

Supplementary Material

Delivering Low-dose CT Screening for Lung Cancer: A Pragmatic Approach

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The SUMMIT Study Pulmonary Nodule and Incidental Finding Management Protocol

The SUMMIT Pulmonary Nodule Protocol

This protocol is based largely on the British Thoracic Society Guideline for the Investigation and Management of Pulmonary Nodules(1). The SUMMIT guidelines have been adapted to a three-year screening programme [baseline (Y0), year 1 (Y1), and year 2 (Y2)] with a randomisation element at the second visit (Y1). Deviations or additions to the BTS guidelines are denoted in **bold** boxes. Evidence for these changes are cited in call-outs at the bottom of each protocol (*, § etc) and incorporate best practice recommendations from the Fleischner Society (2,3).

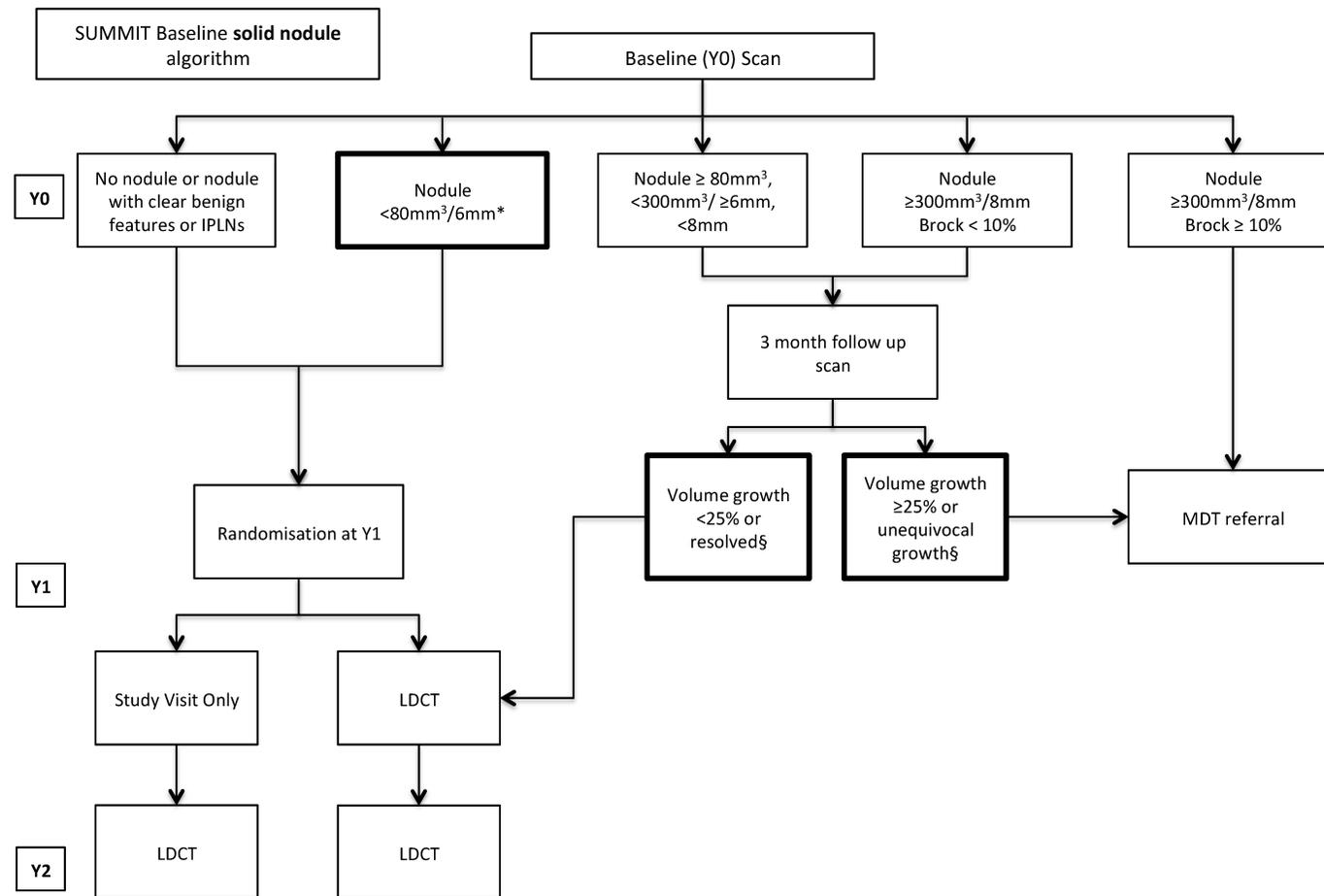
Some general principles when using this protocol:

