

Early Menopause: Reproductive Adaptation of Javanese Women in Oransbari Distric West Papua

Elda Irma Jeanne Joice Kawulur^{1*}, Eka Dewi Kusumawati¹, Eneng Nunuz Rohmatullayaly², Indah Ratih Anggriyani³

¹Department of Biology, Faculty of Mathematics and Natural Science, Papua University, Manokwari 98314, Indonesia

²Department of Biology, Faculty of Mathematics and Natural Science, Padjadjaran University, Sumedang 45363, Indonesia

³Department of Mathematic, Faculty of Mathematics and Natural Science, Papua University, Manokwari 98314, Indonesia

ARTICLE INFO

Article history:

Received June 18, 2022

Received in revised form October 5, 2022

Accepted November 30, 2022

KEYWORDS:

Early menopause,
Javanese women,
Oransbari,
adaptive response

ABSTRACT

Menopause is the permanent cessation of menstruation due to loss of ovarian follicular activity. Assessment of the age of menopause is particularly important because previous studies have shown a high risk of osteoporosis, hypertension, stroke, and coronary heart disease. This study aims to determine the risk factors for early menopause in Javanese women in Oransbari District, West Papua Province. The cross-sectional sampling method was carried out on women aged 51.73 years with an interval of 40.07-78.58 years. Age at menopause was calculated using the Probit Generalized Linear Model (GLM) analysis. We used a binary logit regression (BLR) model to estimate risk factors for early menopause. BLR analysis was fitted to estimate the odds ratio (OR) and 95% confidence interval (CI). Age at menopause is divided into two categories, normal (≥ 45 years) and early (< 45 years). Our results show that the average age of menopause is 43.1 years, or the early menopause category, with an age range of 39.61 to 55.28 years. The results of the partial parameter significance test at the 10% significance level showed that no formal education (OR: 2.348; CI 1.4213.917) had the most significant risk factor for experiencing early menopause, followed by parity (OR: 0.623; CI: 0.377-1.023), contraception (OR: 0.118; CI: 0.038-0.296), and the lowest risk was the age at first delivery (OR: 0.389; CI: 0.207-0.716). The biocultural conditions experienced early in life in Oransbari shape the character of a younger reproductive age as an adaptive response to maximize fitness.

1. Introduction

Menopause is the permanent cessation of menstruation due to the loss of ovarian follicular activity (Nelson 2008; WHO 1981). The natural menopause phase is characterized by not having a menstrual cycle for 12 months, usually occurring at an average age of 50 years, but varies among ethnic groups (Yang *et al.* 2019; Zhu *et al.* 2019). There are 5% of women who experience early menopause between the ages of 40-45 years, and around 1% of women who experience premature menopause that occurs before the age of 40 years (Luborsky *et al.* 2003; Zhu *et al.* 2019).

Assessment of age at menopause is important because several studies reveal a high risk of morbidity and mortality in women due to fluctuations and

decreases in estrogen and progesterone hormones. Early menopause can cause several osteoporosis-related diseases and cardiovascular diseases such as hypertension, stroke, and coronary heart disease, while late menopause is associated with endometrial and breast cancer (Kirchengast 2017; Nisar *et al.* 2012; Zhu *et al.* 2019). Decreased function of the estrogen also causes physiological and psychological changes that triggered adverse effects on women's life quality which was expressed by a decrease in mental health capacities such as irritability, anger, stress, and depression (Du *et al.* 2020).

In general, genetic and environmental factors may affect the age of menopause. Some of these environmental factors include the residential environment in which the woman lives, marital status, race, age at menarche, parity, smoking, contraception, body mass index, occupation, and education (Arnot and Mace 2019; Gold *et al.* 2001; Ortega-Ceballos *et al.* 2006; WHO 1981; Yang *et al.*

* Corresponding Author

E-mail Address: e.kawulur@unipa.ac.id

2019). Each population has different environmental factors that might influence the age of menopause. For instance, lifestyle and reproduction factors are the significant elements in early menopause (Ortega-Ceballos *et al.* 2006). Meanwhile, unfavorable environmental conditions, like stress and the high physical activity, can accelerate reproduction characters as a profitable strategy in maximize fitness (Bolund 2020; Meczekalski *et al.* 2014; Szedga *et al.* 2017).

