Abstract

Background: Pubertal timing is in part mediated by environmental factors, with greater energy availability often associated with earlier or more rapid development. Many indigenous populations are undergoing socioeconomic change that may affect pubertal development and related health risks, necessitating fundamental longitudinal research on growth and development in these populations.

Aim: We describe growth velocity and time to menarche among peri-urban indigenous Qom (Toba) girls in Argentina.

Subjects and Methods: From 2011-2015, monthly anthropometrics and menstrual status were collected from 61 Qom girls aged 7-14. Growth velocity curves were generated using the ‘Super-imposition by translation and rotation’ (SITAR) method. Median time to menarche was estimated by Kaplan-Meier survival analysis.

Results: Mean ages at peak height, weight, and BMI velocity were estimated at 10.8, 10.5, and 10.7 years, and median age at menarche at 11.6 years (95% CI 11.4 – 11.9).
At menarche, 45% of girls were overweight or obese and only one participant was short-statured by international standards.

**Conclusion:** Qom participants in this study exhibit relatively fast pubertal development as compared to other Latin American indigenous populations studied previously by others. Genetic and environmental factors influencing body size, diet, and/or activity levels should be investigated further in this population.

**Keywords:** puberty, growth and development, Latin America, indigenous health, menarche

**Introduction**

The onset and pace of pubertal progression are flexibly attuned to environmental conditions (Ellis, 2004; Ellison et al., 2012), with earlier maturation generally associated with greater available energetic resources and more rapid growth during childhood (Ellison, 1990, 2001). Earlier pubertal maturation in females has been observed globally since the 20th century (Parent et al., 2003; Biro et al., 2012), and is a growing public health concern, since earlier onset of menstruation and gains in adiposity may increase later life risk of reproductive cancers, obesity, and other metabolic diseases (Stoll, 1998; Stöckl et al., 2011; Akter et al., 2012; Glueck et al., 2013). In certain cultural contexts, earlier sexual maturation may also lead to earlier sexual activity and increase risks of early adolescent pregnancy, sexually transmitted diseases, sexual abuse, depression, or anxiety (Angold et al., 1999; Kaestle et al., 2005; Boden et al., 2011).

Variation in pubertal development by socioeconomic class or ethnicity within populations is of further interest, as such variation may both reflect underlying differences in environmental quality or risk exposures, and predict later health
disparities. National surveys from Brazil, Argentina, and Colombia have shown that earlier menarche is associated with higher income, better education, and greater birthweight, height, and BMI (Orden et al., 2011; Castilho and Nucci, 2015; Jansen et al., 2015). However, comparative research on pubertal development in Latin America by ethnicity and genetic ancestry has been limited. Though Latin American indigenous populations are generally economically marginalized, poverty may increase risks of over- or undernutrition depending on the quality of diet and other local conditions (Monteiro et al., 2004; Caballero, 2005), suggesting varying influences on pubertal development. For example, in the U.S. menarche generally occurs earlier among girls of lower socioeconomic status (Obeidallah et al., 2000; Krieger et al., 2015), who also tend have higher obesity risks (Drewnowski and Darmon, 2005; Frederick et al., 2014). In contrast, a study in Chile found that Mapuche indigenous girls were shorter, heavier and had later ages at menarche than their non-indigenous peers, with earlier menarche across both groups associated with higher stature and SES, not greater weight or BMI (Amigo et al., 2010, 2015, Ossa et al., 2010, 2012).

The Qom (Toba) are an indigenous population residing primarily in the northeastern Gran Chaco region of Argentina. Most Qom live below the national poverty level. However, mean height-for-age (HAZ) and BMI-for age z scores (BMIZ) of Qom children aged 0 – 18.9 years are well within normal ranges of international and national growth references (Alfonso-Durruty and Valeggia, 2016), and Qom adult stature is among the highest of small-scale indigenous populations surveyed globally (Walker et al., 2006). The prevalence of obesity and metabolic disorders in this transitioning population has also been steadily increasing (Valeggia et al., 2010; Lagranja et al., 2014a). Qom developmental trajectories may be either relatively slow or fast, given that the Qom are an economically marginalized South American indigenous
population, but conversely relatively tall and well-nourished. In this descriptive study, we analyse patterns of growth velocity, time to menarche, and additional measures of nutritional status and pubertal development from a longitudinal study of pubertal Qom females. We compare Qom pubertal trajectories to those of other sample populations previously published, emphasizing Latin American and indigenous populations where possible.