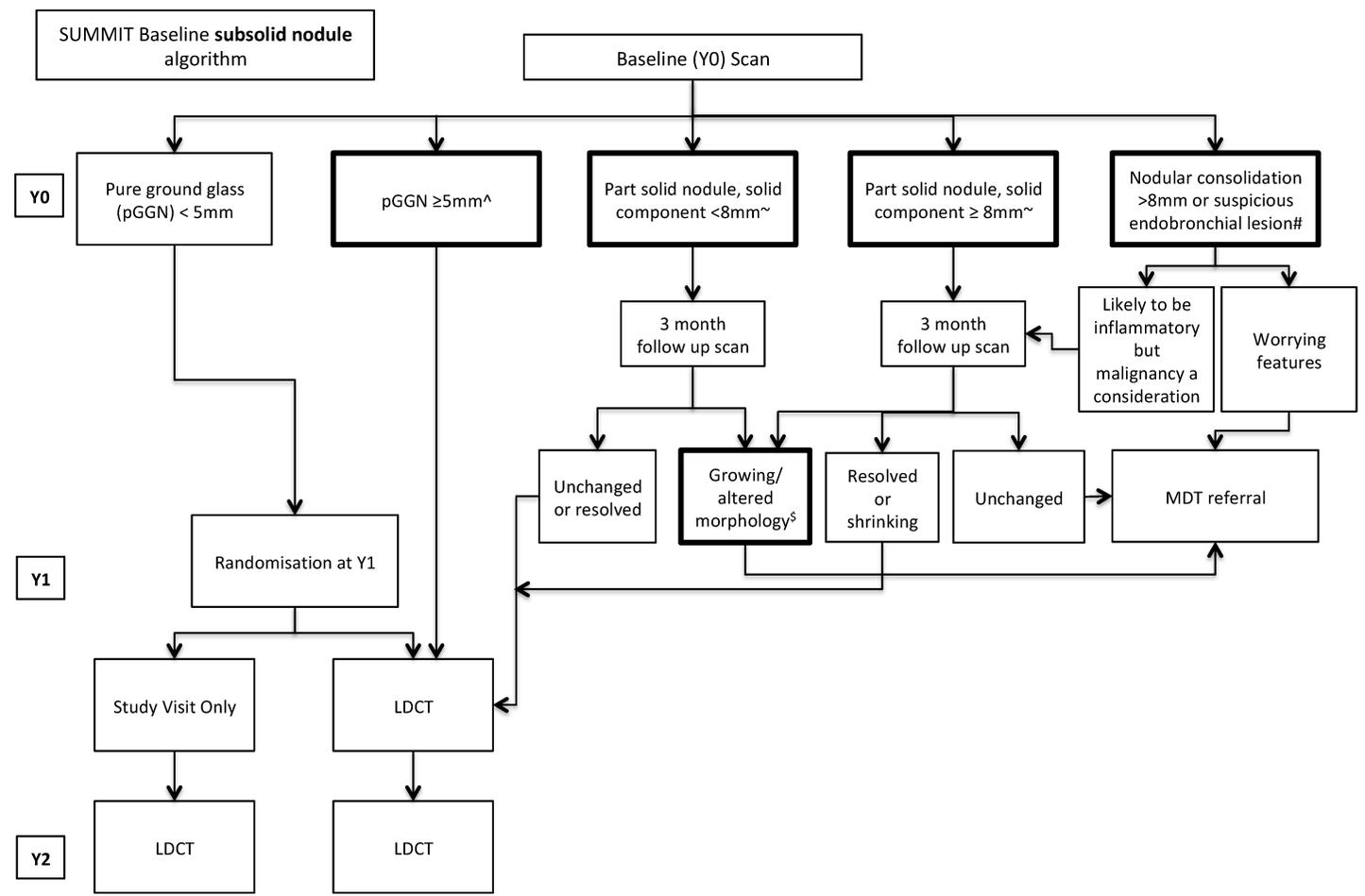
- Overall management is based on the largest nodule, or the nodule requiring most immediate follow-up.
- At any time point, radiologists can upgrade to next level of management if nodules are felt to have suspicious features and recommended management is felt not to be sufficient.
- Growing solid nodules should be $>200\text{mm}^3$ (or 8mm in diameter if unreliably segmented) before referral to multidisciplinary teams (MDTs) in order to prevent unnecessary referrals to secondary care sites. This is because for smaller nodules, MDTs are likely to recommend surveillance CT anyway, in which case this is best delivered within the screening programme. For nodules that have volumetrically grown $\geq 25\%$ at 3 months but are $\leq 200\text{mm}^3$, and nodules with unreliable volumetry that appear to have equivocally grown on visual inspection, a repeat CT in 3 months is performed within the study.
- In cases where volumetry is not possible for a solid nodule and diameter measurements are made, assessment should be based on unequivocal growth (as per BTS Guidelines).
- For sub-solid nodules (SSNs), 'growing morphology' refers to a new or increasing solid component. SSNs with 'altered morphology' refers to bubble-like lucencies or pleural retraction. If the solid component grows but is still $<8\text{mm}$, then the increase should be at least 2mm since the previous LDCT or observed on two CTs before MDT referral.
- Nodular consolidation $>8\text{mm}$ or endobronchial lesions or other nodules $>8\text{mm}$ that appear more likely to be inflammatory, but where malignancy is a consideration, may be scanned again at three months. If unchanged or growing at the follow-up scan, these should be referred to MDT. Opacities that are clearly