The early life of the Javanese transmigration in Oransbari as pioneers in opening residential land that faced severe physical and psychological challenges might have shaped the character of women's reproduction. The population in Oransbari is predominantly Javanese, which has been a transmigration population since 1972. The condition of Oransbari at the time was still covered with forest and no road access, so transmigrants used a boat for one day to get there. Because of limited transportation, they were gone everywhere on foot. They lived as subsistence farmers, and the government provided food aid for several years. However, now they are more dominant as rice and horticultural farmers in the Oransbari traditional market. Men and women work together to manage the fields by preparing the land, planting, tending, and harvesting.

In this study, we tried to assess several factors related to reproductive and socioeconomic status and whether they are associated with the early age of menopause in Oransbari women. Reproductive factors include age of menarche, age of marriage, age during having first birth, parity, and contraception, while socioeconomic factors include occupation, income, and education. Therefore this study aims to determine the age of menopause and the factors that influence the early age at menopause of Javanese women in Oransbari, West Papua Province.

2. Materials and Methods

2.1. Subjects

This research was carried out from December 2020 to July 2021 with a cross-sectional sampling method. Before collecting data, we briefly explained the research's objectives, benefits, and procedures. If they agree, the subject signed a statement of consent (informed consent) to participate in the study data collection through interviews based on questionnaires.

The subject is Javanese who lives in the Oransbari District, South Manokwari, West Papua Province. The ethnic authenticity was confirmed by asking about the mother and father's ethnicity and previous generations (grandmother and father's ethnicity). Data were collected in five of 15 villages in the Oransbari district, which are Sidomulyo, Margorukun, Akeju, Margomulyo, and Sindang Jaya villages. The five villages are dominantly inhabited by Javanese people, while other villages are inhabited by Papuan people or other ethnic. We collected 299 subjects with an average age of 51.73 years old and an interval of 40.07–78.58 years old.

2.2. Age at Reproductive Characters

Determination of age of menopause, age of menarche, and age during having first childbirth/delivery and marriage were based on status quo and recall methods (Malina *et al.* 2014). The definition of menopause, according to WHO (1981), is not having menstruation for 12 months permanently.

2.3. Risk factors of Menopause

The risk factors for age of menopause were contraceptive use, age of menarche, marital status/age at married, age at first childbirth, and parity (number of children). These factors are related to the reproductive status, and other information such as education, occupation, and monthly family income is related to socioeconomic status. All those factors were categorized in Table 1 and 2.

2.4. Data Analysis

The mean age at menopause was calculated using Generalized Linear Model (GLM), while the factors that influencing early menopause were identified

Table 1. Reproductive profile categories of Javanese Women in Oransbari

Reproduction profile	Category
Menopause Status	<45 yo
	≥45 yo
Age at menarche	≤10 yo
	>10 yo
Age at marriage	≥19 yo
	<19 yo
Parity	≥3 child
	<3 child
Age at first delivery	≥20 yo
	<20 yo
Contraception	Yes
	No

Table 2. Socio-demographic Characteristics of Javanese Women in Oransbari

Sociodemography characteristics	Category
Education	Not having a formal education Having formal education
Occupation	Farmer Housewife Others
Family expenditure	≥ UMR West Papua Province < UMR West Papua Prvince

using binary logit regression analysis in the R program (Venables and Ripley 1999). A binary logistic regression model was generated using the logit transformation. The Maximum Likelihood Estimation (MLE) method was used to estimate the parameters in logistic regression. Logit regression was performed to see eight candidate risk factors, including age of menarche, age of marriage, parity, age at first birth, contraception, occupation, income, and education, potentially affecting early menopause. The significance test for each parameter was carried out using the Wald test, with a 69.90% classification accuracy value. The p-values of <0.1 were considered to be statistically significant.