**Materials and Methods**

**Study population**

The Qom of Argentina (referred to as “Toba” by neighbouring, but not related, indigenous groups) were traditionally semi-nomadic hunter-gatherers, who resisted Spanish colonization and Argentinian expansion policies until the late 1800s (Valeggia and Tola, 2003). Since the 1930s, government policy and habitat degradation have forced many Qom into peri-urban settlements. The total population today is around 70,000, with most Qom residing in the provinces of Chaco and Formosa, and in smaller settlements around Santa Fe and Buenos Aires. This study was conducted with girls in the peri-urban village of Namqom, a genetically homogenous Eastern Qom settlement (pop. ~3000), located 11 km outside of the city of Formosa (pop 234,000), and established in the early 1970s (Alfonso-Durruty and Valeggia, 2016).

Namqom families subsist primarily on government subsidies, with additional income generated from men’s temporary wage labor and women’s sales of artisanal crafts. The typical diet in Namqom is high in carbohydrates and fat from staples like *torta frita* (fried bread) (Lagranja et al., 2014b). Thirty-five and 45% of adults are classified as obese and overweight, respectively (Lagranja et al., 2014a). In more rural
Qom communities BMI is positively associated with socioeconomic status (Valeggia et al., 2010), though this relationship may be reversed in peri-urban Namqom. A health center in Namqom offers prenatal and child health care, and the majority of births take place in a local city hospital. The incidence of pre-term births is comparable to that of non-indigenous women in the area. The majority of infants are within normal birth weight range (2500 – 4000 g), with 0-3% classified as low birthweight and 10-12% as more than 4000g. In general infants are exclusively breastfed until about four to six months of age and weaned when the mother gets pregnant again, or the child weans him/herself (Valeggia and Ellison, 2003a; b; Olmedo et al., 2014). Adolescent sexual activity, including prostitution, is not stigmatized but may pose health risks. The average age at first birth is 16. Adolescent mothers usually remain single and live at home, and it is common of them to foster away care of their first born children to parents or other relatives (Valeggia and Tola, 2003).

Ethics approval and consent to participate

Participants and their caretakers were informed that the purpose of the study was to examine pubertal development in the population. All girls and their adult caretakers (usually the mother) provided verbal informed consent to participate. The research protocol was approved by the internal review boards of both the University of Pennsylvania (Protocol # 811200) and Yale University (HSC Protocol # 1406014104). There were no ethics committees available to provide approval in the province of Formosa, where the study took place.

Data collection
Between 2011 – 2015, researchers affiliated with the Chaco Area Reproductive Ecology (CARE) program followed a total of 61 self-identifying Qom girls between the ages of 7 -14. This data was collected as part of a larger study to examine endocrine correlates of female reproductive life history transitions. **Subject recruitment:** All females aged 7-10 in Namqom were eligible for inclusion in the study and invited to participate. As Qom families move frequently among kin residences and across territories, participants were located and recruited into the study between 2011-2013 (Table 1). To our knowledge, there were no girls aged 7-10 living permanently in the community during those years who were approached and excluded based on menarcheal status, or who declined to participate. However, at the start of data collection in January 2011, four pre-menarcheal girls aged 12-13 requested to be part of the study and were also included. To test if inclusion of these subjects biased results, we ran separate survival analysis models of time to menarche both including and excluding these subjects. The average age at first observation across all participants was 9.4 ± 1.2 years (range 7.3 – 13.4; IQR 8.4 – 10.9).

**Subject follow-up:** The original study design protocol called for researchers to follow participants monthly until they reported menstruating three times or for six months after menarche. The total number of observations per subject per year varied due to age at initial observation, age at menarche, age at study exit, and intermittent absences (Table 1). Age at menstruation was reported by 51/61 participants: three participants had still not experienced menarche by the end of the study in 2015 (mean age at last observation 12.3 ± 0.7 years; mean number of observations 37 ± 4); one participant left the study at her mother’s request at age 8.7 after five visits; six participants moved away or were otherwise lost to follow up (mean age at last observation 9.7 ± 1.1 years; mean number of observations 12 ± 13). The mean number
of observations per subject was 24 ± 11 (range 2 - 46, IQR 16 - 29). Among participants
with known age at menarche, the mean number of pre- and post-menarcheal
observations per subject were 20 ± 4 and 4 ± 3, respectively, and the mean age at last
observation was 12.0 ± 1.0 (range 9.9 – 14.4).