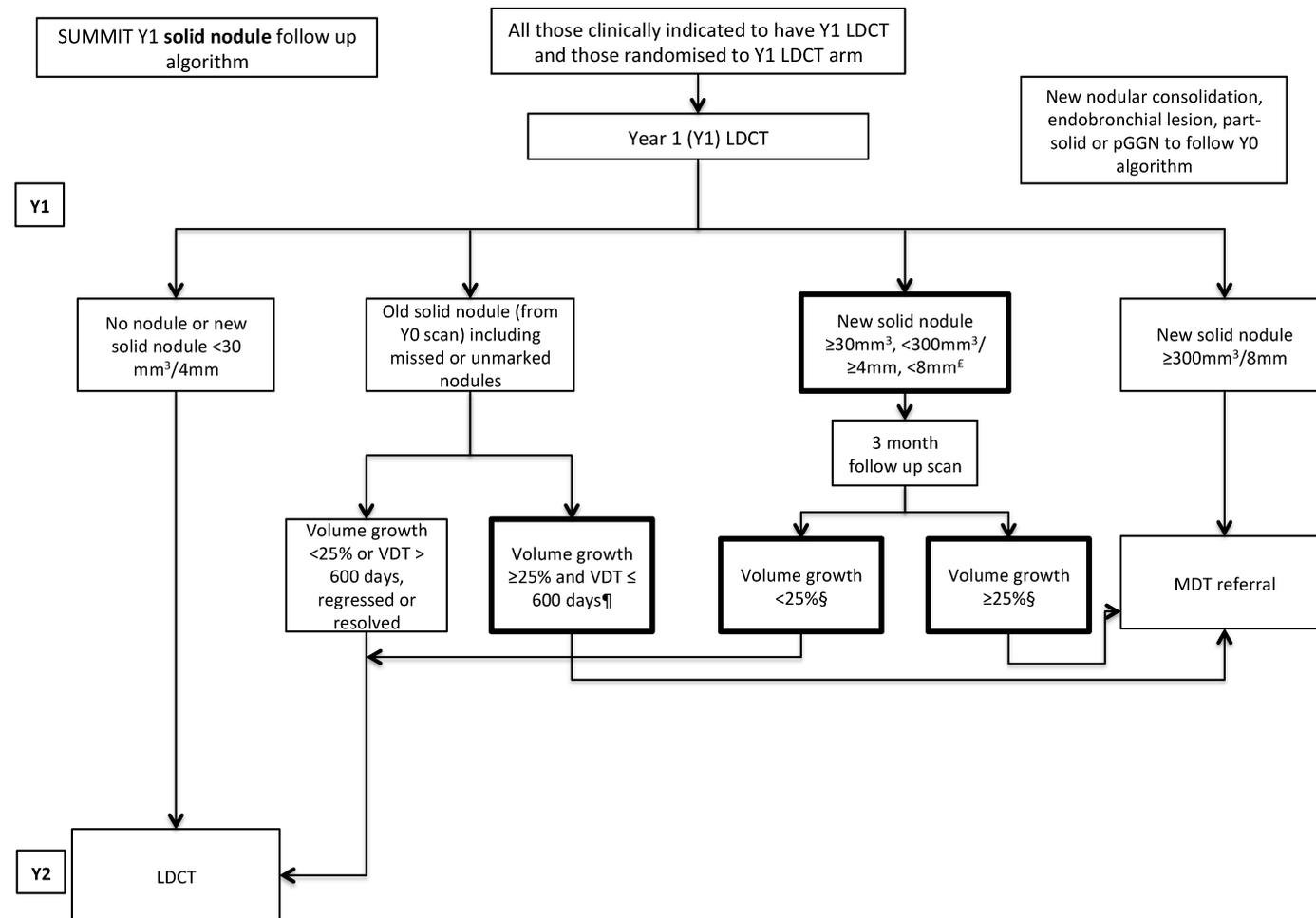
inflammatory (eg tree-in-bud or endobronchial mucous) and where malignancy is not a consideration do not require follow up.