3. Results

The total number of subjects was 299 people, with an age range of 40.07-78.58 years (average = 51.02 years). A total of 38 women used contraception so that they did not experience natural menopause. The results showed that the average age at menopause was 43.1 years (Figure 1), with an age range of 39.61-55.28 years. The percentage of premature menopause was 0.80% (2 individuals); early menopause was 41.69% (106 individuals), while normal menopause was 57.27% (147 individuals). The prevalence of early menopause in Oransbari women was relatively high. The average percentage of early menopause is about 10%.

On average, women in Oransbari have 2-3 children and get married at a younger age (17.8 years). The average age at menarche of Oransbari women was categorized as younger (12.4 years) with a range of 8.96-17.00 years, while the average age of first birth was 21.92 years with a range of 13-35 years. Figure 2 shows the natural history of four reproductive characters, including age at menarche (12.4 years),

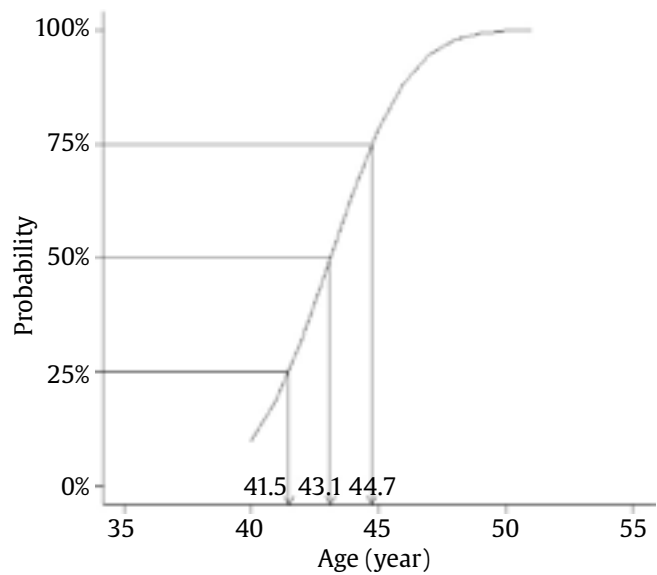


Figure 1. Age at Menopause of Javanese Women

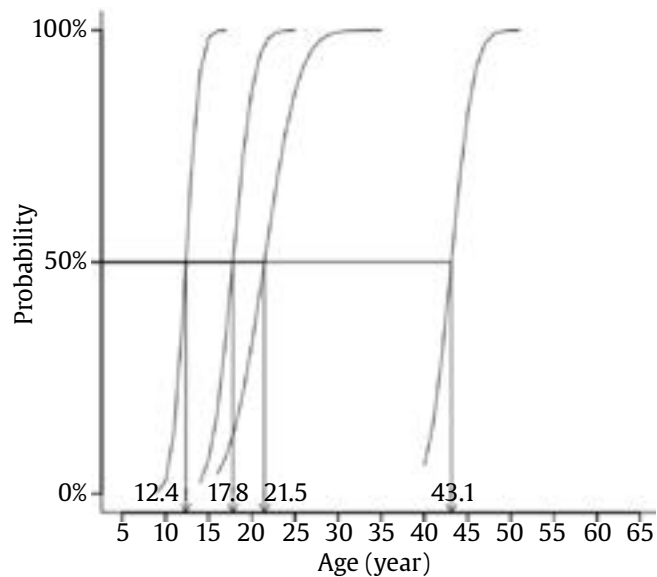


Figure 2. The natural history of four reproductive characters of Javanese Women in Oransbari

age at marriage (17.8 years), age at first birth (21.5 years), and age at menopause (43.1 years).