Measurement protocols: Anthropometric measures and self-reported menstrual
status and Tanner breast stage were collected by researchers during monthly visits to the
participants’ homes. Height was measured to the nearest centimeter using a portable
SECA 213 portable stadiometer. Chest, waist, and hip circumference were measured to
the nearest 0.5 cm using a portable tape measure. Weight (kg) and % body fat (via
electrical impedance) were recorded using TANITA ® body composition scale. Tricep
and subscapular skinfolds were measured in triplicate to the nearest mm using Lange
calipers. Participants were also given photographs of Tanner breast stages digitally
modified with darker skin images to reference, and asked to self-report their own stage
of development. However, in 39% of interviews, participants declined to report this
information. Maternal age at menarche and participants’ birth weight, birth length, and
gestational age from birth records were collected at initial interviews if available.

Statistical analysis
All statistical analyses were run on R (ver. 3.4.1). Descriptive statistics were generated
for each of the following anthropometric measurements at initial observation and at age
of menarche: weight, height, BMI, % body fat, waist, hip, and chest circumference,
waist to hip ratio, and subscapular and triceps skinfold measurements. Triplicate
measures of subscapular and tricep skinfolds were averaged for each observation.
Height-for-age (HAZ) and BMI-for-age z-scores (BMIZ) were calculated using WHO
2007 growth standards (de Onis et al., 2007). HAZ and weight-for-age z scores (WAZ)
were also calculated based on Argentina LMS pediatric growth references (Lejarraga et al., 2009). To account for intermittent missing self-reported Tanner breast stages, we assigned a median breast stage score to each six-month period of observation for each participant. Kaplan-Meier survival analysis was used to estimate median time to menarche to incorporate both censored (n = 10) and non-censored participants (n = 51).

SITAR models of height, weight, and BMI velocity were generated using the sitar package in R (Cole, 2017). The method has been previously used to model height velocities of European and South American children (Cole et al., 2014; Blackwell et al., 2016b). As described in more detail elsewhere (Cole et al., 2010; Pizzi et al., 2014), the SITAR method uses a shape invariant spline curve and a nonlinear random-effects model to fit individual trajectories and estimate an average growth curve for a sample. The model estimates three fixed and random effects (α, β, γ), referred to as size, tempo, and velocity, which define how individual curves deviate from the mean (Cole et al., 2010). For each growth outcome, size is interpreted as a random intercept, with larger values representing larger mean size than average (an upward shift of the curve). Tempo adjusts for differences in the age at peak velocity (APV), with positive values indicative of later maturation and negative values indicative of earlier maturation relative to the mean (right or left shifts of the curve). Velocity adjusts for the duration of the growth spurt, with positive values indicative of faster and negative values of slower growth (stretching or shrinking the curve along the age scale).

To ensure model convergence, we constrained all observations to equivalent intervals by rounding each age at measurement in years to the nearest 1st decimal (e.g. 8.1, 8.2, 8.3). In the case of multiple measures per individual in an interval, only the first measure was retained. We eliminated from the sample any age intervals with fewer than five subjects per interval, and any subjects with fewer than three observations. The
resulting sample included 58 subjects ages 8.0 – 13.0, with 1174 height observations and 1171 weight/BMI observations. Final models for height, weight, and BMI were all fit with a five-degree polynomial curve.

Prior to assembling the database used in this study, raw data points were visually inspected. Biologically implausible measures (monthly deviations of > 2 cm or > 5 kg from previous or subsequent measures) were checked against written records and amended, or removed in extreme cases. For the SITAR models, we examined additional outliers within individual trajectories using custom package functions. Removal of weight and BMI outliers substantially reduced the sample, resulting in an altered weight velocity curve and non-convergence of the BMI velocity model. Since errors appeared randomly distributed across subjects, and there was a high number of discrete data points per subject, we ultimately elected not to remove flagged outliers from the final models. Growth velocities calculated over measurement increments of < 0.85 years are more affected by seasonal shifts and measurement error (Tanner and Davies, 1985).