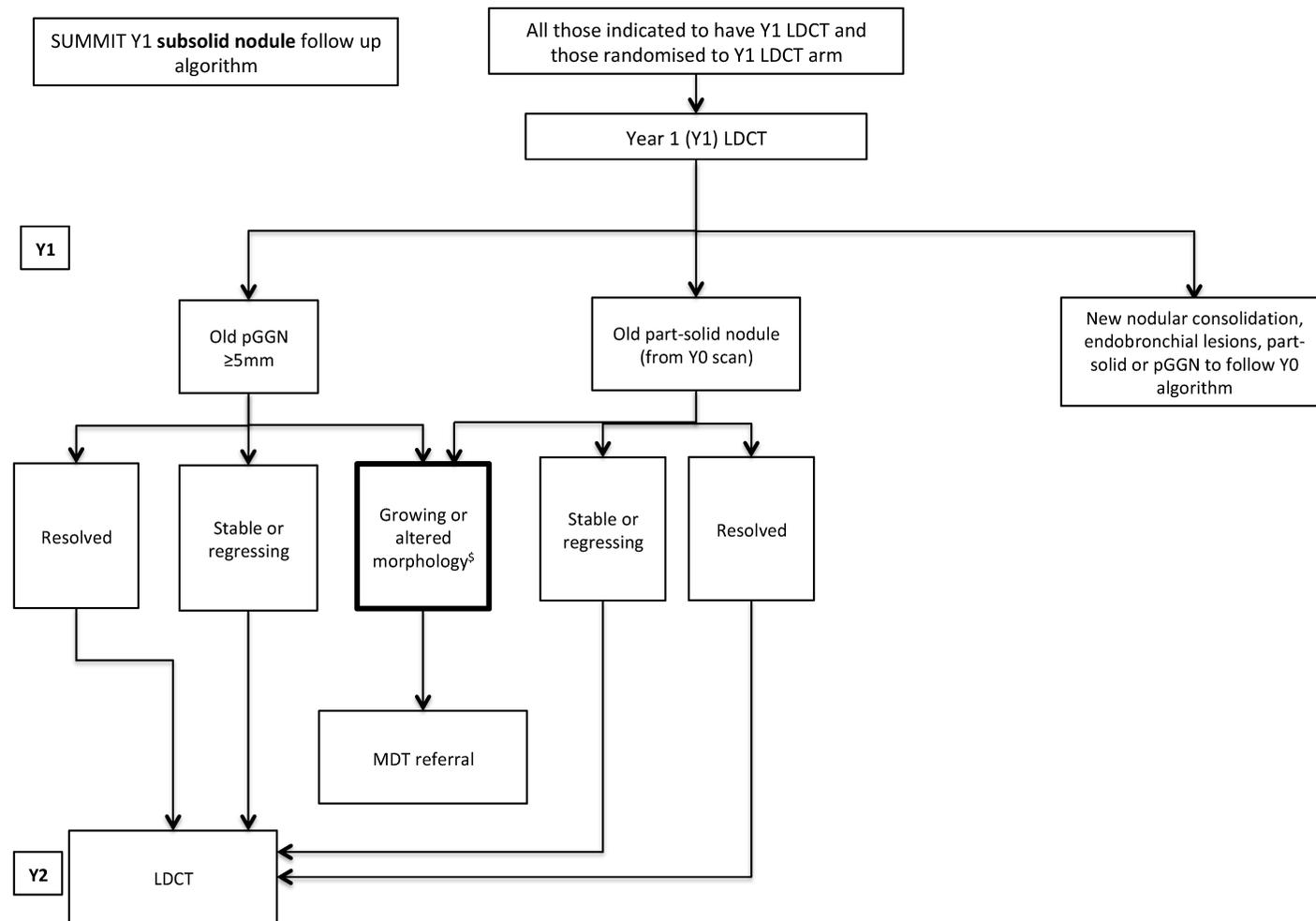
- If a part solid nodule has a solid component that is >90% of the total nodule size, then this nodule is considered solid and is assessed as such(4).
- Intrapulmonary lymph nodes (IPLNs), also known as perifissural nodules, are nodules with specific benign characteristics, including triangular or lentiform shape, often attached to a fissure. Nodules with these characteristics are highly unlikely to be malignant, and therefore can be marked and tagged with the appropriate classifier, but do not affect management and do not confer any follow-up requirement(5). This approach is consistent with BTS guidelines.