Most Javanese women in Oransbari had an education level up to senior high school, and the others had no formal education. They work as housewives (69%), farmers (27%), entrepreneurs (4%), and in the government (11%), but previously they were occupied as subsistence farmers. In addition, the majority of the monthly family income was IDR 1,000,000 (Table 2). As subsistence farmers in a new area, they were gone to the fields on foot because there was no transportation, and their monthly

income was only sufficient for daily consumption. Women in Oransbari work as housewives and participate with their husbands to manage the fields. These activities describe the overload of work and limited food intake of Oransbari people in the new area.

In order to estimate the risk factor of early menopause, we used a binary logistic regression model with eight environmental factors. Each factor was categorized and tested for the significance of the variables simultaneously (Table 3), then a partial test using the Wald test. The parameters partially tested resulted in four risk factors that significantly affected the early age at menopause, including not having a

formal education, less parity, using contraception, and age at first birth (Table 4). The best model is obtained by entering only significant variables into the analysis step.

Table 5 shows the association of each factor to early menopause based on the interpretation of the odds ratio (OR). Not having formal education (OR: 2.348; 95% CI 1.421-3.917) had the most significant risk of early menopause, followed by parity (OR: 0.623; 95% CI: 0.377-1.023) and contraception (OR: 0.118; 95% CI: 0.038-0.296). The lowest risk factor was the age at first birth (OR: 0.389; 955 CI: 0.207-0.716). The results showed that socioeconomic and reproductive status are associated with early menopause.

Table 3. Output binary logistic regression model with significant environmental factors (simultaneous test)

Variables	Estimate	SE	z value	p value	Signif. codes:
(Intercept)	1.826	1.308	1.396	0.163	
Not formal education	0.831	0.274	3.036	0.002	**
Occupation: household	-1.173	0.813	-1.442	0.149	
Occupation: farmer	-1.033	0.970	-1.065	0.287	
Parity	-0.508	0.262	-1.936	0.053	*
Income (based UMR)	-0.297	1.130	-0.263	0.793	
Expenditure	0.090	1.161	0.078	0.938	
Late age at menarche	-2.025	1.429	-1.417	0.156	
Nomal age at menarche	0.116	0.841	0.138	0.890	
Contraception	-2.194	0.526	-4.170	0.000	***
Age at married	-0.279	0.295	-0.948	0.343	
Age at first birth	-1.193	0.353	-3.379	0.001	***
Income (based poverty indicator)	-0.387	0.497	-0.778	0.436	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Table 4. Output binary logistic regression model with significant variables (partial test)

Variables	Estimate	SE	Wald	p value	Signif. codes:
(Intercept)	0.386	0.227	1.702	0.089	.
No having formal education	0.853	0.258	3.305	0.001	***
Parity	-0.474	0.254	-1.862	0.063	*
Contraception	-2.134	0.509	-4.195	0.000	***
Age at first birth	-0.945	0.316	-2.994	0.003	**

Table 5. Odd ratio and Confidence Interval (95%) of significant variables

Variables	Coef	Odds.ratio	95% CI
(Intercept)	0.385	1.470	0.947-2.306
No education	0.853	2.348	1.421-3.917
Parity	-0.474	0.623	0.377-1.023
Contraception	-2.134	0.118	0.039-0.296
Age at first birth	-0.945	0.389	0.207-0.716

4. Discussion

Several reproductive characters of Javanese women in Oransbari showed acceleration when facing environmental pressure as an adaptive response. Socioeconomic and reproductive traits had a significant association with early reproductive aging.

The average percentage of early menopause, about 10% (Pelosi *et al.* 2015), varied. In some countries, such as Australia, Scandinavia, America, and Japan 4-7% based on studies by Mishra *et al.* (2017) and Zhu *et al.* (2019); in Japan, 1.67% (Yasui *et al.* 2012), and America 3.56% (Sezdga *et al.* 2017) showed less than 10% of early menopause.

The age of menopause for Javanese women in Oransbari (43.1 years old) was almost the same as the Agta population, a forager population in Luzon, the Philippines (43.93 years old). The Agta population lives in ecological conditions where women also participated in foraging for food (hunting, gathering, fishing, and slash and burn cultivation) which involved high levels of physical activity (Goodman *et al.* 1985).

