

CLINICAL UPDATE

# Does access to private healthcare influence potential lung cancer cure rates?

T-J John,<sup>1</sup> MB ChB, Dip HIV Man (SA); D Plekker,<sup>2</sup> MB ChB, FCP (SA), MMed (Int), Cert Pulm (SA);  
E M Irusen,<sup>1</sup> MB ChB, FCP (SA), PhD; C F N Koegelenberg,<sup>1</sup> MB ChB, MMed (Int), FCP (SA), FRCP (UK), Cert Pulm (SA), PhD

<sup>1</sup> Division of Pulmonology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Academic Hospital, Cape Town, South Africa

<sup>2</sup> Pulmonologist, Kuils River Hospital, Cape Town, South Africa

Corresponding author: T-J John (jessjohnt@gmail.com)

**Background.** Numerous studies show a link between poor socioeconomic status (SES) and late-stage cancer diagnosis. However, this has not been consistently shown looking at non-small-cell lung cancer (NSCLC) in isolation. Despite the extremely high prevalence of lung cancer and disparities in access to healthcare based on health insurance in South Africa, there is a paucity of data on the influence of health insurance (as a surrogate for SES) on stage at presentation of NSCLC.

**Objective.** To assess the relationship between health insurance status (and invariably SES) and staging (and therefore resectability) of patients with primary NSCLC at the time of initial presentation.

**Methods.** Health-insured patients with NSCLC ( $n=51$ ) were retrospectively compared with NSCLC patients with no health insurance ( $n=532$ ) with regard to demographics, tumour node metastasis (TNM) staging, and cell type at initial presentation.

**Results.** Patients with no health insurance were younger (mean (standard deviation (SD)) 59.9 (10.1) years) than those with private health insurance (64.2 (9.6) years) ( $p=0.03$ ). Poorly differentiated NSCLC was significantly more common in the privately health-insured group (23.6%) than among those with no health insurance (4.6%) ( $p<0.01$ ). Six of 51 NSCLC patients (11.8%) with private health insurance presented with early-stage, potentially curable disease (up to stage IIIA), compared with 55 patients (10.3%) in the uninsured group ( $p=0.75$ ).

**Conclusions.** Access to private health insurance did not have a significant impact on stage at initial presentation. The only significant differences were the relatively advanced age at presentation and relatively higher percentage of poorly differentiated NSCLC seen in patients with health insurance.

*S Afr Med J* 2017;107(8):687-690. DOI:10.7196/SAMJ.2017.v107i8.12277

According to the *World Cancer Report* of 2014,<sup>[1]</sup> lung cancer remains the most common cause of cancer-related death, resulting in >1.59 million reported deaths in 2012. The situation in South Africa (SA) is no different, although studies have consistently shown that SA patients with non-small-cell lung cancer (NSCLC) have an inferior potential cure rate at presentation when compared with the USA and Western Europe.<sup>[2-4]</sup> Only ~10% of patients diagnosed with lung cancer in SA are offered treatment with curative intent.<sup>[2-4]</sup>

The National Institute for Health and Clinical Excellence (NICE) guideline<sup>[5]</sup> recommends radical surgery for stage I - II NSCLC, with chemoradiotherapy with or without surgery (with curative intent) offered to patients with stage IIIA disease. Palliative chemotherapy and radiotherapy are recommended for later-stage NSCLC patients (stage IIIB and IV).<sup>[5]</sup> Stage at diagnosis is therefore an important indicator of survival in lung cancer.<sup>[6]</sup> Diagnosis at an advanced stage (IIIB or IV) usually precludes the possibility of cure and leads to poor long-term outcomes.<sup>[7-9]</sup> Five-year survival rates of patients diagnosed with late-stage disease range from ~4% to 6%, whereas those for early-stage disease range from 40% to 54%.<sup>[6,10-14]</sup>

