presents maps of IRRs for each of the methods used. According to our findings, there was no difference between ZIP and ZINB models, indicating that both ZIP and ZINB have the same prediction and they are successful with the AIC and BIC results, and ZIP was more suitable than the ZINB model to handle the over-dispersion of the bone tumours data. While PH and NBH models suggest there were some provinces which disagree with the results obtained from ZIP and ZINB models, because these two models unsuccessfully with the AIC and BIC results. According to ZIP results, Al-Muthanna and Al-Diwaniyah had a higher incidence rate than the other provinces (Figure 5A); compared to Al-Basrah Province, their incidence was

Table 4. Model selection criteria for childhood bone tumour data of the fitted models for childhood bone tumour data.

Model	AIC (smaller is better)	BIC (smaller is better)	Log-likelihood
ZIP	1381	1467	1337
ZINB	1383	1472	1337
PH	1390	1553	1306
NBH	1394	1557	1310

AIC, Akaike information criterion; BIC, Bayesian information criteria; ZIP, zero-inflated Poisson; ZINB, zero-inflated negative binomial; PH, Poisson hurdle; NBH, negative binomial hurdle.

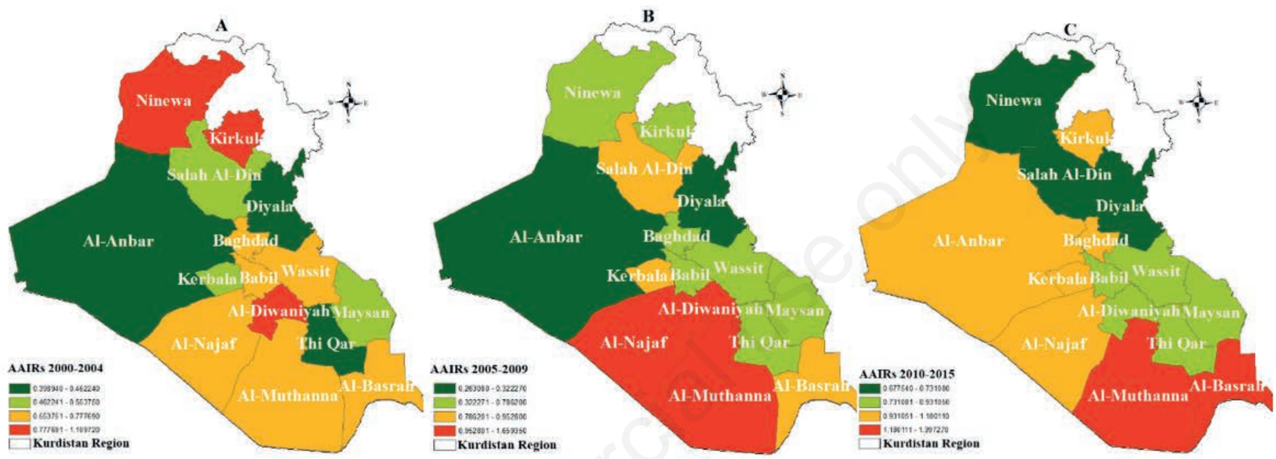

Figure 1. Variation of the geographical distribution of childhood bone cancer incidence between 2000 and 2015. The age-adjusted incidence rate (AAIR) for A) for 2000-2004; B) for 2005-2009; and C) for 2010-2015.