Our results showed four factors that influenced early menopause: no formal education, less parity, contraception, and age at first birth. Not having a formal education was related to low socioeconomic status, while the other factors were related to reproductive status. These findings showed that socioeconomic and reproductive factors were significant elements in the occurrence of early menopause in Javanese women in Oransbari. The effect of low socioeconomic and reproductive status on early menopause was also reported by Pelosi *et al.* (2015); Schoenaker *et al.* (2014); Ortega-Ceballos *et al.* (2006); Zhu *et al.* (2019); while several studies revealed that parity had a significant effect (Harlow and Signorello 2000; Pelosi *et al.* 2015; Sinha *et al.* 2020).

Besides the two factors that affected the early menopause of Javanese women in Oransbari, we also assumed that physical activity might be another significant factor in early menopause. Limited transportation caused most people to go everywhere on foot, including going to the fields. The excessive workload was also experienced by women in Oransbari who worked as housewives while helping their husbands to manage the fields. Therefore, we predicted that the high physical

activity of Oransbari women could affect their reproductive physiology. High physical activity could interfere with hormone function disruption, which had implications for early menopause (Gold *et al.* 2001; Meczekalski *et al.* 2014).

The high percentage of early menopause in Oransbari's women might be related to environmental pressures that interfere with hormone function, as Meczekalski *et al.* (2014). Low body weight, chronic stress, and high physical activity could affect the work function of the hypothalamus and the pituitary glands that produced the reproductive hormones (Sezdga *et al.* 2017).

As pioneer transmigration communities in Oransbari since 1972, they opened forest areas as residential areas, with limited factors such as food, health, and transportation. These described the challenges which could cause chronic stress. There was an association between stress and early menopause related to hormone disruption. Mental stress could disrupt the regulation of the hypothalamus, pituitary, and gonadotropin hormones, so it might cause anovulation, hypoestrogenism, and increased the risk of infertility. Activation of the hypothalamus and pituitary gland led to increase in secretion of corticotropin-releasing hormone (CRH). The CRH further increased the secretion of adrenocorticotropic hormone from the pituitary gland and cortisol from the adrenal gland, and this phenomenon reduced GnRH. Increased levels of cortisol stress hormones also increased the risk of early menopause (Meczekalski *et al.* 2014; Rivier *et al.* 1986; Sezdga *et al.* 2017).

The tremendous challenges that Oransbari women faced in a new isolated environment require an energy investment allocated to grow, reproduce, and survive, while the energy budget was limited. The life history trade-off theory explained that when facing challenges in an unfavorable environment, more energy was allocated to the most profitable traits to maximize fitness (Walker *et al.* 2006). The most prominent life history trade-off involves the cost of reproduction (Bolund 2020; Stearns 1989). In the case of Javanese women in Oransbari, their reproductive strategies, which were younger age at menarche and marriage, might be the most beneficial characteristics to maximize fitness in early life in Oransbari. Both of these younger ages

led to reproductive aging that was accelerated age at menopause in late life. This finding supported the early and late-life trade-off theory, which explained that physiological processes that increase biosynthesis was required for growth and reproduction in early life fitness, which could have adverse effects on late-life fitness or accelerate senescence (Lemaitre *et al.* 2015; Hayward *et al.* 2015; Maklakov and Chapman 2019; Bolund 2020).

Kawulur *et al.* (2012, 2013) also found life history strategies related to a faster growth rate of body weight at the child to juvenile phase and an earlier age at menarche of Arfak girls in Manokwari, West Papua. Walker *et al.* (2006) stated that juvenile mortality was related to faster child-juvenile growth rates, earlier sexual maturation, and age at first reproduction. It means that mortality was the ecological challenge to drive a fast life history strategy (Migliano *et al.* 2007), which Arfak girls and Oransbari women might experience.