Health insurance status is commonly used as a surrogate marker of socioeconomic status (SES).<sup>[15]</sup> In turn, SES has been shown to be an independent contributor to health status, as a surrogate for lifestyle, diet, and working and living conditions.<sup>[16]</sup> Lower SES is known to be associated not only with an increased incidence of cancer but also with worsened survival.<sup>[17,18]</sup> Although numerous

studies across various cancers have shown that poor SES has been associated with late-stage diagnosis, this has not been consistently observed in studies looking at NSCLC in isolation.<sup>[18-21]</sup> Disparities in access to healthcare and its use, as well as lack of preventive healthcare services including cancer screening, may contribute somewhat to differentials in cancer stage distributions, especially in late-stage diagnosis.<sup>[18,22-25]</sup>

## Objective

There is a paucity of SA data comparing the staging of lung cancer patients at the time of presentation based on SES. The objective of this study was to assess the relationship between health insurance status (and invariably SES) and staging of patients (and therefore resectability and potential cure) with primary NSCLC at the time of initial presentation. The study's null hypothesis, based on previous international research, was that there is no notable difference in the resectability rates of patients with v. without private health insurance diagnosed with NSCLC at the time of presentation.

## Methods

All cases of primary lung cancer presenting to Tygerberg Academic Hospital and the Kuils River Respiratory Centre (Kuils River Hospital) in Cape Town, SA, between August 2013 and September 2015 were identified. Tygerberg Academic Hospital, a 1 380-bed public hospital, is a primary referral centre serving approximately three million people. Kuils River Respiratory Centre is based in the suburb of

Kuils River, with patients being admitted to the 180-bed Kuils River Hospital.<sup>[26]</sup> The two centres are in close proximity and serve a patient population group similar in demographics other than their SES.

All patients in the study population diagnosed with an underlying primary NSCLC in either of the institutions were included in the study group. In the study group, all patients who had a confirmed histological diagnosis together with complete staging details were included in the analysis. Patients were excluded if the presentation with primary lung malignancy was not their first presentation to the healthcare service with a malignancy, or if a second underlying malignancy was suspected at the time of presentation.

Information on individual patients was collected retrospectively from medical records, including routine demographic and clinical data. All patients had access to positron emission tomography/computed tomography, bronchoscopy with endobronchial ultrasound-guided transbronchial needle aspiration with rapid on-site evaluation, transthoracic image (ultrasound or tomography)-guided biopsy and related diagnostic techniques that were performed at the discretion of the treating doctors as per standard operating procedures. A combined panel of at least a pulmonologist, thoracic radiologist, thoracic surgeon, specialist oncologist and pathologist staged all patients as per the 2009 International Association for the Study of Lung Cancer tumour node metastasis (TNM) staging system. These findings were recorded prospectively in a lung cancer registry (administered by the investigators), which was retrospectively used to identify cases anonymously.

Pathological analyses were performed by the National Health Laboratory Services at Tygerberg Hospital (state patients) and Ampath Laboratories at N1 City Hospital in Cape Town (insured patients).

**Statistical analysis**

Data were collected on a customised Microsoft Excel spreadsheet, version 15.0.4797.1000 (Microsoft, USA). Chi-square or Fisher’s exact tests (where indicated) were performed on dichotomous categorical variables, and *t*-testing on continuous data. A 5% significance level (*p*<0.05) was applied.

**Ethical approval**

Ethical approval for this retrospective analysis was provided by the Stellenbosch University Research Ethics Committee (ref. no. S16/04/077). The application included a

waiver of consent owing to the retrospective nature and anonymity of the study design.

**Results**

During the 2-year study period, 665 patients were seen between the two institutions with a confirmed histological diagnosis of primary lung malignancy. All the patients who presented to Tygerberg Hospital (*n*=610) had no health insurance, whereas all the patients who presented to Kuils River Respiratory Centre (*n*=55) had access to private health insurance.