However, SITAR growth models for Qom girls did not converge when the dataset was reduced to measurements taken every 3 or 6 months, likely due to the resulting small sample size. Removal of one subject observed to be an extreme outlier for weight (mean 84.7 ± 11.4 kg) and BMI (mean 37.0 ± 2.8) resulted in biomodal growth velocity distributions or nonconvergence of models. In general, the SITAR models were highly sensitive to any data reduction. A model of fat velocity, with % body fat measured from bioelectrical impedance, also failed to converge. Velocity curves and estimates for peak velocity and age at peak velocity were generated from sitar package custom commands. Datasets and R code used to generate analyses are publically available on figshare (https://doi.org/10.6084/m9.figshare.4757164.v2).
Results

Eighty percent of Qom girls with known age at menarche (40/51) experienced menarche before age 12. The median time to menarche estimated by survival analysis for censored and non-censored subjects was 11.6 years (95% CI 11.4 – 11.9) (Fig.1), which was largely concordant with mean and median ages from girls with known age at menarche (Table 2). Median time to menarche was slightly decreased by removing the four pre-menarcheal subjects who were aged 12-13 at first observation from the survival analysis (11.4, 95% CI 11.3 – 11.8). There are no standard cut-offs for defining early menarche, with researchers varyingly using population cut-offs of < 11 to < 12 years (Ibáñez et al., 2006; Stöckl et al., 2011; Akter et al., 2012; Glueck et al., 2013). We estimate that 77% (66 – 89% 95% CI) of Qom girls are still premenarchal at age 11, and only 31% (21-47%) at age 12. (Figure 1). For subjects’ mothers with available data (n = 48), their average age of menarche reported by recall was 12.81 ± 1.08, suggesting a secular trend towards earlier pubertal development. Participants and their mothers’ reported ages at menarche were weakly correlated (Pearson’s r = 0.337, 95% CI = 0.041 – 0.579; p = 0.027).

Precocious thelarche is frequently diagnosed if breast development is observed before age 8, ideally confirmed by palpation in a supine position (Kaplowitz and Bloch, 2015). We lack appropriate diagnoses for precocious thelarche based on these criteria, and only two subjects observed at age seven ever self-reported breast stage, both reporting stage I development. Across all participants observed from ages 7-9 (n = 57), in 59% of monthly observations (226/381) participants reported Tanner Stage I breast development, 36% (138/381) reported Stage II, and 5% (17/381) reported Stage III-V. Among subjects reporting menarche, 7% (3/51) reported Stage I breast development in
the month of menarche, 64% (29/51) Stage II, 27% Stage III (12/51), and 2% (1/51) Stage IV.

For participants with available data, most were born within normal birthweight ranges, though 5% (3/58) would be classified as low birthweight (< 2.5 kg) and 9% (5/58) as macrosomic (> 4 kg). For subjects with known gestational ages, 23% (9/39) were classified as preterm at < 37 weeks. At initial observations, 26% of participants were overweight and 8% were obese, with only 7% classified as short-statured (Table 3). By menarche, the percentage of short-statured girls slightly decreased while percentages of obese and overweight girls slightly increased (Table 3). Mean HAZ scores at menarche were well within normal ranges as calculated by either WHO standards or Argentina growth references (Table 2).

There have been limited studies to determine cut-offs for abdominal obesity based on waist circumference or waist/height ratios in children, and cut-off values may vary with age and ethnicity (Lear et al., 2010; Lewitt et al., 2012; Magalhães et al., 2014). Waist circumference cut-offs of ≥ 70.1 and ≥ 69.9 cm have been recommended for Mexican girls aged 8-9 and 10 year-old, respectively (Gomez-Diaz et al., 2005), and 65.1 – 69.1 cm for mixed-ethnicity Chinese girls aged 7 – 18 (Yan et al., 2008). Waist-height ratio cut-offs of > 0.44 and > 0.43 cm have been recommended for Brazilian girls aged 8 and 9 (Sant’Anna et al., 2010), and 0.475 – 0.50 for Chinese, Spanish, and Italian children up to age 18 (Yan et al., 2007; Maffeis et al., 2008; Marrodán et al., 2013). Conservatively, we applied cut-off values of ≥70 cm for waist circumference and ≥ 0.50 for waist/height ratio as potentially indicative of abdominal obesity. At first observation (n = 61), 11% of participants had a waist circumference of ≥70 cm and 25% had a waist/height ratio ≥ 0.50. For participants reporting menarche (n = 51), the prevalence was 43% and 25%, respectively, at month of menarche. Waist/height ratio at
first observation was not associated with age at menarche after adjusting for age at first
observation (Est. = -2.2, 95% CI = -7.21 – 2.28; p = 0.381).