Based on our findings, the average age at menarche (12.2 years) was approximately three decades ago, relatively earlier than those girls from rural Maybrat (13.1 years), rural Padaido (13.2 years), or the same with urban Manokwari (12.0 years) (Baransano *et al.* 2015, Rumayauw 2019; Siahaan *et al.* 2017). Thus, we could argue that Javanese women in Oransbari had a younger age at menarche than other populations in Papua. The association between early menarche and early menopause was still contradictory. However, Chang *et al.* (2007) found a significant association between both, while Sinha *et al.* (2020) stated that age at menarche indirectly affects the natural age at menopause.

We concluded that the early menopause of Javanese women in Oransbari West Papua was an adaptive response to environmental challenges as a pioneer transmigration community. In facing environmental challenges, energy was allocated to the beneficial characteristics of younger age at menarche, marriage, and menopause. Biocultural conditions experienced at the beginning of life in Oransbari shaped a younger age of reproductive character as an adaptive response to maximize fitness. These results were consistent with the previous studies that early reproduction accelerates senescence in late life.

References

- Arnot, M., Mace R., 2019. Sexual frequency is associated with age of natural menopause: result from the study of women's health across the nation. *R. Soc. Open.Sci.* 7, 1-10. <https://doi.org/10.1098/rsos.191020>
- Baransano, L., Kawulur E.I.J., Sinuraya S., 2015. Pertumbuhan fisik dan kejadian menarke anak perempuan maybrat. In: *Prosiding Seminar Nasional Biologi Perhimpunan Biologi Indonesia*. Jayapura: Uncen Press. pp 72-79.
- Bolund, E., 2020. The challenge of measuring trade-offs in human life history research. *Evolution and Human Behavior.* 41, 502-512. <https://doi.org/10.1016/j.evolhumbehav.2020.09.003>
- Chang, S.H., Kimb, C., Lee, K., Kima, H., Yimc, S.V., Limd, Y.J., Park, S.Y., 2007. Premenopausal factors influencing premature ovarian failure and early menopause. *Maturitas.* 58, 19-30. <https://doi.org/10.1016/j.maturitas.2007.04.001>
- Du, L., Xu, B., Huang, C., Zhu, L., He, N., 2020. Menopausal symptoms and perimenopausal healthcare-seeking behavior in women aged 40-60 years: a community-based cross-sectional survey in Shanghai, China. *International Journal of Environmental Research and Public Health.* 17, 8-10. <https://doi.org/10.3390/ijerph17082640>
- Gold, E.B., Bromberger, J., Crawford, S., Samuels, S., Greendale, G.A., Harlow, S.D., Skurnick, J., 2001. Factors associated with age at natural menopause in a multiethnic sample of midlife women. *American Journal of Epidemiology.* 153, 865-874. <https://doi.org/10.1093/aje/k1153>
- Goodman, M., Estioko, A.G., Bion, P.G., Grove, J.S., 1985. Menarche, pregnancy, birth spacing and menopause among the agta women foragers of Cagayan Province, Luzon, the Philippines. *Annals of Human Biology.* 12, 169-177. <https://doi.org/10.1080/03014468500007661>
- Harlow, B.L., Signorello, L.B., 2000. Factors associated with early menopause. *Maturitas.* 35, 6-9. [https://doi.org/10.1016/S0378-5122\(00\)00092-X](https://doi.org/10.1016/S0378-5122(00)00092-X)
- Hayward, A.d., Nenko, I., Lummaa, V., 2015. Early-life reproduction is associated with increased mortality risk but enhanced lifetime fitness in pre-industrial humans. *Proc. R. Soc. B.* 282, 20143053. <https://doi.org/10.1098/rspb.2014.3053>
- Kawulur, E.I.J., Suryobroto, B., Budiarti, S., Hartana, A., 2012. Association of sexual maturation and body size of arfak children. *Hayati Journal Bioscience.* 19, 124-130. <https://doi.org/10.4308/hjb.19.3.124>
- Kawulur, E.I.J., Suryobroto, B., Budiarti, S., Hartana, A., 2013. Pola pertumbuhan fisik pada anak-anak suku Arfak Papua Barat. *Makara Seri Kesehatan.* 17, 41-48. <https://doi.org/10.7454/msk.v17i1.2144>
- Kirchengast, S., 2017. Menopause female reproductive senescence from the viewpoint of evolutionary anthropology, in: Rodriguez-Landa, J.F., Jonathan, Cueto-Escobedo, J. (Eds.), *A Multidisciplinary Look at Menopause*. London: InTechOpen. pp. 7-23. <https://doi.org/10.5772/intechopen.68682>
- Lemaitre, J., Berger, V., Bonenfant, C., Douhard, M., Gamelon, M., Plard, F., Gaillard J., 2015. Early-late life trade-offs and the evolution of ageing in the wild. *Proc. R. Soc. B.* 282, 20150209. <https://doi.org/10.1098/rspb.2015.0209>
- Luborsky, J.L., Meyer, P., Sowers, M.F., Gold, E.B., Santoro, N., 2003. Premature menopause in a multi-ethnic population study of the menopause transition. *Human Reproduction.* 18, 199-206. <https://doi.org/10.1093/humrep/deg005>

