

4. Banerjee S, Couturier P, Steenkeste F et al. Measuring nocturnal activity in Alzheimer's disease patients in a 'smart' hospital room. *Gerontechnology* 2004;3:29–35.
5. Motohashi Y, Maeda A, Wakamatsu H et al. Circadian rhythm abnormalities of wrist activity of institutionalized dependent elderly persons with dementia. *J Gerontol A Biol Sci Med Sci* 2000;55A:M740–M743.

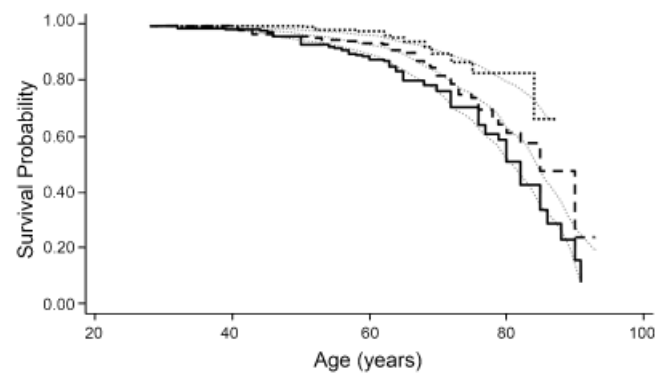
SURVIVAL AND MORTALITY IN OLDER ADULTS LIVING AT HIGH ALTITUDE IN BOLIVIA: A PRELIMINARY REPORT

To the Editor: Approximately 400 million people live permanently at altitudes above 1,500 m.¹ High-altitude communities reportedly have higher prevalence of Parkinson's disease,² migraine,³ chronic obstructive pulmonary disease,⁴ and chronic mountain sickness,⁵ which may affect survival and mortality, although epidemiological evidence is lacking. To address this limitation of the literature, data relating to age at death and causes of death were obtained for grandparents of participants in the Bolivian Children Living at Altitude (BoCLA) Study.⁶

Information regarding the grandparents of 280 children participating in BoCLA was requested from parents, including whether grandparents were alive or dead, current age or age at death, municipality of residence, major health concerns, and cause of death. Families recruited to BoCLA were selected from mid to high socioeconomic strata to limit the effect of cultural diversity and to prevent bias from differences in nutrition and education. For this retrospective report on children's grandparents, the altitude of current or last municipality of residence was coded as low (LA; 0–1,499 m), moderate (MA; 1,500–2,999 m), or high (HA; $\geq 3,000$ m) altitude. Lifetime data on age at survey for living participants and life duration for participants who had died were obtained. Sex, frequent diseases, family income, housing standards, and access to medical care described by BoCLA participant families were used as predictors in subsequent multivariate regression models. Distributions of these variables are frequently different between altitude populations in Bolivia.⁷

The sample consisted of 555 distinct grandparents (mean age \pm standard deviation 64.4 ± 11.0 ; 54% women) distributed across LA (alive/dead $n = 143/12$), MA ($n = 138/36$), and HA ($n = 161/65$) categories. Income level, housing standards, and medical care access, estimated from that of the son or daughter (BoCLA parents), were comparable across altitude locations (Wilcoxon, Mann-Whitney tests, $P > .05$). Hypertension and diabetes mellitus were the only prevalent diseases, but two- and three-way nonparametric comparisons across altitude groups were not significant ($P > .05$). The most frequently reported causes of death involved cardiovascular system disease or complications (including myocardial infarction and stroke), cancer, and respiratory disease (including pneumonia). Cardiovascular system disease or complications as cause of death were less common at HA and MA than LA (Kruskal-Wallis, $P < .001$).

Presentation at a meeting: Virues-Ortega J, Hogan AM, Baya-Botti A, Kirkham FJ, Baldeweg T, & Bucks R (August 2007). Survival rates and causes of death in older adults living at high altitude in Bolivia: A preliminary study. Poster presented at the Annual Meeting of the British Association of Cognitive Neuroscience. Dundee, Scotland.