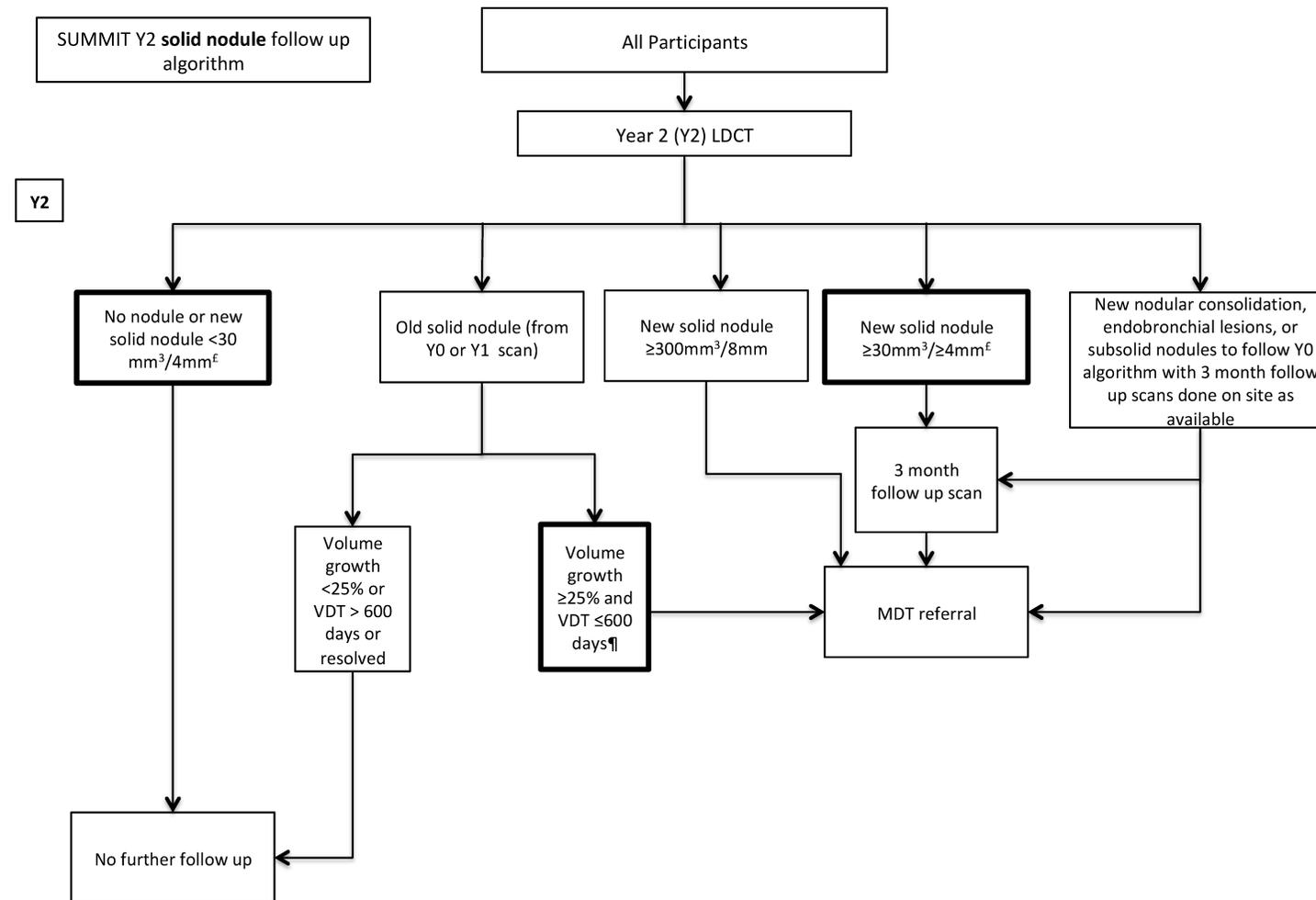
Figure S1—SUMMIT Pulmonary Nodule Protocol Flow Diagrams