The patients with no health insurance were younger (mean (standard deviation (SD)) 59.9 (10.1) years) than those with private health insurance (64.15 (9.6) years) (*p*=0.03). There was no significant difference in gender distribution between the two groups (Table 1). Overall, adenocarcinoma was the commonest form of lung malignancy (48.1%), followed by squamous cell carcinoma (29.2%). In the privately health-insured group, poorly differentiated NSCLC (25.5%) was more common than squamous cell carcinoma (23.6%). Poorly differentiated NSCLC was also significantly more common

in the privately health-insured group (23.6%) compared with those with no health insurance (4.6%) (*p*<0.01).

Sixty-one (10.5%) of the 583 patients with NSCLC were staged as early-stage disease (up to stage IIIA, Table 1). In total, 477 of 532 NSCLC state patients (89.7%) had incurable disease at presentation, compared with 45 of 51 privately insured patients (88.8%) (*p*=0.75). Conversely, 55 state patients (10.3%) presented with early-stage, potentially curable disease (up to stage IIIA) compared with 6 patients in the privately insured group (11.8%) (*p*=0.75).

**Discussion**

In this retrospective, observational study in patients with NSCLC, access to private health insurance (medical aid in SA) was shown not to have a significant effect on staging at initial presentation. The only significant differences were the relatively advanced age at presentation and relatively higher percentage of poorly differentiated NSCLC seen in private practice.

Potential theories regarding why a later-stage diagnosis would have been expected in

**Table 1. Demographics, cell types and staging for all lung cancer patients by health insurance type (N=665)**

	All* (N=665)	No health insurance (n=610)	Private health insurance (n=55)	<i>p</i> -value
<b>Demographics</b>				
Age (yr), mean (SD)	60.49 (10.1)	59.9 (10.1)	64.15 (9.6)	0.03
Gender male, <i>n</i> (%)	404 (60.8)	372 (61.0)	32 (58.2)	0.68
<b>Cell type, <i>n</i> (%)</b>				
NSCLC ( <i>n</i> =583)				
Adenocarcinoma	320 (48.1)	298 (48.9)	22 (40.0)	0.26
Squamous cell carcinoma	194 (29.2)	181 (29.7)	13 (23.6)	0.35
Poorly differentiated	42 (6.3)	28 (4.6)	14 (25.5)	<0.01
Other	27 (4.1)	25 (4.1)	2 (3.6)	1
SCLC	82 (12.3)	78 (12.8)	4 (7.3)	0.28
<b>Stage, <i>n</i> (%)</b>				
NSCLC ( <i>n</i> =583)				
I	8 (1.4)	7 (1.3)	1 (2.0)	1
II	15 (2.6)	15 (2.8)	0 (0.0)	0.38
IIIA	38 (6.5)	33 (6.2)	5 (9.8)	0.37
IIIB	128 (22.0)	115 (21.6)	13 (25.5)	0.52
IV	394 (67.6)	362 (68.0)	32 (62.7)	0.44
SCLC ( <i>n</i> =82)				
Limited	11 (13.4)	10 (12.8)	1 (25.0)	1
Extensive	71 (86.6)	68 (87.2)	3 (75.0)	1

SD = standard deviation; NSCLC = non-small-cell lung cancer; SCLC = small-cell lung cancer.  
\*Stage I - IIIA v. stages IIIB - IV NSCLC.

those of lower SES include fatalistic views and medical mistrust, which has been shown to be more common among the poor and minorities<sup>[27,28]</sup> and leads to delays in seeking care for symptoms suggestive of lung cancer as well as delaying prompt work-up once a tumour has been identified. The poor may also prioritise health to a lesser degree and therefore postpone seeing a doctor, which can contribute to later stage of presentation.<sup>[6,28]</sup> However, these findings were not reproducible in this study, which showed that although patients without health insurance presented with later-stage disease, there was no significant difference between the privately insured and uninsured groups.

