Actinic keratosis on the rise in Australia [version 1; referees: 2 approved with reservations]

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Abstract

Objectives: To report the burden and cost of actinic keratosis (AK) treatment in Australia and to forecast the number of AK treatments and the associated costs to 2020.

Design and setting: A retrospective study of data obtained from medicare Australia for AK treated by cryotherapy between 1 January 1994 and 31 December 2012, by year and by state or territory.

Results: The total number of AK cryotherapy treatments increased from 247,515 in 1994 to 643,622 in 2012, and we estimate that the number of treatments will increase to 831,952 (95% CI 676,919 to 986,987) by 2020. The total Medicare Benefits Schedule (MBS) benefits paid out for AK in 2012 was $19.6 million and we forecast that this will increase to $24.7 million by 2020 (without inflation).

Conclusion: The number of AK cryotherapy treatments increased by 160% between 1994 and 2012. We forecast that the number of treatments will increase by 30% between 2012 and 2020. The rates of non-melanoma skin cancer (NMSC) and AK appear to be increasing at the same rate. During the period 2010 to 2015 AK is anticipated to increase by 17.8% which follows a similar trend to published data that forecasts an increase in NMSC treatments of 22.3%.

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Competing interests: No competing interests were disclosed.

Introduction

Actinic keratosis (AK), is one of the most common and most expensive skin diseases to treat. This places a high burden on the Australian population, health care system and government. Up to 60% of Australians in subtropical Queensland over the age of 40 have AK\(^2\). AK lesions are rough scaly and generally less than 1 cm in diameter. They are caused by chronic sun exposure and prevented by regular sunscreen use\(^3\). Multiple lesions are common. Some lesions regress spontaneously, but others progress to invasive squamous cell carcinoma (SCC). Hypertrophic AK may contain occult foci of SCC\(^4\). A systematic review of the natural history of AK estimated the risk of malignant transformation to range from 0% to 0.0075%/lesion/year\(^5\). In individuals with a history of non-melanoma skin cancer (NMSC), the risk is up 0.53% per lesion per year\(^6\). Organ transplant recipients on systemic immuno-suppressive therapies are at increased risk of malignant transformation\(^7\).

Indications for treatment include prophylaxis of SCC, uncertainty of diagnosis, symptomatic relief and to improve cosmetic appearance. Detectable lesions are frequently associated with alterations of the surrounding skin. These surrounding subclinical lesions, or field changes, can be identified histologically and also clinically with the application of topical field therapy for AK\(^8\).

Cryosurgery with liquid nitrogen is the most widely used therapy. Clinical response varies with the duration of application, as does morbidity. One study reported cure rates of 39% for freeze times less than 5 seconds, 69% for freeze times between 5 and 25 seconds and 83% for freeze times greater than 25 seconds\(^9\).

Medicare Australia is a universal health insurance scheme that reimburses patients for medical fees incurred. Benefits are paid according to the Medicare Benefits Schedule (MBS)\(^10\). The total number of claims and cost of Medicare benefits for the treatment of 10 or more premalignant lesions with an ablative therapy (MBS item number 30192) was obtained for the period 1994 to 2012 inclusive\(^10\).

The historical Medicare benefit payment data were inflated to 2012 Australian dollars, using the Reserve Bank of Australia Inflation calculator\(^11\). For each of the SK numbers and costs historical data sets, three Auto-regressive Integrated Moving Average (ARIMA) models\(^12\) were fitted and forecasts produced for the years 2013 to 2020. The models were ARIMA(1,1,1), ARIMA(0,1,1) and ARIMA(1,1,0). For each forecast series, the best fitting model was chosen on the basis of the Akaike Information Criterion (AIC)\(^13\). For both time series the AIC differences between models were extremely small and the model forecasts very similar.

Total numbers of non-melanoma skin cancer (NMSC) treatment was obtained from a study conducted by Fransen et al.\(^14\). These are illustrated in the graph in Figure 1 to compare the trends of AK to Field therapy is most useful for multiple AK lesions. Agents approved by the Therapeutics Goods Administration for field therapy include topical 5-Fluorouracil (5-FU), diclofenac sodium, ingenol mebutate and photodynamic therapy (PDT). Field therapy is not subsidized by the PBS and does not contribute directly to the cost to Government of treatment of AK in Australia.

There is no current published estimate of the direct cost of AK to the Australian government. We aimed to use Medicare data to report the annual numbers of AK treatments between 1994 and 2012, calculate the direct costs associated with these treatments and predict the numbers and costs from 2013 to 2020.