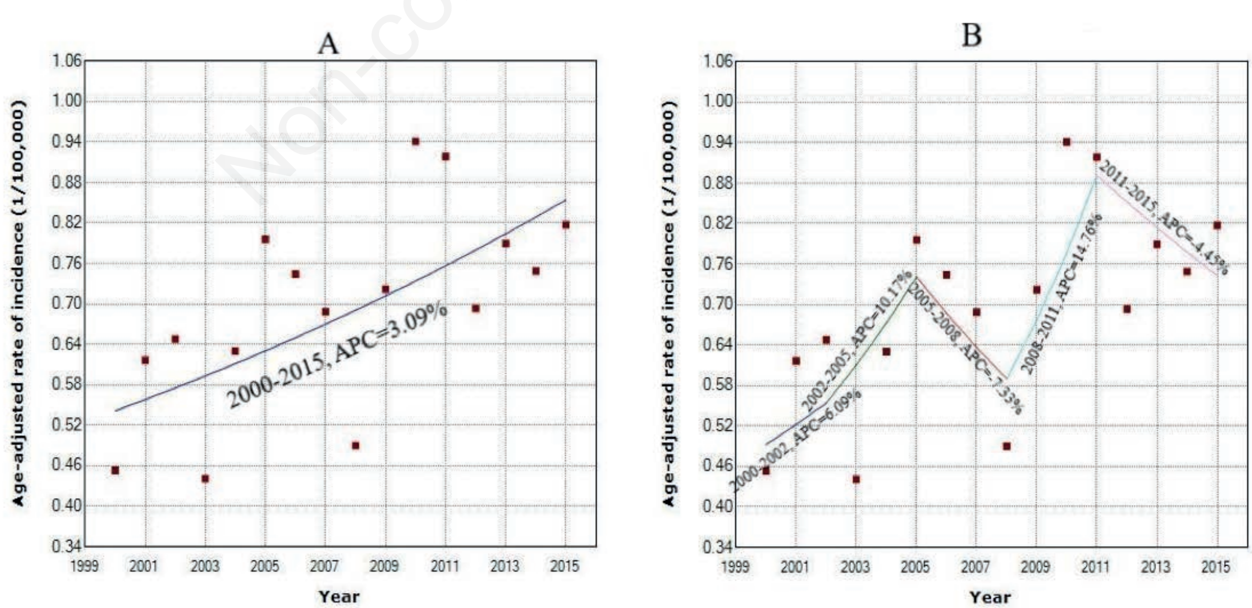

Figure 2. Join point analysis of the age-adjusted incidence rate of childhood bone cancer in Iraq between 2000 and 2015. A) The general temporal trend of the average percentage change (APC) of the age-adjusted incidence rates over the whole period; B) The short-term trend changes in five sub-divisions of the time.

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higher, although it was statistically insignificant by 1.7% (IRR=1.0168, 95% CI: 0.8121, 1.4311) and 2.0% (IRR=1.0204, 95% CI: 0.8184, 1.4510), respectively. The incidence rate was lower among the remaining provinces; the lowest one being Diyala, situated in the East, at 51.7% (IRR=0.4829, 95% CI: 0.2934, 0.7952); AL-Anbar, 40.8% (IRR=0.5917, 95% CI: 0.3691, 0.7842) in the West; Thi-Qar, 36.9% (IRR=0.63610, 95% CI: 0.4846, 0.8903) in the South; Babil, 32.76% (IRR=0.6724, 95% CI: 0.4794, 0.8242) in central Iraq and Ninewa 31.5% (IRR=0.6852, 95% CI: 0.4214, 0.8976) in the North (Table 5 and Figure 5A).

Discussion

This is the first study of bone tumours in 0-19 years old in Iraq, with incidence distributed into age groups, year-periods and gender across fifteen provincial areas, covering the entirety of the country with the exception of three Kurdish province, for which data were not available. Four models were applied to analyse the data over a 15-year period. The data showed over-dispersion with excessive zeros where the ZIP performed better than the other regression models because it handled the extra zeroes and the over-dispersion in a superior way.

The situation in Iraq was similar with respect to the worldwide data on osteosarcoma and Ewing's sarcoma, but Ewing's sarcoma

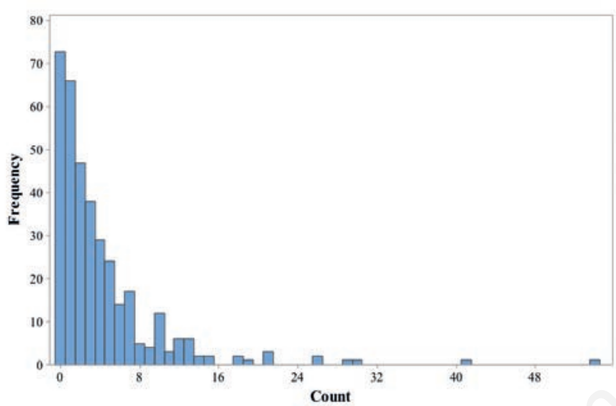

Figure 3. Bone tumour frequency counts from 2000 to 2015.