A systematic review of the literature from 1995 to 2005 by Woods *et al.*<sup>[15]</sup> found that most studies report an association between low SES and later stage at diagnosis of various cancers. As with our study, this does not always hold true when looking at NSCLC in isolation. Various studies of lung cancer from Canada, Denmark and Sweden have only indicated limited socioeconomic differences in advanced-stage diagnosis.<sup>[17,29,30]</sup> Other studies from the UK have in fact shown a lower frequency of advanced stage at diagnosis in more deprived patients.<sup>[31]</sup> The findings of our study, although not showing independent evidence of an association ( $p=0.75$ ), may reflect a lack of power due to the lack of numbers in the privately insured group. To our knowledge, there are no available local data looking at the influence of SES or health insurance on the stage of presentation of primary lung malignancy.

The proportion of early-stage (up to stage IIIA) disease in the study group was calculated at 10.3% in our patients with no health insurance and 11.8% in those with private health insurance. This corresponds with reported resectability rates in patients with NSCLC in SA literature, where operability rates between 10% and 11% have been quoted in other studies from Johannesburg and Cape Town.<sup>[2-4,32,33]</sup> In the developed world, the proportion of patients who present with potentially curable disease is much higher. A study detailing >12 800 cases of lung cancer from Nebraska, Canada, revealed early-stage disease in 23.04% of patients.<sup>[34]</sup> Other studies from the developed world have revealed resectable disease in up to 33% of patients.<sup>[13]</sup> It must be noted that in the SA setting, other factors including the effect of the HIV pandemic on the stage of presentation must be kept in mind. A previous study from the Western Cape Province, SA, has shown that HIV-positive lung cancer patients were significantly less likely to have early-stage lung cancer compared with their HIV-negative counterparts.<sup>[4]</sup> Limited resources in the state sector and restricted funding by medical aids in the private sector also pose significant barriers to early detection of disease.

The present study revealed that poorly differentiated NSCLC was significantly more common in the privately health-insured group (23.6%) compared with those with no health insurance (4.6%) ( $p<0.01$ ). Our data also support current worldwide lung cancer trends that have revealed an increase in the proportion of patients being diagnosed with adenocarcinoma in comparison with squamous cell carcinoma.<sup>[35-40]</sup> A steady decrease in daily smoking prevalence in association with switching to low-tar and filter cigarettes (enhancing delivery of smoke to peripheral regions of the lung) is believed to contribute to the decrease in rates of squamous cell carcinoma and the increase in rates of adenocarcinoma.<sup>[41-44]</sup> It has been postulated that filter tips effectively reduce deposition of larger particles in the central airway, resulting in a reduced risk of squamous cell carcinoma, but increase deposition of small-size particles in the deeper parts of the lung where adenocarcinoma preferentially occurs.<sup>[41,42]</sup>

### Study limitations

A limitation of the study is possible selection bias, in that data from a single region that only includes <10% of the SA population may

not be generalisable to the whole population. Furthermore, the lack of documentation of race makes it even more difficult to generalise the results and findings to the SA population as a whole. Access to and quality of healthcare institutions may also vary between metropolitan areas. A further potential limitation may be the fact that different laboratories were used for analysis and typing of lung cancer.

Health insurance type as a measure of SES has limitations in that it may be affected by the wide lack of homogeneity within each group. In future studies, a multilevel framework examining individual and area-specific socioeconomic variables, including housing standards, family income, etc., may be a better classification of SES. Further, larger-scale studies involving multiple centres (both public and privately run) from around the country may aid in proving significance of the above findings and minimise any selection bias that may be present. A multilevel assessment of SES as outlined above may also give a better indication of the true impact of SES on stage of presentation with underlying malignancy.

### Conclusions

We found a nominal and statistically insignificant difference between the stage of presentation in patients who had health insurance compared with those who did not have access to private health insurance. Larger-scale studies involving multiple centres may need to be carried out to identify whether a true difference exists between the two groups; this is of great importance, as a difference may have important public health implications for the future. It is also evident that lung cancer screening as well as other methods to improve early-stage disease detection remains one of the most important tools in improving lung cancer cure rates.