The risk of AK increases with age and the ageing of the Australian population may increase the burden of AK on the Australian health system.

Methods

Medicare Australia issues the total number of claims and benefits paid for each Medicare item number according to the Medicare Benefits Schedule (MBS)\(^10\). The total number of claims and cost of Medicare benefits for the treatment of 10 or more premalignant lesions with an ablative therapy (MBS item number 30192) was obtained for the period 1994 to 2012 inclusive\(^10\).

The historical Medicare benefit payment data were inflated to 2012 Australian dollars, using the Reserve Bank of Australia Inflation calculator\(^11\). For each of the SK numbers and costs historical data sets, three Auto-regressive Integrated Moving Average (ARIMA) models\(^12\) were fitted and forecasts produced for the years 2013 to 2020. The models were ARIMA(1,1,1), ARIMA(0,1,1) and ARIMA(1,1,0). For each forecast series, the best fitting model was chosen on the basis of the Akaike Information Criterion (AIC)\(^13\). For both time series the AIC differences between models were extremely small and the model forecasts very similar.

Total numbers of non-melanoma skin cancer (NMSC) treatment was obtained from a study conducted by Fransen et al.\(^14\). These are illustrated in the graph in Figure 1 to compare the trends of AK to

![Figure 1. Total number of AK treatments from 1994–2020.](image-url) Estimated treatment numbers from the period of 1994–2020. Estimated treatment numbers with 95% CI from 2013–2020 is shaded in grey.

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NMSC treatment. All statistical analysis was carried out with JMP® v 9.0.0.

Results
The total number of item 30192 treatment services billed to Medicare in 1994 was 247,515, increasing to 643,622 in 2012. This represents an increase of 160%. Rates remained relatively stable during the period of 2005–2009 and then began increasing again after 2010. It was estimated that the cost of treatments would reach $24.7 million in 2020 for roughly 831,953 treatment services – an increase of 29% over the next 8 years (Table 1 and Figure 1 and Figure 2).

The total number of AK treatments billed to Medicare showed a similar increase over time to the increase seen in total NMSC treatments over the same period of time (Figure 3). NMSC treatment services continued to rise during 2005–2009 while AK treatment services remained stable.

The number of treatment services billed for each of the Australian states and territories is illustrated in Figure 4. Approximately 293,933 treatment services were billed in NSW in 2012 and 184,233 services in Queensland compared to 1,548.

The number of AK treatments per 1,000 head was the highest in New South Wales compared to Queensland (Table 2). The number of AK treatments per 1,000 people in the Northern Territory was remarkably low, almost comparable to the number of AK treatments seen in Tasmania.

Table 1. Total number of AK treatments, total costs inflated, total costs without inflation and forecasts of AK numbers and costs with upper and lower 95% confidence limits (UCL95 and LCL95).