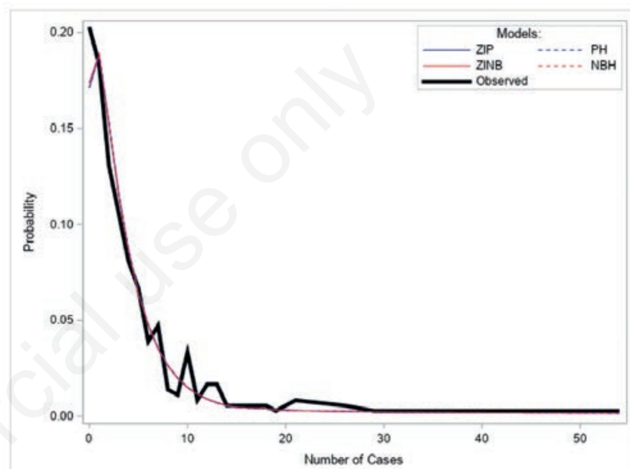

Figure 4. Average predicted count probability.

Table 5. Parameter estimates of the zero-inflated Poisson model fitted to childhood bone tumour data.

Variable	Level	IRR	P-value	95% CI	
Age group	5-9	2.3438	<0.0001	1.5830	2.9441
	10-14	5.9008	<0.0001	4.0213	6.9092
	15-19	8.2292	<0.0001	6.4094	9.7651
Gender	Male	1.4912	<0.0001	1.1880	3.0073
Time-period	2005-2009	1.2286	0.0055	0.9603	1.4244
	2010-2015	1.4967	<0.0001	1.1690	1.8656
Province	Baghdad	0.7792	0.0104	0.6296	0.8911
	Ninewa	0.6852	0.0013	0.4214	0.8976
	Maysan	0.6935	0.0355	0.4903	0.8275
	Al-Diwaniyah	1.0204	0.8862	0.8184	1.4510
	Diyala	0.4829	<0.0001	0.2934	0.7952
	Al-Anbar	0.5917	0.0004	0.3691	0.7842
	Babil	0.6724	0.0038	0.47941	0.8242
	Kerbala	0.793422	0.1505	0.6803	0.9092
	Kirkuk	0.925584	0.6075	0.6474	1.0102
	Wassit	0.689285	0.0184	0.4923	0.8099
	Thi-Qar	0.636100	0.0010	0.4846	0.8903
	Al-Muthanna	1.01679	0.9206	0.8121	1.4311
	Salah Al-Din	0.701173	0.0184	0.5232	0.8930
	Al-Najaf	0.974715	0.8552	0.6742	1.0188

IRR, incidence rate ratio; CI, confidence interval.

in Iraq was found to be most common in the 10-14 age group. In accordance with studies carried out in Africa (Mohammed *et al*., 2010; Ghert *et al*., 2019), USA (Mirabello *et al*., 2009) and Europe (Stiller *et al*., 2006), it was noted that bone tumours in childhood and adolescence were more frequent in males than females. Our results that bone tumour incidence peaks in the 15-19 years olds are also similar to findings by others (Katchy *et al*., 2005; Rhutso *et al*., 2013; Wilhelm *et al*., 2014; Ramdass *et al*., 2015; Pruksakorn *et al*., 2016). The incidence rates had a fluctuating pattern, generally showing an increasing annual trend, with peaks in 2010 and relatively small peak in 2011.

The distribution of the incidence of bone tumours in children and adolescents is different among the provinces in Iraq. However, very little is known about the aetiology of bone tumours in children; there are few papers that have implicated a role of environment. A Spanish study (García-Pérez *et al*., 2017) have suggested a probable risk of bone tumours in children living near metal processing plants, cement and combustion plants, waste management, energy generating sector and plantations using pesticides. Eyre *et al*. (2009) and Ottaviani and Jaffe (2009) have put forward the possible role of genetic/environment interaction. These reports support the idea of agricultural, industrial and conflict-related contam-