**Acknowledgements.** None.

**Author contributions.** CFNK and T-JJ conceived the idea. All authors collected the data. T-JJ and CFNK analysed the data and prepared the manuscript, and EMI and DP were responsible for critical revision of the manuscript.

**Funding.** None.

**Conflicts of interest.** None.

- Stewart B, Wild C. World Cancer Report 2014. Lyon: World Health Organization, 2014.
- Nanguzambo AB, Aubeleack K, Grootte-Bidlingmaier F, et al. Radiologic features, staging and operability of primary lung cancer in the Western Cape, South Africa. *J Thorac Oncol* 2011;6(2):343-350. <https://doi.org/10.1097/jto.0b013e3181fd40ec>
- Koegelenberg CFN, Aubeleack K, Nanguzambo AB, et al. Adenocarcinoma the most common cell type in patients presenting with primary lung cancer in the Western Cape. *S Afr Med J* 2011;101(5):321. <https://doi.org/10.7196/SAMJ.4554>
- Koegelenberg CFN, van der Made T, Taljaard JJ, Irusen EM. The impact of HIV infection on the presentation of lung cancer in South Africa. *S Afr Med J* 2016;106(7):666-668. <https://doi.org/10.7196/samj.2016.v106i7.10737>
- National Institute for Health and Clinical Excellence. Clinical Guideline: Lung Cancer: The Diagnosis and Treatment of Lung Cancer. Manchester: NICE, 2006.
- Efird JT, Landrine H, Shiue KY, et al. Race, insurance type, and stage of presentation among lung cancer patients. *Springerplus* 2014;3:710. <https://doi.org/10.1186/2193-1801-3-710>
- Halpern MT, Ward EM, Pavluck AL, Schrag NM, Bian J, Chen AY. Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: A retrospective analysis. *Lancet Oncol* 2008;9(3):222-231. [https://doi.org/10.1016/S1470-2045\(08\)70032-9](https://doi.org/10.1016/S1470-2045(08)70032-9)
- Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* 2010;60(5):277-300. <https://doi.org/10.3322/caac.20073>
- Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin* 2012;62(1):10-29. <https://doi.org/10.3322/caac.20138>
- Ward EM, Fedewa SA, Cokkinides V, Virgo K. The association of insurance and stage at diagnosis among patients aged 55 to 74 years in the national cancer database. *Cancer J* 2010;16(6):614-621. <https://doi.org/10.1097/PPO.0b013e3181f2aac>
- Billing JS, Wells FC. Delays in the diagnosis and surgical treatment of lung cancer. *Thorax* 1996;51(9):903-906. <https://doi.org/10.1136/thx.51.9.903>
- Melamed MR, Flehinger BJ, Zaman MB, Heelan RT, Hallerman ET, Martini N. Detection of true pathologic stage I lung cancer in a screening program and the effect on survival. *Cancer* 1981;47(5 Suppl):1182-1187. [https://doi.org/10.1002/1097-0142\(19810301\)47:5+<1182::aid-cnrcr2820471322>3.0.co;2-4](https://doi.org/10.1002/1097-0142(19810301)47:5+<1182::aid-cnrcr2820471322>3.0.co;2-4)
- Salomaa ER, Sallinen S, Hiekkänen H, Liippo K. Delays in the diagnosis and treatment of lung cancer. *Chest* 2005;128(4):2282-2288. <https://doi.org/10.1378/chest.128.4.2282>
- Myrdal G, Lambe M, Hillerdal G, Lambert K, Agustsson T, Stahle E. Effect of delays on prognosis in patients with non-small cell lung cancer. *Thorax* 2004;59(1):45-49.
- Woods LM, Rachet B, Coleman MP. Origins of socio-economic inequalities in cancer survival: A review. *Ann Oncol* 2006;17(1):5-19. <https://doi.org/10.1093/annonc/mdj007>