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of AK Treatments</th>
<th>Number of AK Treatments LCL95</th>
<th>Number of AK Treatments UCL95</th>
<th>Total cost in non-deflated AUS</th>
<th>Total cost in 2012 AUS UCL95</th>
<th>Total cost in 2012 AUS LCL95</th>
<th>Total cost in 2012 AUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>247,515</td>
<td>.</td>
<td>.</td>
<td>5,592,597</td>
<td>9,094,440</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>1995</td>
<td>269,252</td>
<td>.</td>
<td>.</td>
<td>6,168,831</td>
<td>9,587,787</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>1996</td>
<td>299,863</td>
<td>.</td>
<td>.</td>
<td>6,975,529</td>
<td>10,565,260</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>1998</td>
<td>326,626</td>
<td>.</td>
<td>.</td>
<td>7,724,620</td>
<td>11,574,041</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>1999</td>
<td>358,525</td>
<td>.</td>
<td>.</td>
<td>8,593,104</td>
<td>12,687,151</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2000</td>
<td>390,535</td>
<td>.</td>
<td>.</td>
<td>9,439,584</td>
<td>13,342,203</td>
<td>.</td>
<td>.</td>
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<tr>
<td>2001</td>
<td>442,486</td>
<td>.</td>
<td>.</td>
<td>10,757,315</td>
<td>14,562,918</td>
<td>.</td>
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<tr>
<td>2002</td>
<td>484,561</td>
<td>.</td>
<td>.</td>
<td>11,857,056</td>
<td>15,586,976</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2003</td>
<td>516,626</td>
<td>.</td>
<td>.</td>
<td>12,851,675</td>
<td>16,445,098</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2005</td>
<td>588,726</td>
<td>.</td>
<td>.</td>
<td>15,470,476</td>
<td>18,835,852</td>
<td>.</td>
<td>.</td>
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<tr>
<td>2006</td>
<td>597,756</td>
<td>.</td>
<td>.</td>
<td>15,991,419</td>
<td>18,801,665</td>
<td>.</td>
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<tr>
<td>2007</td>
<td>596,683</td>
<td>.</td>
<td>.</td>
<td>16,304,737</td>
<td>18,733,990</td>
<td>.</td>
<td>.</td>
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<tr>
<td>2008</td>
<td>591,497</td>
<td>.</td>
<td>.</td>
<td>16,618,138</td>
<td>18,298,064</td>
<td>.</td>
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<tr>
<td>2009</td>
<td>589,286</td>
<td>.</td>
<td>.</td>
<td>16,865,300</td>
<td>18,247,035</td>
<td>.</td>
<td>.</td>
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<tr>
<td>2010</td>
<td>609,820</td>
<td>.</td>
<td>.</td>
<td>17,770,443</td>
<td>18,681,155</td>
<td>.</td>
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<tr>
<td>2011</td>
<td>614,843</td>
<td>.</td>
<td>.</td>
<td>18,327,107</td>
<td>18,650,174</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2012</td>
<td>643,622</td>
<td>.</td>
<td>.</td>
<td>19,602,097</td>
<td>19,602,097</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2014</td>
<td>694,371</td>
<td>643,980</td>
<td>744,763</td>
<td>21,037,418</td>
<td>19,324,949</td>
<td>22,749,887</td>
<td>.</td>
</tr>
<tr>
<td>2015</td>
<td>718,078</td>
<td>645,821</td>
<td>790,335</td>
<td>21,669,511</td>
<td>19,309,150</td>
<td>24,029,872</td>
<td>.</td>
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<tr>
<td>2016</td>
<td>741,260</td>
<td>649,137</td>
<td>833,382</td>
<td>22,282,359</td>
<td>19,360,513</td>
<td>25,204,205</td>
<td>.</td>
</tr>
<tr>
<td>2019</td>
<td>809,422</td>
<td>668,121</td>
<td>950,724</td>
<td>24,083,673</td>
<td>19,829,435</td>
<td>28,337,912</td>
<td>.</td>
</tr>
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</table>
The total Medicare benefits paid for the 30192 item number in 1994 was $5.6 million and $19.6 million in 2012. This represents an increase of 250%. NSW and Queensland received the highest amount of benefits at $9 million and $5.6 million respectively) while NT received the lowest amount of Medicare benefits at $49 thousand (Figure 5).

**Discussion**

AK is a chronic disease. Patients with multiple AK require multiple treatment episodes. The number of item 30192 treatments for AK has increased by 160% since 1994 and is predicted to increase by a further 29% between 2012 to 2020. NMSC has similarly been increasing over time. During the period 2010 to 2015 AK is anticipated to increase by 17.8% compared with an increase in NMSC treatments of 22.3% which was predicted by Fransen et al. 14.

Interestingly, the rates of ablative treatment for premalignant lesions of the skin remained virtually stable during the period 2005 to 2009, whilst the rates for NMSC treatments continued to rise during this period. One possible explanation for the trend in AK billing treatments is the introduction of new field treatment options during this period. The Therapeutic Goods Administration approved PDT with Methyl aminolevulinate (Metvix®) for the treatment of AK in 2003 and Imiquimod (Aldara®) for treatment of AK in 2004.
Table 2. Number of AK treatments per 1,000 people for each Australian state.