As estimated by SITAR models, mean age at peak velocity and mean peak
velocity were estimated at 10.8 years and 9.4 cm/years for height, and 10.5 years and
8.5 kg/year for weight. Mean age at BMI velocity was estimated at 10.7 years. Velocity
and distance curves for each growth measure are shown in Figures 2a-c. The models
explained 98.8%, 99.1, and 97.8% of variance in height, weight, and BMI, respectively.
Random effects for size and tempo were positively correlated in models of height
(0.63), weight (0.61), and BMI velocity (0.60), indicating that later maturation is
associated with greater average body size. Growth velocity was more strongly
correlated with size and tempo in models of weight (size/tempo 0.62/0.80) and BMI
(0.58/0.56) than in models of height (0.14/0.32).

Discussion

There have been relatively few longitudinal studies on growth and menarcheal
onset in indigenous populations, limiting knowledge of normative variation in pubertal
development globally. Pubertal development among the Qom girls observed here
appears relatively accelerated when compared to available published estimates of
growth velocity in indigenous and non-indigenous populations. To our knowledge, only
two studies have used similar methods—i.e. SITAR curves or pseudo-velocity curves
from median LMS values—to characterize pubertal growth in indigenous populations.
These were conducted with neotropical horticulturalist populations, the Tsimane of
Bolivia and the Shuar of Ecuador. For both height and weight, mean peak velocities are
greater and mean ages of peak velocity are earlier in Qom as compared to Tsimane
females (height: 8.2 cm/yr, 11.3 years; 6.5 kg/yr, 12.0 years) (Blackwell et al., 2016b).
Comparatively, Shuar females exhibited a slightly earlier mean age of peak height velocity (10.2 years), but later mean age at peak weight velocity (12.1 years) and substantially lower velocities for height and weight (5.4 cm/yr, 2.2 kg/yr, 12.1 years) (Urlacher et al., 2015).

Differences in pubertal growth between the Qom and these indigenous populations are expected due to substantial intra-and inter-population environmental and genetic variation. For example, the Tsimane and the Shuar are characterized by short adult stature, a high prevalence of childhood stunting and infectious diseases, and relatively low prevalence of overweight/obesity (Godoy et al., 2006; Blackwell et al., 2010, 2016a; Liebert et al., 2013; Rosinger et al., 2013; Urlacher et al., 2016). In contrast, the average height of Qom adults are among the highest documented for indigenous groups globally (Walker et al., 2006), and 35% and 45% of Qom adults are obese and overweight, respectively (Lagranja et al., 2014a).

Estimated peak height velocity for these participants is also earlier as compared to estimates of 11.5 – 12.1 years published in seminal studies of American and European girls observed from the 1960s – 1990s (Tanner, 1989; Abbassi, 1998; Granados et al., 2015). The SITAR method was recently applied to a study of English girls measured in the 1970s (Cole et al., 2014), and estimated age at peak height velocity and peak velocity in those subjects at 11.9 years and 7.6 cm/year, respectively.