	HR*	SE*	95% CI*	P value
Altitude of residence				
..... (Low altitude 0-1,499 m)*				
- - - Mid altitude 1,500-2,999 m	1.98	0.664	1.03, 3.83	0.040
— High altitude $\geq 3,000$ m	2.92	0.922	1.58, 5.43	0.001

Figure 1. Survival curves for older residents living at low, moderate, and high altitude in Bolivia. Dashed-dotted lines represent predicted survival according to univariate Cox regression. *Reference category in parenthesis. Proportional hazards chi-square (χ^2) (2) = 1.63, $P = .44$. Sex, access to medical care, self-reported income, basic housing standards (electricity, piped water, flush toilet, nondirt floor), and offspring-reported diagnosis of hypertension and diabetes mellitus did not improve goodness of fit when entered one by one into the model (likelihood ratio χ^2 , $P > .10$). HR = hazard ratio; SE = standard error; CI = confidence interval.

Cumulative survival functions were estimated using the Kaplan-Meier method to compare explanatory factors. Altitude of residence was the only significant predictor (Figure 1). Lower survival is apparent throughout a wide age range, with a several-fold difference between LA and HA. Survival proportions varied significantly across altitude groups, from 91% at LA to 60% at HA (log rank test, chi-square (χ^2) = 13.92, $P < .001$; Wilcoxon test, $\chi^2 = 13.44$, $P < .001$). Two-way comparisons showed that survival was lower in the MA and HA samples than LA (log rank test, $\chi^2 = 4.01$, $P = .05$; Wilcoxon test, $\chi^2 = 4.38$, $P < .05$; $\chi^2 = 13.27$, $P < .001$; $\chi^2 = 12.83$, $P < .001$, respectively). There was no difference between MA and HA samples ($P > .05$). The log rank test was nonsignificant for all other predictors. Independent univariate Cox regression analyses showed no prognostic value for sex, self-reported income, housing standards, access to medical care, or prevalent diseases, including hypertension and diabetes mellitus ($P > .5$). The final Cox regression model included altitude of residence as the only predictor (see predicted curves, Figure 1).

This study shows that, in older adults, life span is shorter over 1,500 m, indicating that high-altitude living may be detrimental to health despite the otherwise expected protection offered by physiological adaptations to chronic hypoxia. Comparable with earlier reports of greater prevalence of common ischemic and coronary conditions at high altitude,^{8,9} the data from the current study show greater frequency of cardiovascular system disease and complications in the living but less likelihood of this being described as cause of death. This requires more-detailed investigation

in larger prospective epidemiological studies. Overall, the data suggest greater all-cause mortality at higher altitudes.

The retrospective design of this study, its reliance on offspring report rather than medical record, and a lack of control for potential confounders such as genetic admixture and diet are significant limitations and mean that the results must be interpreted cautiously, but this preliminary report, using opportunistic data obtained as part of the BoCLA study, suggests that a combination of environmental and physiological stressors, present across the life span, may account for shorter survival at high altitude. This may provide the impetus for further research to determine the nature of these stressors and the mechanisms by which they reduce lifespan in those living at high altitude and perhaps also in those living at the sea level with diseases causing pathological chronic hypoxia at sea level.

*Javier Virues-Ortega, PhD
Centro de Investigaciones Biomédica en Red sobre
Enfermedades Neurodegenerativas (CIBERNED)*

*Alexandra M. Hogan, PhD
Developmental Cognitive Neuroscience Unit
Institute of Child Health
University College London
London, United Kingdom*

*Ana Baya-Botti, MS
Prince Leopold Institute of Tropical Medicine
Antwerp, Belgium*

*Fenella J. Kirkham, MD, PhD
Neuroscience Department
Institute of Child Health
University College London
London, United Kingdom*

*Torsten Baldeweg, MD
Developmental Cognitive Neuroscience Unit
Institute of Child Health
University College London
London, United Kingdom*

*Ignacio Mahillo-Fernandez, MS
Jesus de Pedro-Cuesta, MD, PhD
Carlos III Institute of Health
National Center of Epidemiology
CIBERNED
Madrid, Spain*

*Romola S. Bucks, PhD
School of Psychology
University of Western Australia
Crawley, Australia*

*On behalf of the Bolivian Children Living at Altitude
Project (BoCLA 2006)*

ACKNOWLEDGMENTS

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has

determined that the authors have no financial or any other kind of personal conflicts with this letter.