- Malina, R.M., Bouchard, C.B., Oder, B., 2004. *Growth, Maturation, and Physical Activity*, second ed. Human Kinetics, United States.
- Maklakov, A.A., Chapman, T., 2019. Evolution of ageing as a tangle of trade-offs: energy versus function. *Proc. R. Soc. B.* 286, 20191604. <https://doi.org/10.1098/rspb.2019.1604>
- Meczekalski, B., Katulski, K., Czyzyk, A., Podfigurna-Stopa, A., Maciejewska-Jeske, M. 2014. Functional hypothalamic amenorrhea and its influence on women's health. *J Endocrinol Invest.* 37, 1049-1056. <https://doi.org/10.1007/s40618-014-0169-3>
- Migliano, M.B., Vinicius, L., Lahr, M.M., 2007. Life history trade-offs explain the evolution of human pygmies. *PNAS.* 104, 20216-20219. <https://doi.org/10.1073/pnas.0708024105>
- Mishra, G.D., Pandeya, P., Dobson, A.J., Chung, H., Anderson, D., Kuh, D., Sandin S., Giles, G.G., Bruinsma, F., Hayashi K., Lee, J.S., Mizunuma, H., Cade, J.E., Burley, V., Greenwood, D.C., Goodman, A., Simonsen, M.K., Adami, H., Demakakos, P., Weiderpass, E., 2017. Early menarche, nulliparity and the risk for premature and early natural menopause. *Human Reproduction.* 32, 679-686. <https://doi.org/10.1093/humrep/dew350>
- Nelson, H.D., 2008. Menopause. *Journal Lancet.* 371, 760-770. [https://doi.org/10.1016/S0140-6736\(08\)60346-3](https://doi.org/10.1016/S0140-6736(08)60346-3)
- Nisar, N., Sohoo, N.A., Sikandar, R., 2012. Age and symptoms at natural menopause: a cross-sectional survey of rural women in Sindh Pakistan. *J. Ayub. Med. Coll. Abbottabad.* 24, 90-94.
- Ortega-Ceballos, PA., Morán, C., Blanco-Muñoz, J., Yunes-Díaz, E., Castañeda-Iñiguez, MS., Salmerón, J., 2006. Reproductive and lifestyle factors associated with early menopause in Mexican women. *Salud Pública de México.* 48, 300-307. <https://doi.org/10.1590/S0036-36342006000400004>
- Pelosi, E., Simonsick, E., Forabosco, A., Garcia-Ortiz, J.E., Schlessinger, D., 2015. Dynamics of the ovarian reserve and impact of genetic and epidemiological factors on age of menopause. *Biology of Reproduction.* 92, 1-9. <https://doi.org/10.1095/biolreprod.114.127381>
- Rivier, C., Rivier, J., Vale, W., 1986. Stress-induced inhibition of reproductive functions: role of endogenous corticotropin-releasing factor. *Science.* 23, 607-609. <https://doi.org/10.1126/science.3003907>
- Rumayauw, I.B., Kawulur, E.I.J.J., Ratnawati, S., 2019. Dimensi Tubuh dan Kematangan Seksual Pada Anak Suku Biak di Daerah Kepulauan Padaido Kabupaten Biak [Skripsi]. Manokwari, Indonesia: Univesitas Papua.