<table>
<thead>
<tr>
<th>Year</th>
<th>NSW</th>
<th>VIC</th>
<th>QLD</th>
<th>SA</th>
<th>WA</th>
<th>TAS</th>
<th>NT</th>
<th>ACT</th>
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</thead>
<tbody>
<tr>
<td>1994</td>
<td>21.8</td>
<td>4.7</td>
<td>18.7</td>
<td>7.2</td>
<td>10.5</td>
<td>3.6</td>
<td>3.9</td>
<td>12.6</td>
</tr>
<tr>
<td>1995</td>
<td>23.3</td>
<td>5.1</td>
<td>19.7</td>
<td>7.9</td>
<td>11.5</td>
<td>3.9</td>
<td>3.8</td>
<td>12.2</td>
</tr>
<tr>
<td>1996</td>
<td>25.4</td>
<td>5.8</td>
<td>21.3</td>
<td>9.3</td>
<td>13.1</td>
<td>4.8</td>
<td>3.5</td>
<td>14.2</td>
</tr>
<tr>
<td>1997</td>
<td>26.4</td>
<td>5.7</td>
<td>22.4</td>
<td>9.2</td>
<td>12.4</td>
<td>5.3</td>
<td>3.0</td>
<td>14.7</td>
</tr>
<tr>
<td>1998</td>
<td>27.6</td>
<td>6.0</td>
<td>23.0</td>
<td>9.4</td>
<td>12.6</td>
<td>6.3</td>
<td>3.4</td>
<td>13.4</td>
</tr>
<tr>
<td>1999</td>
<td>30.7</td>
<td>6.4</td>
<td>24.7</td>
<td>9.8</td>
<td>12.1</td>
<td>6.7</td>
<td>3.0</td>
<td>14.5</td>
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<tr>
<td>2000</td>
<td>32.7</td>
<td>6.5</td>
<td>28.4</td>
<td>9.7</td>
<td>12.6</td>
<td>6.0</td>
<td>3.6</td>
<td>16.4</td>
</tr>
<tr>
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<td>35.5</td>
<td>7.1</td>
<td>33.8</td>
<td>11.5</td>
<td>13.7</td>
<td>6.3</td>
<td>4.4</td>
<td>17.5</td>
</tr>
<tr>
<td>2002</td>
<td>37.1</td>
<td>7.3</td>
<td>38.1</td>
<td>12.9</td>
<td>17.6</td>
<td>6.5</td>
<td>4.3</td>
<td>18.3</td>
</tr>
<tr>
<td>2003</td>
<td>38.9</td>
<td>7.7</td>
<td>40.7</td>
<td>12.7</td>
<td>19.4</td>
<td>6.4</td>
<td>3.7</td>
<td>17.1</td>
</tr>
<tr>
<td>2004</td>
<td>41.6</td>
<td>8.6</td>
<td>43.7</td>
<td>14.1</td>
<td>21.5</td>
<td>7.4</td>
<td>4.3</td>
<td>15.9</td>
</tr>
<tr>
<td>2005</td>
<td>42.4</td>
<td>9.5</td>
<td>44.6</td>
<td>15.7</td>
<td>22.4</td>
<td>8.3</td>
<td>3.8</td>
<td>14.3</td>
</tr>
<tr>
<td>2006</td>
<td>42.3</td>
<td>10.1</td>
<td>43.5</td>
<td>16.2</td>
<td>23.0</td>
<td>9.1</td>
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<td>2007</td>
<td>41.2</td>
<td>10.6</td>
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<td>23.0</td>
<td>10.6</td>
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<tr>
<td>2008</td>
<td>39.8</td>
<td>10.4</td>
<td>40.5</td>
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<td>22.9</td>
<td>9.9</td>
<td>3.7</td>
<td>13.0</td>
</tr>
<tr>
<td>2009</td>
<td>38.6</td>
<td>10.6</td>
<td>39.9</td>
<td>14.0</td>
<td>22.2</td>
<td>9.4</td>
<td>4.3</td>
<td>13.2</td>
</tr>
<tr>
<td>2010</td>
<td>39.1</td>
<td>11.1</td>
<td>40.9</td>
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<td>22.2</td>
<td>9.3</td>
<td>6.0</td>
<td>12.5</td>
</tr>
<tr>
<td>2011</td>
<td>39.0</td>
<td>11.6</td>
<td>39.5</td>
<td>15.6</td>
<td>21.8</td>
<td>9.9</td>
<td>5.8</td>
<td>12.9</td>
</tr>
<tr>
<td>2012</td>
<td>40.0</td>
<td>12.6</td>
<td>40.0</td>
<td>16.6</td>
<td>21.8</td>
<td>10.2</td>
<td>6.5</td>
<td>13.8</td>
</tr>
</tbody>
</table>

Topical 5-FU and PDT are funded by the RPBS but not the PBS for the treatment of AK in repatriation members\(^\text{15}\). The contribution of these agents to the overall cost to Government of treatments of premalignant skin conditions is therefore negligible.

Also notable is the significantly higher number of AK treatment services, provided by NSW compared to Queensland. This is particularly surprising as the number of NMSC treatments recorded in Queensland continued to increase at a faster rate and the number of NMSC treatments was greater than in NSW after 2011\(^\text{10}\).