BoCLA 06 was supported by grants from the Gerald Kerkut Charitable Trust and the British Academy, to Dr. Alexandra M. Hogan. Funding to Dr. Javier Virues was also obtained from CIBERNED.

Author Contributions: Javier Virues-Ortega: study design, data collection and analysis, writing the first draft, coordination of all co-authors. Alexandra M. Hogan: Principal Investigator of BoCLA 06 project, study design, assistance with writing the introduction and discussion sections. Ana Baya-Botti: leader of the study in Bolivia during data collection, helped write introduction and discussion sections. Fenella J. Kirkham: medical consultant of the study, helped design the study, analyzed medical data (particularly causes of death and health conditions), wrote significant sections of the discussion. Torsten Baldeweg: medical consultant, helped during the data collection and proofed the manuscript. Ignacio Mahillo-Fernandez: statistician of the study, designed and conducted most of the analysis (Cox model, survival analysis). Jesus de Pedro-Cuesta: epidemiological consultant, helped design the study and wrote significant sections throughout the manuscript. Romola S. Bucks: data manager and statistician for BoCLA, and jointly with Javier Virues-Ortega, took the lead in analyzing and interpreting grandparent data, for this ancillary study of BoCLA.

Sponsor's Role: The sponsor had no direct role in the design, methods, subject recruitment, data collections, analysis and preparation of the letter. The role of the sponsor was confined to accepting the initial project and obtaining regular reports on the progress of the study.

REFERENCES

1. Cohen JE, Small C. Hypsographic demography: The distribution of human population by altitude. *Proc Natl Acad Sci U S A* 1998;95:14009–14014.
2. Cuba JM, Corbera JC, Cosentino C. Neuroepidemiologic Approach on Parkinson's Disease, Huntington's Disease and Epilepsy at High Altitude. National Congress of Altitude Medicine. Lima, Peru: Medical Board Chulee Hospital at La Oroya, 1992.
3. Leon-Velarde F, Arregui A. Adaptación a la vida en altura. Lima, Peru: EFEEA/UPCH, 1994.
4. Cote TR, Stroup DF, Dwyer DM et al. Chronic obstructive pulmonary disease mortality: A role for altitude. *Chest* 1993;103:1194–1197.
5. Monge C, Arregui A, Leon-Velarde F. Pathophysiology and epidemiology of chronic mountain sickness. *Int J Sports Med* 1992;13(Suppl 1):S79–S81.
6. Hogan AM, Virues-Ortega J, Baya-Botti A et al. Development of aptitude at altitude. *Dev Sci* in press.
7. Urquiola M, Andersen L, Antelo E et al. Geography and Development in Bolivia. Inter-American Development Bank Research Network [on-line]. Available at <http://www.iadb.org/res/publications/pubfiles/pubR-385.pdf> Accessed March 1, 2009.
8. Al-Tahan A, Buchur J, el Kwsy F et al. Risk factors of stroke at high and low altitude areas in Saudi Arabia. *Arch Med Res* 1998;29:173–177.
9. Al-Huthi MA, Raja'a YA, Al-Noami M et al. Prevalence of coronary risk factors, clinical presentation, and complications in acute coronary syndrome patients living at high vs low altitudes in Yemen. *Med Gen Med* 2006;8:28.

DELIRIUM IN NURSING HOME RESIDENTS ACROSS CARE TRANSITIONS: A PRELIMINARY REPORT

To the Editor: Delirium affects patients in many settings,^{1–3} leading to adverse outcomes. Nursing home (NH) patients are three times more likely to present to an emergency department (ED) with delirium than community-dwelling