In an early study of pubertal growth in North American children, early maturation was noted to coincide with greater peak height velocity (Tanner and Davies, 1985). In Qom girls, the estimated age at peak weight velocity preceded age at peak height velocity by ~ four months, whereas elsewhere peak height velocity has been reported to precede peak weight velocity by about six months elsewhere (Rogol et al., 2000). Average peak height velocity of Qom girls also preceded average age at menarche by approximately
9.6 months, whereas an average difference of about one year between these events was estimated for English girls measured in the 1970s (Cole et al., 2014). The growth differences observed in these comparisons may reflect local genetic and obesogenic conditions, but also general secular trends operating across disparate observation periods. At ~11.5 years, menarche also occurs on average about 6 months to 2 years earlier in these Qom girls than as reported in recent studies for girls in the U.S., Europe, and Latin America, including Argentina (Ossa et al., 2010; Orden et al., 2011; Torres et al., 2011; Currie et al., 2012; Cabrera et al., 2014; Castilho and Nucci, 2015; Jansen et al., 2015; Krieger et al., 2015), and may reflect the influence of obesogenic conditions as observed elsewhere. For example, average ages of menarche around 11.5 years or earlier have been observed and associated with excess weight and/or body fat in girls from the Brazilian Amazon (Barcellos Gemelli et al., 2016), Yucatán, México (Datta Banik et al., 2015), Italy (Rigon et al., 2010), and Argentina (Figueroa Sobrero et al., 2016). Similarly, a comparative study of pubertal development in children from Bolivia (Takana and Esse ejja ethnicities) and Senegal (Tokolor, Wolof, and Serer ethnicities), all of whom lived in rural, tropical environments, found that the characteristically “short and plump” Bolivian girls had much earlier ages of menarche (median 12.9 years) than the characteristically “tall and thin” Senagalese girls (median 15.9 years) (Benefice et al., 2011). Average ages of menarche around 11.5 years have also been associated with relative affluence in specific demographic groups within populations—e.g.: Saudi Arabian girls attending private schools (Shaik et al., 2015), and Mexican girls born after 1990 (Marván et al., 2016). Finally, while Mapuche girls in Chile experience menarche 2-4 months later on average than non-indigenous neighbouring girls (Amigo et al., 2010, 2012; Ossa et al., 2012), among the Mapuche themselves, researchers have
observed a secular trend in decreasing age at menarche since the 1960s (Ossa et al., 2010), and earlier menarche in association with obesity and higher socioeconomic status (Amigo et al., 2012).

Qom environmental and genetic conditions influencing infant and childhood growth patterns may influence relatively accelerated pubertal development. The present study suggests a picture of sufficient to excess nutrition in later childhood, as at first observations 24% of participants were overweight, 8% were obese, and only 7% were short-statured. A previous survey showed that mean HAZ in Qom children increased in each successive age group following infancy, while mean WAZ was u-shaped (with a nadir during ages 3-6), and mean BMIZ was lower in each age group following infancy, levelling off after age 11. Mean BMIZ in infants (0-2.9 years) of both sexes and across all regions was 1.64 ± 1.18, which is notable because Qom infants are exclusively breastfed for about six months and breastfed for about 2-3 years. Mean HAZ was also significantly higher among more rural Western Qom than among peri-urban Eastern Qom (Alfonso-Durruty and Valeggia, 2016), suggesting a wider underlying genetic influence.

We have previously proposed that Qom growth patterns—i.e. decreasing mean BMIZ and increasing mean HAZ after infancy—may reflect an evolutionarily selected strategy (Alfonso-Durruty and Valeggia 2016). Life-history theory posits that somatic energy expenditure at key phases of the life course may be shaped by selection to maximize survival or reproduction through differential energy allocation. Energy trade-offs can occur between investment in growth, reproduction, or maintenance, but also within those individual categories, for example between linear growth and adiposity. Preferential investment in adiposity (maintenance) relatively to linear growth during infancy may buffer against energy losses related to infectious disease and nutritional
scarcity, and therefore may be common strategy in risky environments (Ellison 2001; Walker et al., 2006). Conversely, the observed gains in linear height during childhood and adolescence—which result in larger adult body size relative to other small-scale populations (Walker et al., 2006)—may reflect energetic adaptations to the Chacoan ecology and/or relaxed selection pressures from infectious disease burdens post-infancy.

**Limitations and Future Directions**

A strength of our study is the longitudinal design with multiple, discrete measurements per subject. Longitudinal research on growth and development in indigenous populations in particular has been limited. While participants in this study represented all available female subjects in the study village at the time, the study design is unbalanced due to participants entering and exiting the study at different ages, rather than according to set observational windows. Analysis of pubertal development according to Tanner stages was not possible because of cultural sensitivity issues, which limited data collection to self-reported breast development, with participants frequently declining to report this information. Finally, though recall bias for age at menarche was minimized through monthly visits, we cannot rule out inaccurate self-reporting.