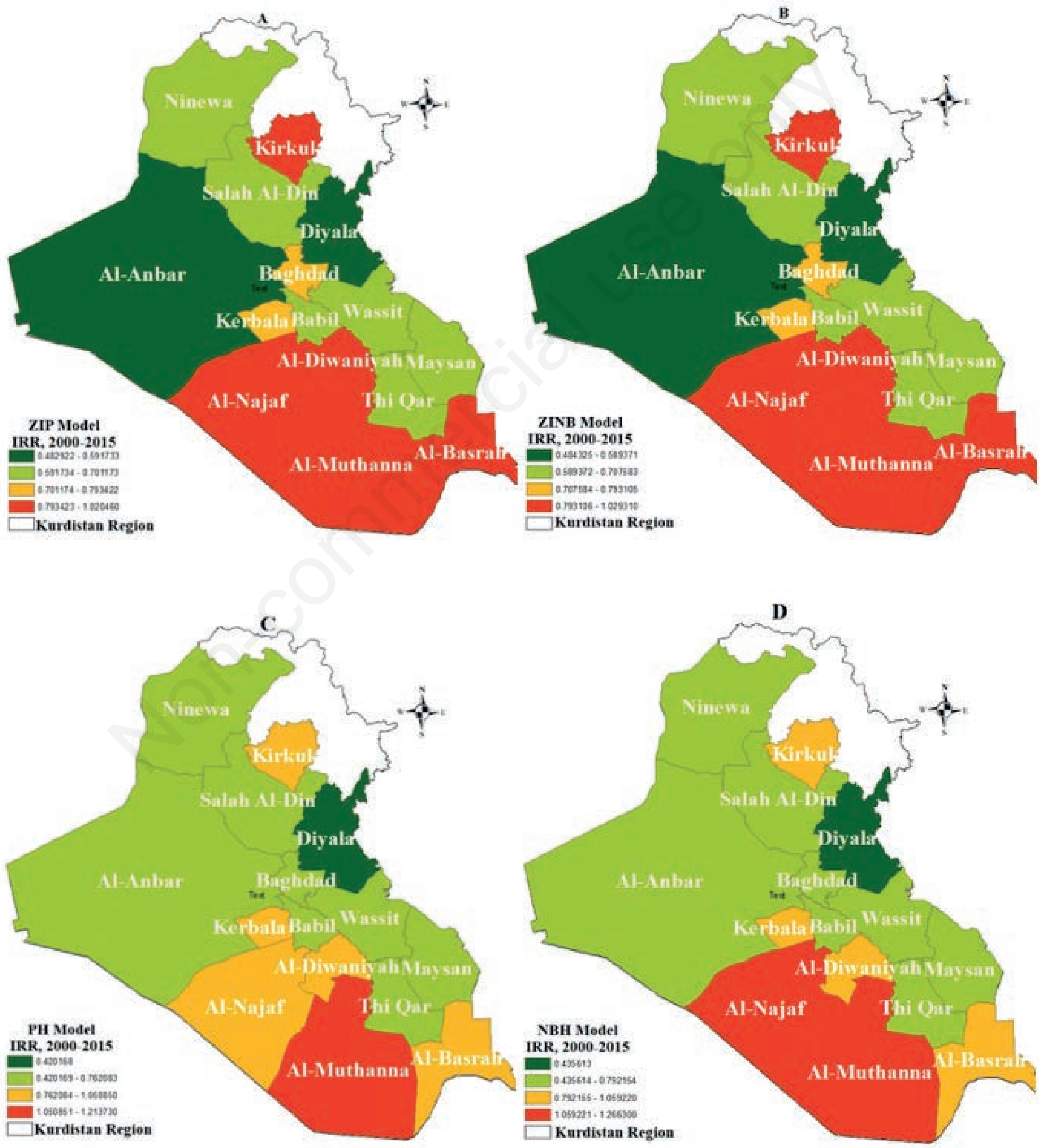

Figure 5. Incidence rate ratio (IRR) of bone cancer, childhood using four models between 2000 and 2015, using A) the zero-inflated Poisson (ZIP) model; B) the zero-inflated negative binomial (ZINB) model; C) the Poisson hurdle (PH) model; D) the negative binomial hurdle (NBH) model.

ination that environmental pollutants could be a factor contributing to the differences of bone tumour incidence among Iraqi provinces.