16. Mao Y, Hu J, Ugnat AM, Semenciw R, Fincham S, Canadian Cancer Registries: Epidemiology Research Group. Socioeconomic status and lung cancer risk in Canada. *Int J Epidemiol* 2001;30(4):809-817. <https://doi.org/10.1093/ije/30.4.809>
17. Booth CM, Li G, Zhang-Salomons J, Mackillop WJ. The impact of socioeconomic status on stage of cancer at diagnosis and survival: A population-based study in Ontario, Canada. *Cancer* 2010;116(17):4160-4167. <https://doi.org/10.1002/cncr.25427>
18. Clegg LX, Reichman ME, Miller BA, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: Selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. *Cancer Cause Control* 2009;20(4):417-435. <https://doi.org/10.1007/s10552-008-9256-0>
19. Mandelblatt J, Andrews H, Kao R, Wallace R, Kerner J. The late-stage diagnosis of colorectal cancer: Demographic and socioeconomic factors. *Am J Public Health* 1996;86(12):1794-1797. <https://doi.org/10.2105/ajph.86.12.1794>
20. Mandelblatt J, Andrews H, Kerner J, Zauber A, Burnett W. Determinants of late stage diagnosis of breast and cervical cancer: The impact of age, race, social class, and hospital type. *Am J Public Health* 1991;81(5):646-649. <https://doi.org/10.2105/ajph.81.5.646>
21. Merkin SS, Stevenson L, Powe N. Geographic socioeconomic status, race, and advanced-stage breast cancer in New York City. *Am J Public Health* 2002;92(1):64-70. <https://doi.org/10.2105/ajph.92.1.64>
22. Greenwald HP, Borgatta EF, McCorkle R, Polissar N. Explaining reduced cancer survival among the disadvantaged. *Milbank Q* 1996;74(2):215-238. <https://doi.org/10.2307/3350247>
23. Hoffman-Goetz L, Breen NL, Meissner H. The impact of social class on the use of cancer screening within three racial/ethnic groups in the United States. *Ethn Dis* 1998;8(1):43-51.
24. Liu L, Cozen W, Bernstein L, Ross RK, Deapen D. Changing relationship between socioeconomic status and prostate cancer incidence. *J Natl Cancer Inst* 2001;93(9):705-709. <https://doi.org/10.1093/jnci/93.9.705>
25. Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. Progress in cancer screening practices in the United States: Results from the 2000 National Health Interview Survey. *Cancer* 2003;97(6):1528-1540. <https://doi.org/10.1002/cncr.11208>
26. Barnard DA, Iruken EM, Bruwer JW, et al. The utility of Xpert MTB/RIF performed on bronchial washings obtained in patients with suspected pulmonary tuberculosis in a high prevalence setting. *BMC Pulm Med* 2015;15(1):103. <https://doi.org/10.1186/s12890-015-0086-z>
27. Bergamo C, Lin JJ, Smith C, et al. Evaluating beliefs associated with late-stage lung cancer presentation in minorities. *J Thorac Oncol* 2013;8(1):8-12. <https://doi.org/10.1097/JTO.0b013e3182762ce4>
28. Dalton SO, Frederiksen BL, Jacobsen E, et al. Socioeconomic position, stage of lung cancer and time between referral and diagnosis in Denmark, 2001 - 2008. *Br J Cancer* 2011;105(7):1042-1048. <https://doi.org/10.1038/bjc.2011.342>
29. Drew EM, Schoenberg. Deconstructing fatalism: Ethnographic perspectives on women's decision making about cancer prevention and treatment. *Med Anthropol Q* 2011;25(2):164-182. <https://doi.org/10.1111/j.1548-1387.2010.01136.x>
30. Berglund A, Holmberg L, Tishelman C, Wagenius G, Eaker S, Lambe M. Social inequalities in non-small cell lung cancer management and survival: A population-based study in central Sweden. *Thorax* 2010;65(4):327-333. <https://doi.org/10.1136/thx.2009.125914>