- Schoenaker, D.A.J.M., Jackson, C.A., Rowlands, J.V., Mishra, G.D., 2014. Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and meta-analyses of studies across six continents. *International Journal of Epidemiology.* 43, 1542-1562. <https://doi.org/10.1093/ije/dyu094>
- Siahaan, A., Kawulur, E.I.J.J., Maker, U., 2017. Usia menarke remaja putri di daerah perkotaan Manokwari Papua Barat. In: *Prosiding Seminar Nasional MIPA UNIPA, Manokwari.* Jakarta: Sinar Grafika. pp. 235-248.
- Sinha, I., Tigga, P., Mondal, N., Jaydip, S., 2020. Association between age at menarche and age at menopause among women of an indigenous population of North Bengal, India. *Journal of Biosocial Science.* 53, 319-335. <https://doi.org/10.1017/S002193202000019X>
- Stearns, S.C., 1989. Trade-offs in life-history evolution. *Functional Ecology.* 3, 259-268. <https://doi.org/10.2307/2389364>
- Szegda, K.L., Whitcomb, B.W., Boutot, M.E., Purdue-Smithe, A.C., Bertone-Johnson, E.R., Manson, J.E., Hankinson, S.E., Rosner, B.A., 2017. Adult adiposity and risk of early Menopause. *Human Reproduction.* 32, 2522-2531. <https://doi.org/10.1093/humrep/dex304>
- Venables, W.N., Ripley, B.D., 1999. *Modern Applied Statistic with SPlus.* Springer Inc, New York.
- Walker, R., Gurven, Hill, K., Migliano, A., Chagnon, N., Souza, N., Djurovic, G., Hames, R., Hurtado, A.M., Kaplan, H., Kramer, K., Oliver, W.J., Valeggia, C., Yamauchi, T., 2006. Growth rates and life histories in twenty two small scale societies. *Am. J. Hum. Biol.* 18, 295-311. <http://doi.org/10.1002/ajhb.20510>
- [WHO] World Health Organization, 1981. *Research on the Menopause.* World Health Organization, Geneva.
- Yang, Y., Arnot, M., Mace, R., 2019. Current ecology, not ancestral dispersal patterns, influences menopause symptom severity. *Ecology and Evolution.* 12503-125014. <https://doi.org/10.1002/ece3.5705>
- Yasui, T., Hayashi, K., Mizunuma, H., Kubota, T., Aso, T., Matsumura, Y., Lee, J., Suzuki, S., 2012. Factors associated with premature onset ovarian failure, early menopause and earlier of menopause in Japanese women. *Maturitas.* 72, 249-255. <http://doi.org/10.1016/j.maturitas.2012.04.002>
- Zhu, D., Chung, H. F., Dobson, A. J., Pandeya, N., Giles, G. G., Bruinsma, F., Brunner, E. J., Kuh, D., Hardy, R., Avis, N. E., Gold, E. B., Derby, C. A., Matthews, K. A., Cade, J. E., Greenwood, D. C., Demakakos, P., Brown, D. E., Sievert, L. L., Anderson, D., Hayashi, K., Lee, J. S., Mizunuma, H., Tillin, T., Simonsen, M. K., Adami, H. O., Weiderpass, E., Mishra G. D. 2019. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. *Journal Lancet Public Health.* 4, 555-563. [https://doi.org/10.1016/S2468-2667\(19\)30155-0](https://doi.org/10.1016/S2468-2667(19)30155-0)