Al-Diwaniyah Province is a rural environment and is heavily cultivated, increasing the probable risk factors such as exposure to pesticides and various agrochemicals. Many articles have reported that Al-Diwaniyah Province suffers from environmental pollution. Walli (2015) found highly pollution of surface water in many sites in the Al-Dalmaj Marshes, Al-Diwaniyah province. The river is neither suitable for drinking nor swimming due to the high-level of pollution (Hussein *et al*., 2019). Polynuclear aromatic hydrocarbons, considered a soil contaminant, have been discovered in Al-Diwaniyah city centre (Afak, Al-Shamiya and Al-Hamza) (Karam & Kadhim, 2014). Another study found chemical pollutants in different types of food (Karam, 2015).

In Al-Muthanna Province, cement and brick factories use black oil, which is usually not efficiently combusted leading to air pollution. Through the southernmost provinces, there are multiple sites where raw sewage is discharged directly into the rivers which flow through them. The use of pesticides in agriculture is unregulated and rife. These are all polluting factors in Iraq, particularly in Al-Muthanna, Al-Diwaniyah and Al-Basrah provinces (Al-Daghir, 2013).

Iraq that is heavily contaminated with pollutants related to the wars (Al-Shammari, 2016). Many researchers have written about environmental pollution levels in Al-Basrah (Al-Aasadi *et al*., 2015; Al-Hassen *et al*., 2015; Al-Shammari, 2016). All these sources confirm air pollution in Al-Basrah during the years 1980 to 2003 when it suffered wars and their aftermath. Subsequently, there was an expansion of industrial and petrochemical plants accompanied by increased traffic density and air pollutants caused by daily activities (Douabul *et al*., 2013).

Iraq's unique geographical situation with two major rivers that cross the country transporting waste of various kinds flow from their catchment areas that include large parts of Turkey, eastern Syria and western Iran. For this reason, the water in Iraq, in particular in the southern part, is loaded with the results of industrial and natural activities in these areas. This element has the potential to affect the health of the population, especially children and young adults. Not surprisingly, the highest incidence was observed is in the southernmost provinces of Al-Muthanna, Al-Diwaniyah and Al-Basrah.

Although understanding the reasons for the variation of the incidence of bone tumours across Iraqi governorates is not the primary aim of this research, the detection of higher incidence rates in different areas is suggestive of the need to provide services for diagnosis and treatment in the locations with higher incidence. It also highlights the need for more research into the causes behind such variation to develop the necessary public health strategies including diagnostic and therapeutic services, besides the necessary policies regarding any contributory environmental factors.

There is no clear evidence for the relationship between cases and geographical and temporal differences, that may be traced to the development of inconsistent criteria for bone tumour registration across the country, because of variation in the accuracy of registration from one governorate to another. This research is a positive endeavour in that direction, which may strongly suggest the role of environmental factors such as exposure to radiation, chemical agents, and pollution. Further research in that area is well worth pursuing.

Conclusions

This study establishes that ZIP model is the preferred model over others. Osteosarcoma and Ewing Sarcoma are the most common type of bone cancer in children and adolescents in Iraq. Bone tumours showed incidence patterns variation among age groups, with peak in the 15-19 age group. The distribution of the incidence of bone tumours in children and adolescents is different between Iraqi provinces. The highest incidence was observed in Al-Muthanna, Al-Diwaniyah, and Al-Basrah provinces in the south of Iraq. The annual incidence of bone tumours from 2000-2015 showed a fluctuating pattern over the period of study, with significant increasing trend.

The study suggests further research into childhood tumours, and especially bone tumours, is needed to look at the effect of environmental factors in this group of disorders beside establishing the impact of availability of specialist local services on the reported incidence of this group of disorders.

References

Al-Aasadi KA, Alwaeli AA, Kazem HA, 2015. Assessment of air pollution caused by oil investments in Basra Province-Iraq. J Novel Appl Sci 4:82-6.

Al-Daghir HA, 2013. The environmental influences on the incidence of cancer in AL-Muthana governate April 2010. Almuthanna J Pure Sci (MJPS) 1:1.

Al-Hassen SI, Sultan AW, Ateek AA, Al-Saad HT, Mahdi S, Alhello AA, 2015. Spatial analysis on the concentrations of air pollutants in Basra province (southern Iraq). Open J Air Pollut 4:139.