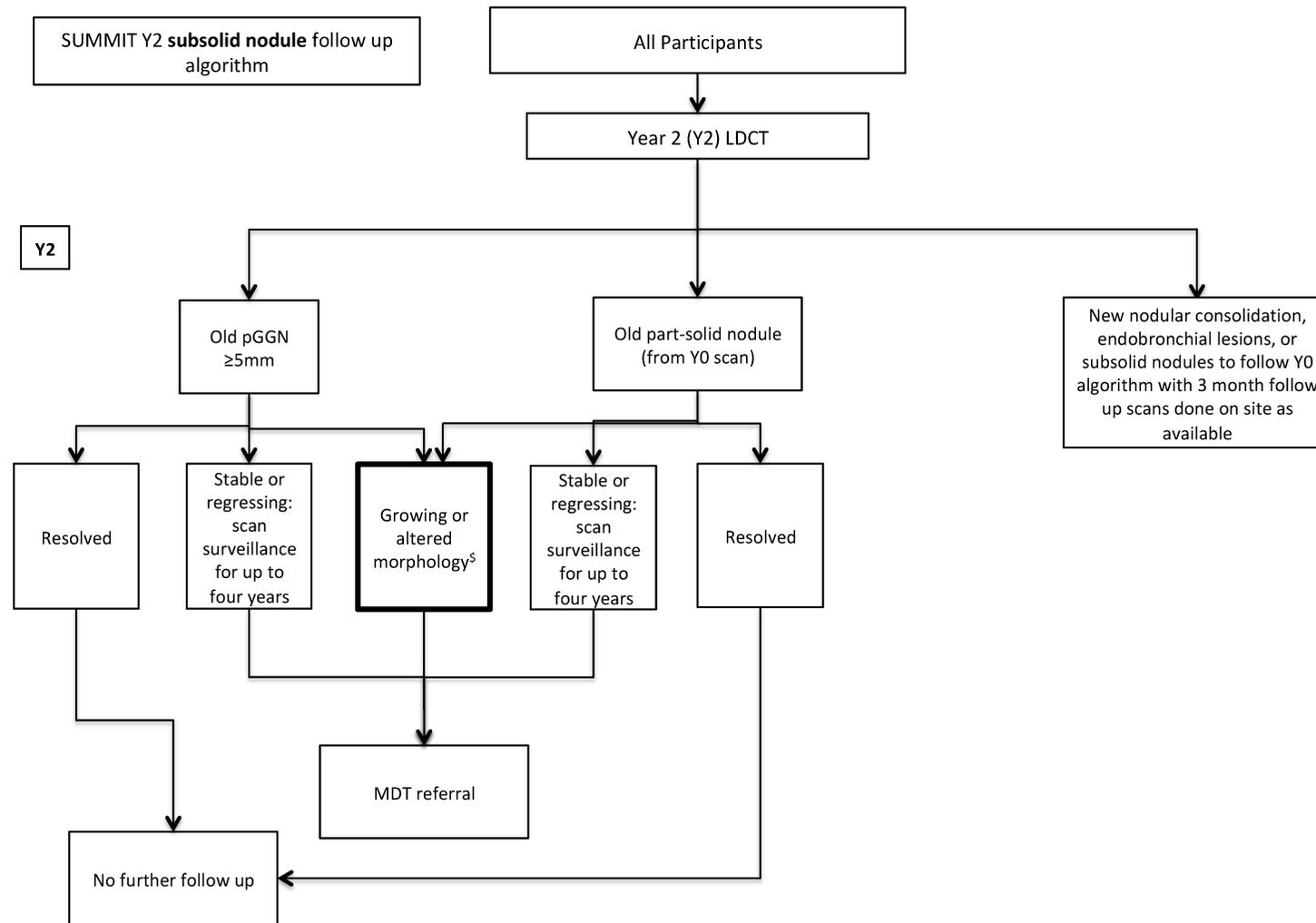












KEY

* Deviation from BTS: no provision for nodules 5-6mm in diameter (where volume not measured) to have 12 month follow up. These will be randomised at Y1 to annual or biennial scans.

§ Simplification of BTS: Volume doubling time (VDT) is not used for growth assessments at 3 month follow up for new or baseline nodules, as $\geq 25\%$ growth at 3 months implies a VDT of less than 400 days. If volume growth is $\geq 25\%$ but the nodule still has a volume $\leq 200\text{mm}^3$, a repeat scan within the study is indicated, as an MDT referral for a nodule of that size is likely only to instigate further surveillance, which can take place within the study.

^ Deviation from BTS: GGNs $\geq 5\text{mm}$ in diameter will be scanned at Y1 and Y2 for monitoring, but not before. Data has shown that GGNs, if persistent, are likely to represent adenocarcinoma in situ (AIS) and are therefore unlikely to require immediate intervention (4,6).

~ Deviation from BTS: The Brock Score is not used for assessing PSNs, due to its likelihood of underestimating malignancy in this nodule type. Instead, a distinction has been made regarding the solid component diameter ($< 8\text{mm} \geq$) to try to minimise unnecessary referrals to MDTs, for nodules with small solid components that are stable, and may represent indolent or overdiagnosed cancers. For PSNs with larger solid components that persist, referral to MDT is indicated.

Addition to BTS: Opacities that are clearly inflammatory (eg tree-in-bud or endobronchial mucous) and where malignancy is not a consideration do not require follow up. Nodular consolidation $> 8\text{mm}$ or endobronchial lesions or other nodules $> 8\text{mm}$ that appear more likely to be inflammatory, but where malignancy is a consideration, may be scanned again at three months. If these nodules remain unchanged or are growing at the follow-up scan, they should be referred to MDT. Such opacities if $< 8\text{mm}$ should follow the normal nodule algorithm.