Northern Territory (NT) had the lowest number of AK treatments per 1,000 a figure that was comparable to treatment numbers seen in Tasmania. It was expected that the number of AK treatments per head would have been similar to that of Queensland because of the association between AK and ultraviolet (UV) light and the higher levels of UV exposure in NT. Aboriginal and Torres Strait Islanders make up 30% of the population in the NT\(^\text{16}\). Although there is limited literature on the incidence of AK in the Indigenous population\(^\text{17}\), it is likely that the incidence of AK would be less that the Caucasian population as the incidence rates of NMSC and melanomas are reduced in the Indigenous population\(^\text{17}\), however this still does not account for the lower than expected treatment numbers. Most of the NT is considered rural or remote under the Australian government’s remoteness classification\(^\text{18}\) and the AK treatment numbers may reflect the reduced access to healthcare in the NT. Furthermore, the lower number of AK treatments may also reflect the behavioural patterns of health seeking in populations living in remote areas.

There were three major limitations of the study. The data set did not include data on cryotherapy item numbers charged to the
Data availability
The data in this study and the study by Fransen et al. can be accessed via Medicare Australia Statistics. http://www.medicareaustralia.gov.au/statistics/mbs_item.shtml. The item number used was 30192; the dates used were 1994–2012.

Author contributions
The authors Eshini Perera and Rodney Sinclair were involved in writing and editing the draft of this manuscript. Sean McGuigan was responsible for the methodology and statistical calculations used in this manuscript. All authors of this research paper have directly participated in the planning, execution, or analysis of this study. All authors of this paper have read and approved the final version submitted.

Competing interests
No competing interests were disclosed.

Grant information
The author(s) declared that no grants were involved in supporting this work.

References


Open Peer Review

Current Referee Status:  

Version 1

Referee Report 12 August 2014
doi:10.5256/f1000research.4992.r5704

Giuseppe Argenziano
Department of Dermatology, Second University of Naples, Naples, Italy

This is an interesting study outlining the rising number of treatments of actinic keratoses (AK) and non melanoma skin cancers in Australia. The paper reads well and deals with an important issue.

It would be useful to understand whether the increasing number of treated AKs actually corresponds to a decrease of invasive squamous cell carcinomas. If this is not the case, then the burden and cost of AK treatment may be not completely justified. This issue should be shortly addressed in the discussion.

Please check in the abstract, results section, "...by 202" should read "2020".

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Competing Interests: No competing interests were disclosed.

Author Response 16 Aug 2014

Eshini Perera, The University of Melbourne, Australia

Thank you kindly for reviewing our article.

We have amended the article to include your suggestions:

- Incidence of SCC was briefly mentioned in the discussion. Unfortunately there is no recent data on the incidence of cutaneous SCC. There is also no data which was collected during the time frame of our study. The increasing number of AK treatments could not be correlated to the number of SCC.
- The abstract was corrected to read 2020.

Competing Interests: No competing interests were disclosed.

Referee Report 06 August 2014
doi:10.5256/f1000research.4992.r5703
Luigi Naldi
Department of Dermatology, Centro Studi GiSED, Bergamo, Italy

This is an interesting study dealing with the number of treatments reimbursed by Medicare for AK in Australia over time, and paralleling those treatments with number of treatments for SCC. As discussed by the Authors, the data presented have several limitations mainly connected with the nature of the claims data available (there is a lack of information on treatments of less than 10 AKs, and a lack of information on treatment modalities other than cryotherapy). In addition, a few points are worth of consideration:

- The Title does not accurately reflect the contents of the paper. I would change it to: “Costs for the treatment of AKs on the rise in Australia”
- The study is restricted to treatment of 10 or more AKs by cryotherapy. Is there any estimate of the number of treatments for modalities other than cryotherapy (including field therapy)?
- Is there any indication that some lesions were not treated at all?
- Were repeated treatments of the same lesions counted separately or did they simply sum up to the total?
- Introduction, 5th paragraph: what does “PBS” stand for?
- Methods, 3rd paragraph: as far as I understand the meaning, the reference should be to Figure 3 and not to Figure 1.
- Discussion, penultimate paragraph: “treatment of early treatment and prevention of AK is prudent” should read “treatment of early lesions and prevention of AK is prudent”

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Competing Interests: No competing interests were disclosed.

Author Response 16 Aug 2014
Eshini Perera, The University of Melbourne, Australia

Thank you for reviewing our article.
We have made the following changes to our article, as per your recommendation:
- The title was amended to reflect the content of the paper.
- There are no estimates for the number of treatments for modalities other than cryotherapy. This was mentioned in the article.
- It is possible that some lesions were not treated and this was mentioned in the article.
- It is possible that some lesions could have been treated twice and this was mentioned in the article.
- The 3rd paragraph in the methods section was amended so that the meaning reflected what was seen in Figure 1.
- The error in the discussion paragraph was corrected.

We thank you for your suggestions.
Competing Interests: No competing interests were disclosed.