Upper Airway Width	Lower Airway Width	Upper airway Area	Lower Airway Area
	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability	Heritability
GonialAngle	6%	5%	12%	17%	20%	-13%	6%	14%	-9%	-29%	-42%	-16%
SnGoGn	-22%	-1%	7%	-10%	-3%	-48%	-12%	10%	-2%	-22%	-16%	-22%
ANB	15%	11%	5%	14%	10%	23%	26%	25%	-10%	2%	-43%	-18%
SNA	30%	-2%	5%	-3%	13%	20%	-1%	0%	-14%	-9%	-1%	-9%
SNB	20%	-19%	18%	8%	23%	2%	-9%	6%	10%	7%	24%	19%
U1NA	28%	-3%	0%	30%	22%	6%	8%	13%	-10%	-21%	-37%	-8%
IMPA	22%	-1%	18%	6%	17%	13%	10%	3%	6%	20%	6%	8%
UpperlipEplane	19%	15%	37%	-14%	13%	-6%	-16%	-2%	-2%	-23%	1%	-25%

THANK YOU!