\$ Addition to BTS: 'Growing morphology' refers to a new or increasing solid component. SSNs with 'altered morphology' refers to bubble-like lucencies or pleural retraction. If the solid component grows but is still $< 8\text{mm}$, then the increase should be at least 2mm since the previous LDCT or observed on two CTs before MDT referral, as a repeat surveillance scan is the most likely outcome from MDT for a nodule of this size, and this can be performed within the study.

£ Addition to BTS for a screening programme: new nodules which have developed since the previous annual scan should have a lower threshold ($\geq 30\text{mm}^3$ or 4mm diameter) for follow up, due to increased likelihood of malignancy (7).

¶ Deviation from BTS: VDT is applied at annual follow up scans and compared to baseline (or Y1) scans, as per BTS. VDT \leq 600 days and volume growth of \geq 25% is required for MDT referral to be made.; BTS has two VDT cut-offs (400 days and 600 days), which we have amalgamated into one cutoff for simplicity.

The SUMMIT Study Incidental Findings Management Protocol

The SUMMIT Study Incidental Findings Management Protocol was developed using guidelines and evidence available at the time of protocol development (2018). Where evidence or guidelines were not available, expert opinion was sought. The table below captures the clinically actionable findings that we are either following up within the study, or are asking that primary or secondary care colleagues follow up, where appropriate. Other data points, not listed here, are being collected for research purposes only, for example coronary artery calcification (CAC) and emphysema, as described in the main article text.