Analysis of causal factors associated with variation in pubertal growth is beyond the scope of this dataset. While shorter gestational age, low birth weight, and more rapid postnatal catch-up growth have been associated with earlier pubertal maturation (Wehkalampi et al., 2011; Addo et al., 2014), we lacked sufficient data to investigate these relationships among our participants. Similarly, while over a third of participants in our study were overweight or obese at initial observations, additional longitudinal research beginning in mid-childhood would be necessary to assess whether the patterns of pubertal development observed here are reflective of age at pubertal onset, the pace...
of pubertal development, or both. Ongoing research stemming from this study will investigate the relationship between growth velocity and concordant changes in metabolic, reproductive, and immunological urinary biomarkers, which may provide more insight into cumulative energetic influences on pubertal development.

Additional longitudinal research would be necessary to assess differences in pubertal maturation between Qom and more affluent non-Qom residents of Formosa. If pubertal development among the Qom does indeed occur relatively earlier, the pattern may be more analogous to that observed in the U.S., in which lower SES and minority groups tend to have earlier ages at menarche but also greater BMI and earlier skeletal maturation (Bogin, 1999; Obeidallah et al., 2000; Kelly et al., 2014). In this case, future research should also explore local patterns of pubertal development in relation to variation in diet, activity, early growth trajectories, and exposure to endocrine disrupting chemicals or specific dietary components. Such research may help determine to what extent early pubertal development in the Qom may be genetic or owing to modifiable socioeconomic and cultural factors. Finally, while early adolescent sexual activity and pregnancy among Qom girls are common and culturally accepted, additional research may examine if differences in pubertal trajectories within the population influence variation in subsequent sexual activity, timing of first births, or later life metabolic or reproductive health risks.

Conclusions

We have described pubertal growth and age at menarche in a sample of indigenous Qom girls from a peri-urban village in Formosa, Argentina. Mean ages at peak height velocity (10.8 years) and menarche (11.6 years) of participants were relatively early compared to estimates reported in several other studies of girls in Latin America, U.S.,
and Europe. Accelerated pubertal development in these girls may reflect local energetic
factors—including a high carbohydrate-high fat diet and sedentarism—and population
specific growth patterns, characterized by marked adiposity in infancy and gains in
linear height in later childhood. However, additional research on diet, activity, growth,
and environmental exposures in a wider Qom sample and other local non-indigenous
populations is needed to both confirm this pattern and illuminate possible causal
relationships. This study underscores the importance of conducting longitudinal studies
with diverse populations to better understand current global secular trends and variation
in pubertal development.

Acknowledgements
We thank all participants and the study community for their cooperation. This study
would not have been possible without the many contributions of the research
coordinators and assistants of the Chaco Area Reproductive Ecology Program: Mirella
Aglietta, Florencia Cirigliano, Rocio Davichi, Mandi Davichi, Marisa Galeano, Angie
Jaimez, Silvia Mansilla, Fernanda Medina, Rosaura Medina, Cara McGuinness, Sofia
Olmedo, Florencia Orlando, Alfonsina Salvarredy, Noemí Trope, and Monika Wasik.
The staff at the Centro de Salud Namqom graciously provided access to clinical
histories (with permission from participants). We thank Fundación ECO for their
logistical, administrative, and moral support throughout data collection. Veronika
Shabanova and Aaron Blackwell provided helpful analytical advice.

Funding:
This research was supported by NSF BCS-0952264. The Yale Institute of
Biospheric Studies (YIBS) funded a postdoctoral fellowship for MAM
Disclosure statement:
The authors have no financial or other competing interests to declare.

Supplemental online material
All datasets and code available on figshare
(https://figshare.com/projects/Qom_Puberty_Shared_Data/19756)

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Table 1. Number of participants entering and exiting study and total observed per study year.