Al-Shammari AM, 2016. Environmental pollutions associated to conflicts in Iraq and related health problems. Rev Environ Health 31:245-50.

Arora RS, Alston RD, Eden TO, Geraci M, Birch JM, 2012. The contrasting age□incidence patterns of bone tumours in teenagers and young adults: Implications for aetiology. Int J Cancer 131:1678-85.

Cameron AC, Trivedi PK, 2013. Regression analysis of count data. Cambridge University Press, Cambridge, UK, pp 112.

Damron TA, Ward WG, Stewart A, 2007. Osteosarcoma, chondrosarcoma, and Ewing's sarcoma: national cancer data base report. Clin Orthop Relat Res 459:40-7.

Diallo AO, Diop A, Dupuy JF, 2019. Estimation in zero-inflated binomial regression with missing covariates. Statistics 53:839-65.

Douabul AA, Maarofi SS, Al-Saad HT, Al-Hassen S, 2013. Gaseous pollutants in Basra city, Iraq. Air Soil Water Res ASWR-S10835.

Du J, Park YT, Theera-Ampornpunt N, McCullough JS, Speedie SM, 2012. The use of count data models in biomedical informatics evaluation research. J Am Med Inform Assoc 19:39-44.

Evola FR, Costarella L, Pavone V, Caff G, Cannavò L, Sessa A, Avondo S, Sessa G, 2017. Biomarkers of osteosarcoma, chondrosarcoma, and Ewing sarcoma. Front Pharmacol 8:150.

Eyre R, Feltbower RG, Mubwandarikwa E, Eden TO, McNally RJ, 2009. Epidemiology of bone tumours in children and young adults. Pediatr Blood Cancer 53:941-52.

García-Pérez J, Morales-Piga A, Gómez-Barroso D, Tamayo-Uria I, Romaguera EP, López-Abente G, Ramis R, 2017. Risk of