Table S1—SUMMIT Actionable Incidental Findings Protocol

Condition/finding	Description	Action by	Recommended action	Rationale
Lung cancer	Abnormality suggestive of lung cancer including consolidation and pleural thickening with worrying features, or unilateral pleural effusion.	Study team	Urgent referral to local lung cancer MDT.	Routine standard of care
Other cancer (non-lung)	Abnormality suggestive of cancer (non-lung) including breast lesions requiring triple assessment	Study team	Urgent referral to local site-specific cancer MDT.	Routine standard of care
Emphysema and COPD	Evidence of airflow limitation on pre-bronchodilator spirometry (FEV ₁ /FVC<70%) who are not known to have COPD and report persistent chronic cough (duration > 6 weeks) and/or breathlessness (MRC score >1)	GP	Clinical review and consider post bronchodilator spirometry assessment for COPD.	NICE guidelines (8)
Bronchiectasis	Severe = luminal diameter relative to the accompanying artery diameter is greater than three times the size.	GP	Clinical review and if symptomatic a non-urgent referral to the local respiratory team.	Relationship between bronchiectasis imaging and disease severity(9)
Interstitial lung	>10% reticulation with fibrotic features i.e. traction	GP	Clinical review and non-urgent referral to local	ILD studies

disease	bronchiectasis, as this denotes significant degree of ILD that may be clinically significant.(10,11)		respiratory team.	(10,11) Specialist opinion
Diffuse Pleural Thickening	Diffuse pleural thickening without overtly worrying features.	Study team	Annual scan within the study.	Specialist opinion
Bilateral pleural effusions	Bilateral pleural effusions.	GP	Participant and GP informed of finding and a recommendation made to investigate further for transudative causes, as per British Medical Journal (BMJ) article.	BMJ(12)
Lower respiratory tract infection (LRTI)	Self-reported acute (or deterioration in chronic) cough <3 weeks duration plus one or more of; fever, pleuritic pain, increased sputum production, shortness of breath or wheeze OR currently taking antibiotics prescribed for LRTI.	Study team	Delay study enrolment and LDCT by 6 weeks on one occasion only. Advise individual to seek review by usual pathway e.g. GP where required for antibiotic treatment if concerned.	SIGN guidelines (13)
Anterior mediastinal mass (suspected thymoma)	<3cm maximum diameter	Study team	Annual scan within study. Inform participant and GP. If stable on successive scans no further action.	ACR White Paper(14)
	≥3cm maximum diameter at baseline, OR <3cm but growing on successive scans OR with suspicious features (invasion, irregularity) OR changing morphology.	Study team	Urgent referral to local lung cancer MDT.	
Ascending thoracic aortic dilatation	<4cm	N/A	No further action required.	ACR Paper(15)
	≥4cm <5.5cm	GP	Non-urgent referral to cardiology team.	
	≥5.5cm	Study team	Urgent referral to local cardiothoracic team.	
Thyroid nodules	Punctate calcification or associated with local lymphadenopathy.	GP	Request outpatient ultrasound scan of neck.	ACR White Paper(16), specialist opinion
Adrenal opacities	<1cm	N/A	No action required.	NLST (17), ACR White Paper (18)
	1-4cm or Hounsfield Units (HU)>10	Study team	Annual scan within study. Inform participant and GP. If stable on successive scans no further action.	

	>4cm	Study team	Refer to local endocrine team.	
Abdominal aortic dilatation	<3cm	N/A	No action required.	NICE guideline(19)
	≥3cm <5cm	GP	Refer to local vascular team for surveillance.	
	≥5cm	Study team	Urgent referral to local vascular team for assessment.	
Abdominal solid organ abnormalities (kidney, liver, spleen)	Case by case basis. Radiologists are encouraged only to refer renal lesions if HU>10 (20) or if very likely to be abnormal (21).	Study team	Any abnormalities will be managed on a case by case basis.	NELSON (21), ACR White Paper (20)
Osteoporotic (wedge) vertebral fracture(s)	If reduction in height is >50% normal	GP	Refer for bone density assessment.	Specialist opinion
Additional notes				
<ul style="list-style-type: none"> - Where the reporting radiologist has a high index of suspicion for cancer, but the study management protocol does not lead to an automatic urgent referral, they have the ability to override the protocolised management plan and the study team will arrange the relevant urgent referral. - As this is a lung cancer screening programme, every attempt is made to limit the images to the thoracic cavity in order to decrease detection of clinically uncertain incidental findings, and to decrease radiation exposure to non-relevant areas - Any emergency or very urgent findings will be managed by the study team on a case by case basis according to local services 				

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