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Recruited n</th>
<th>Exited Study n</th>
<th>Total Followed/Yr n</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>41</td>
<td>2</td>
<td>41</td>
</tr>
<tr>
<td>2012</td>
<td>16</td>
<td>10</td>
<td>55</td>
</tr>
<tr>
<td>2013</td>
<td>4</td>
<td>22</td>
<td>49</td>
</tr>
<tr>
<td>2014</td>
<td>15</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>2015</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>
Table 2. Descriptive statistics of nutritional & developmental markers at menarche, among participants with known age at menarche (n = 51 out of 61 original participants).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>9.6 – 13.8</td>
<td>11.5 ± 0.9</td>
<td>11.3 (10.9 - 11.9)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>136 – 157</td>
<td>146.7 ± 6.7</td>
<td>147 (143 – 151)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>29.3 – 100.7</td>
<td>44.5 ± 11.2</td>
<td>41.2 (38.1 – 46.9)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>15.6 – 40.9</td>
<td>20.6 ± 4.3</td>
<td>20.0 (17.9 – 21.5)</td>
</tr>
<tr>
<td>HAZ (WHO)a</td>
<td>-2.34 – 2.49</td>
<td>-0.12 ± 0.105</td>
<td>-0.11 (-0.71 – 0.33)</td>
</tr>
<tr>
<td>HAZ (Argentina)b</td>
<td>-0.89 – 3.61</td>
<td>0.89 ± 1.00</td>
<td>0.84 (0.33 – 1.29)</td>
</tr>
<tr>
<td>WAZ (Argentina)b</td>
<td>-1.71 – 4.73</td>
<td>1.02 ± 1.25</td>
<td>1.16 (0.31 – 1.50)</td>
</tr>
<tr>
<td>BMIZ (WHO)a</td>
<td>-1.98 – 4.64</td>
<td>0.83 ± 1.22</td>
<td>0.93 (0.22 – 1.45)</td>
</tr>
<tr>
<td>Body fat %</td>
<td>13 – 52</td>
<td>20.6 ± 6.9</td>
<td>25 (22 – 30)</td>
</tr>
<tr>
<td>Waist circ. (cm)</td>
<td>59 – 112</td>
<td>70.0 ± 8.8</td>
<td>69 (64 – 73)</td>
</tr>
<tr>
<td>Hip circ. (cm)</td>
<td>68 – 118</td>
<td>78.3 ± 8.3</td>
<td>76 (73 – 82)</td>
</tr>
<tr>
<td>Chest circ. (cm)</td>
<td>60 – 119</td>
<td>78.5 ± 8.6</td>
<td>76.5 (75 – 119)</td>
</tr>
<tr>
<td>Bicep circ. (cm)</td>
<td>17 – 37</td>
<td>23.1 ± 3.2</td>
<td>23 (21 – 25)</td>
</tr>
<tr>
<td>Waist/height ratio</td>
<td>0.39 – 0.71</td>
<td>0.48 ± 0.05</td>
<td>0.48 (0.44 – 0.50)</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.79 – 0.97</td>
<td>0.89 ± 0.04</td>
<td>0.89 (0.87 – 0.92)</td>
</tr>
<tr>
<td>Subscapular skinfold (mm)</td>
<td>6.7 – 28.3</td>
<td>14.5 ± 4.9</td>
<td>13.5 (11.0 – 16.8)</td>
</tr>
<tr>
<td>Tricep skinfold (mm)</td>
<td>6.7 – 25.0</td>
<td>13.3 ± 4.7</td>
<td>12.0 (10.0 – 25.0)</td>
</tr>
</tbody>
</table>

aWHO 2007 standards were used to calculate height-for-age (HAZ) and BMI-for-age (BMIZ) z scores. bArgentina 2009 pediatric growth references used to calculate HAZ and weight-for-age z scores (WAZ).
Table 3. Prevalence of thinness, overweight, obese, and short stature among participants at first observation (n = 61) and at first report of menarche (n = 51).

<table>
<thead>
<tr>
<th>BMIZ cut-off</th>
<th>First observation</th>
<th>At menarche</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thinness (&lt; - 2 SD)</td>
<td>2 (3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Overweight (&gt; 1 SD)</td>
<td>16 (26%)</td>
<td>17 (33%)</td>
</tr>
<tr>
<td>Obese (&gt; 2 SD)</td>
<td>5 (8%)</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>HAZ &lt; -2SD</td>
<td>4 (7%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

**Figure 1.** Age at menarche survival curve for Qom girls estimated from 61 subjects (n events = 51, n censored subjects = 10). The graph depicts the Kaplan-Meier survival function (black line) with 95% of confidence interval (grey band), and median survival (dashed horizontal and vertical lines).

![Survival curve for Qom girls](image)

**Figure 2 A-C.** SITAR models of age at peak growth velocity, APGV (black dashed line), and peak velocity, PV (solid grey line), for (A) height (APGV = 10.8 years, PV = 9.4 cm/year), (B) weight (APGV = 10.5 years, PV = 8.5 kg/year, and (C) BMI (APGV = 10.7 years). Models were estimated from 1174 and 1171 observations, respectively, for height and weight/BMI from 58 Qom girls ages 8 – 13.