

# The national Targeted Lung Health Checks programme: Focusing on the lungs does not mean missing adrenal lesions

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## ABSTRACT

Recently, the UK's national Targeted Lung Health Checks programme produced recommendations for the management of incidental findings identified during the scans performed as part of the lung cancer screening programme. We identified significant discrepancies between the recommendations for adrenal incidentaloma management and those currently implemented into UK practice (2016 European Society of Endocrinology guidelines).

This may create conflict and confusion between referrers (respiratory clinicians) and receivers (endocrinologists), with potential negative impact on patients, delay and inefficient use of resources. We also address the potential cost implications of adopting a more vigilant approach as advised by the European Society of Endocrinology.

Urgent multidisciplinary and unified guidelines should be established in the interest of clinical- and cost-effectiveness.

**KEYWORDS:** Adrenal, incidentaloma, lung cancer, screening

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The NHS Long Term Plan included the target that 'by 2028, the proportion of cancers diagnosed at stages 1 and 2 will rise from around half now to three-quarters of cancer patients'.<sup>1</sup> As a result, the national Targeted Lung Health Checks programme, offers the opportunity of a lung health check to individuals aged 55–74 years who have ever smoked.<sup>2</sup> The programme recently published its quality assurance standards, including action on incidental findings.<sup>2</sup>

Among those, adrenal incidental findings were included with the advice that, apart from lesions smaller than 1 cm, all other lesions require review at the 'screening review meeting'. When reviewed

in the meeting, the recommendation is that lesions <1 cm or <10 Hounsfield units (HU), no further action is required. For lesions 1–4 cm and >10 HU, no action is warranted but for a repeat scan in 12 months. Lesions >4 cm need to be referred to endocrinology.<sup>2</sup>

These recommendations contradict the recently published European Society of Endocrinology (ESE) guidelines that are widely used in the UK.<sup>3</sup> According to these, all patients with adrenal incidentaloma >1 cm should have excess cortisol and catecholamines investigated (via overnight dexamethasone suppression test together with plasma metanephrines or urinary fractionated metanephrines). In addition, patients with hypertension or unexplained hypokalaemia will require aldosterone excess explored with aldosterone:renin ratio. Furthermore, measurement of sex hormones and steroid precursors is recommended if there are manifestations suggestive of adrenocortical cancer (clinical or radiological).<sup>3</sup>

Furthermore, the ESE recommends that the density and homogeneity of an adrenal lesion is assessed on non-contrast computed tomography (CT). If the lesion is lipid-rich (<10 HU) and is <4 cm in size, then no further imaging is required. However, if indeterminate on non-contrast CT (ie >10 HU), with no evidence of hormone over-production, a multidisciplinary team (MDT) meeting should decide, with the clinical context, whether to proceed with further imaging, arrange interval non-contrast CT or magnetic resonance imaging (MRI) in 6–12 months or refer for surgery.<sup>3</sup>

Accordingly, the NHS lung cancer programme risks overlooking whether lesions between 1–4 cm are associated with hormone excess, or indeed whether they are malignant (either primary or metastatic). In lung cancer patients, 4% had adrenal incidentalomas, with almost three-quarters being metastatic; only ~25% were benign adenomas.<sup>4</sup> Based on this, lesions >1 cm with density >10 HU should not be left merely to have repeat CT in 12 months. Expert adrenal MDTs could have an important role of providing recommendations on which patients should undergo further investigations in an endocrine centre. Establishing tumour functionality, together with considering the risk of malignancy in this category (1–4 cm with HU of >10) is crucial. In addition to the potential for these missed cases, the conflicting guidance will create confusion in clinical practice.

While more than 80% of adrenal incidentalomas are non-functioning, the commonest functional abnormality is excess cortisol in >10% of cases.<sup>3</sup> A 15-year retrospective study demonstrated that, even with subclinical hypercortisolism, adrenal incidentalomas patients had an increased cardiovascular morbidity and mortality.<sup>5</sup> More recently, a prospective cohort

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study revealed that the frequency of adrenal incidentalomas was 7.3%, significantly higher than previous reports. With multivariate regression analysis, diabetes was significantly associated with the presence of adrenal incidentalomas ( $p=0.003$ ). Failure to suppress in overnight dexamethasone suppression test was observed in 50% of patients; again, significantly higher than the previously reported incidence of ~10%. The study did not have ascertainment bias as the prospectively drawn adrenal incidentalomas cohort had the same risk of diabetes similar to the general population.<sup>6</sup> While less common, hyperaldosteronism and particularly pheochromocytoma have serious morbidity and mortality implications, so cannot be ignored. They could be associated with lesions <4 cm.

We want to emphasise that this will apply to individuals who have screened negative for lung cancer. The management would potentially be different if lung cancer is detected. In these cases, close interaction between the lung and adrenal MDTs will be required.

Paradoxically, it would be important to recognise that the caseload generated through this programme is not insignificant. This proactive programme is targeting individuals aged 55 years and above where adrenal incidentaloma prevalence rises, from being rare in children to ~3% at 50 years and 10% in the elderly.<sup>7</sup> Planning for this increased workload should be considered from the outset, acknowledging that current guidelines on adrenal incidentalomas rely mostly on large case series with limited systematic data and cost-effectiveness analysis. To address this gap, we have recently developed a cost-effectiveness tool for adrenal incidentaloma management.<sup>8</sup> We have initiated discussions with the lung cancer screening programme to support their efforts in establishing a clinically- and cost-effective strategy to address adrenal incidentalomas. Such initiatives are essential if the NHS is to address this potential clinical risk. ■

## References

- 1 NHS England. *The NHS Long Term Plan*. NHS, 2019. [www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf](http://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf)
- 2 NHS England. *Targeted screening for lung cancer with low radiation dose computed tomography: quality assurance standards prepared for the Targeted Lung Health Checks programme*. NHS, 2020. [www.england.nhs.uk/wp-content/uploads/2019/02/targeted-screening-for-lung-cancer-quality-assurance-standard.pdf](http://www.england.nhs.uk/wp-content/uploads/2019/02/targeted-screening-for-lung-cancer-quality-assurance-standard.pdf) [Accessed 21 January 2020].
- 3 Fassnacht M, Arlt W, Bancos I *et al*. Management of adrenal incidentalomas: European Society of Endocrinology clinical practice guideline in collaboration with the European Network for the study of adrenal tumors. *Eur J Endocrinol* 2016;175:G1–34.
- 4 Gillams A, Roberts CM, Shaw P, Spiro SG, Goldstraw P. The value of CT scanning and percutaneous fine needle aspiration of adrenal masses in biopsy-proven lung cancer. *Clin Radiol* 1992;46:18–22.
- 5 Di Dalmazi G, Vicennati V, Garelli S *et al*. Cardiovascular events and mortality in patients with adrenal incidentalomas that are either non-secreting or associated with intermediate phenotype or subclinical Cushing's syndrome: a 15-year retrospective study. *Lancet Diabetes Endocrinol* 2014;2:396–405.
- 6 Reimondo G, Castellano E, Grosso M *et al*. Adrenal incidentalomas are tied to increased risk of diabetes: findings from a prospective study. *J Clin Endocrinol Metab* 2020;105:dgz284.
- 7 Mansmann G, Lau J, Balk E *et al*. The clinically inapparent adrenal mass: update in diagnosis and management. *Endocr Rev* 2004;25:309–40.
- 8 Hanna FWF, Issa BG, Lea S *et al*. Adrenal lesions found incidentally; how to improve clinical and cost-effectiveness. *BMJ Open Qual* 2020;9:e000572.

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