bone tumours in children and residential proximity to industrial and urban areas: New findings from a case-control study. Sci Total Environ 579:1333-42.
Ghert M, Mwita W, Mandari FN, 2019. Primary bone tumors in children and adolescents treated at a referral center in Northern Tanzania. J Am Acad Orthop Surg Glob Res Rev 3:3.
Grimer R, Athanasou N, Gerrand C, Judson I, Lewis I, Morland B, Peake D, Seddon B, Whelan J, 2010. UK guidelines for the management of bone sarcomas. Sarcoma 1:2010.
Hussein KM, Fadhil SA, Salih SA, 2019. Assessing water quality for Al-Diwaniyah River, Iraq using GIS technique. Eng Technol J (ETJ) 37:256-64.
Ibp I, 2012. Iraq country study guide, Volume 1. Strategic information and developments. International Business Publications, Inc., Alexandria, VA, USA.
Iraqi Cancer Board, 2018. Annual Report: Iraqi Cancer Registry 2016. Ministry of Health and Environment, Republic of Iraq.
Kaatsch P, Strothotte J, Becker C, Bielack S, Dirksen U, Blettner M, 2016. Pediatric bone tumours in Germany from 1987 to 2011: incidence rates, time trends and survival. Acta Oncol 55:1145-51.
Karam FF, 2015. The concentrations, distribution and sources of Benzo (a) pyrene in vegetables from Al-Diwaniya Province, Iraq. J Al-Qadisiyah Pure Sci Q 2:86-91.
Karam FF, Kadhim MI, 2014. Determination of Chrysene by Gas Chromatography in Selected Soils from Al-Diwaniya Province, Iraq, 2014. Asian J Chem 26:S259-61.
Katchy KC, Ziad F, Alexander S, Gad H, Mota'al MA, 2005. Malignant bone tumours in Kuwait. Int Orthop 29:406-11.
Klakattawi HS, Vinciotti V, Yu K, 2018. A simple and adaptive dispersion regression model for count data. Entropy 20:142.
Lambert D, 1992. Zero-inflated Poisson regression, with an application to defects in manufacturing. Technometrics 34:1-4.
Martin J, Hall DB, 2017. Marginal zero-inflated regression models for count data. J Appl Stat 44:1807-26.
Meyers PA, Gorlick R, 1997. Osteosarcoma. Pediatr Clin North Am 44:973-89.
Mirabello L, Troisi RJ, Savage SA, 2009. Osteosarcoma incidence and survival rates from 1973 to 2004: data from the Surveillance, Epidemiology, and End Results Program. Cancer 115:1531-43.
Mohammed A, Sani MA, Hezekiah IA, Enoch AA, 2010. Primary bone tumours and tumour-like lesions in children in Zaria, Nigeria. Afr J Paediatr Surg 7:16.
Mouatassim Y, Ezzahid EH, 2012. Poisson regression and Zero-inflated Poisson regression: application to private health insurance data. Eur. Actuar. J. 2(2):187-204.
Mullahy J, 1986. Specification and testing of some modified count data models. J Econom 33:341-65.
Ottaviani G, Jaffe N, 2009. The etiology of osteosarcoma. In: Jaffe N, Bruland OS, Bielack S, eds. Pediatric and adolescent osteosarcoma. Springer, Boston, MA, USA, pp 15-32.
Özkan EA, Göret CC, Özdemir ZT, Yanık S, Doğan M, Gönültaş A, Akkoca AN, 2015. Pattern of primary tumours and tumor-like lesions of bone in children: retrospective survey of biopsy results. Int J Clin Exp Patho 8:11543.
Pittman B, Buta E, Krishnan-Sarin S, O'Malley SS, Liss T, Gueorguieva R, 2018. Models for analyzing zero-inflated and overdispersed count data: an application to cigarette and marijuana use. Nicotine Tob Res 22:1390-8.
PosthumaDeBoer J, Graat HC, Bras J, Saouti R, 2010. Small cell osteosarcoma of a toe phalanx: a case report and review of literature. J Orthop Surg Res 5:36.
Pruksakorn D, Phanphaisarn A, Pongnikorn D, Daoprasert K, Teeyakasem P, Chaiyawat P, Katruang N, Settakorn J, 2016. Age Standardized incidence rates and survival of osteosarcoma in northern Thailand. Asian Pac J Cancer Prev 17:3455-8.
Ramdass MJ, Mooteeram J, Beharry A, Mencia M, Barrow S, 2015. An 8-YEAR analysis of bone tumours in a Caribbean island. Ann Med Surg 4:414-6.
Rhutso Y, Laishram RS, Sharma LD, Debnath K, 2013. Histopathological evaluation of bone tumours in a tertiary care hospital in Manipur, India. J. Med. Soc 27:135.
Rose CE, Martin SW, Wannemuehler KA, Plikaytis BD, 2006. On the use of zero-inflated and hurdle models for modeling vaccine adverse event count data. J Biopharm Stat 16:463-81.
Steliarova-Foucher E, Colombet M, Ries LA, Moreno F, Dolya A, Bray F, Hesseling P, Shin HY, Stiller CA, Bouzbid S, Hamdi-Cherif M, 2017. International incidence of childhood cancer, 2001-10: a population-based registry study. Lancet Oncol 18:719-31.
Stiller CA, Bielack SS, Jundt G, Steliarova-Foucher E. Bone tumours in European children and adolescents, 1978-1997, 2006. Report from the Automated Childhood Cancer Information System project. Eur J Cancer 42:2124-35.
Walli HA, 2015. Determination of PAHs in Surface Water of Al-Dalmaj Marsh, Al-Diwaniya Province, Iraq. J Enviro Earth Sci (JEES) 5:67-72.
Wilhelm M, Dirksen U, Bielack SS, Whelan JS, Lewis IJ, Jürgens H, Ferrari S, Sundby Hall K, Cleton-Jansen AM, Stark D, 2014. ENCCA WP17-WP7 consensus paper on teenagers and young adults (TYA) with bone sarcomas. Ann Oncol 25:1500-5.
Xie H, Tao J, McHugo GJ, Drake RE, 2013. Comparing statistical methods for analyzing skewed longitudinal count data with many zeros: An example of smoking cessation. J Subst Abuse Treat 45:99-108.
Yesilova A, Kaydan MB, Kaya Y, 2010. Modeling insect-egg data with excess zeros using zero-inflated regression models. Hacettepe J Math Stat 39:273-82.