31. Brewster DH, Thomson CS, Hole DJ, Black RJ, Stroner PL, Gillis CR. Relation between socioeconomic status and tumour stage in patients with breast, colorectal, ovarian, and lung cancer: Results from four national, population based studies. *BMJ* 2001;322(7290):830-831. <https://doi.org/10.1136/bmj.322.7290.830>
32. Wilcox PA, O'Brien JA, Abratt RP. Lung cancer at Groote Schuur Hospital: A local perspective. *S Afr Med J* 1990;78(12):716-720. [https://doi.org/10.1016/0169-5002\(91\)90384-i](https://doi.org/10.1016/0169-5002(91)90384-i)
33. Mukansi M, Smith C, Feldman C. A study of lung cancer in Johannesburg, South Africa. *South Afr J Infect Dis* 2013;29(1):43-47. <https://doi.org/10.1080/23120053.2014.11441566>
34. Wen J, Lin G, Islam K. Social determinants of non-small cell lung cancer stage at diagnosis and survival in Nebraska. *Ann Public Health Res* 2015;2(1):1011-1017.
35. Tse LA, Mang OW, Yu IT, Wu F, Au JS, Law SC. Cigarette smoking and changing trends of lung cancer incidence by histological subtype among Chinese male population. *Lung Cancer* 2009;66(1):22-27. <https://doi.org/10.1016/j.lungcan.2008.12.023>
36. Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143(5 Suppl):1S-29S. <https://doi.org/10.1378/chest.12-2345>
37. Borras J, Borras JM, Galceran J, Sanchez V, Moreno V, Gonzalez JR. Trends in smoking-related cancer incidence in Tarragona, Spain, 1980 - 96. *Cancer Cause Control* 2001;12(10):903-908. <https://doi.org/10.1023/a:1013764220293>
38. Li X, Mutanen P, Hemminki K. Gender-specific incidence trends in lung cancer by histological type in Sweden, 1958 - 1996. *Eur J Cancer* 2001;10(3):227-235. <https://doi.org/10.1097/00008469-200106000-00005>
39. Myrdal G, Lambe M, Bergstrom R, Ekblom A, Wagenius G, Stahle E. Trends in lung cancer incidence in Sweden with special reference to period and birth cohorts. *Cancer Cause Control* 2001;12(6):539-549. <https://doi.org/10.1023/a:1011238525498>
40. Nguyen AM, Luke CG, Roder D. Time trends in lung cancer incidence by histology in South Australia: Likely causes and public health implications. *Aust N Z J Public Health* 2003;27(6):596-601. <https://doi.org/10.1111/j.1467-842x.2003.tb00605.x>
41. Blizzard L, Dwyer T. Lung cancer incidence in Australia: Impact of filter-tip cigarettes with unchanged tar yields. *Int J Cancer* 2002;97(5):679-684. <https://doi.org/10.1002/ijc.10095>
42. Hart CL, Hole DJ, Gillis CR, Smith GD, Watt GC, Hawthorne VM. Social class differences in lung cancer mortality: Risk factor explanations using two Scottish cohort studies. *Int J Epidemiol* 2001;30(2):268-274. <https://doi.org/10.1093/ije/30.2.268>
43. Joshua AM, Boyer MJ, Subramanian R, Clarke SJ. Smoking reduction does work: Resulting alterations in the incidence and histological subtypes of lung cancer in New South Wales in the last 20 years. *Respirology* 2005;10(2):233-238. <https://doi.org/10.1111/j.1440-1843.2005.00672.x>
44. Zheng T, Holford TR, Boyle P, et al. Time trend and the age-period-cohort effect on the incidence of histologic types of lung cancer in Connecticut, 1960-1989. *Cancer* 1994;74(5):1556-1567. [https://doi.org/10.1002/1097-0142\(19940901\)74:5<1556::aid-cncr2820740511>3.0.co;2-0](https://doi.org/10.1002/1097-0142(19940901)74:5<1556::aid-cncr2820740511>3.0.co;2-0)

Accepted 7 April 2017.