National Institute for Health and Clinical Excellence

Idiopathic Pulmonary Fibrosis
Guideline Consultation Comments Table
28.01.11 – 25.02.11

Type (NB this is for internal purposes – remove before posting on web)

SH = Registered Stakeholders. These comments and responses will be posted on the NICE website when the guideline is published.
PR = Peer Reviewers or Experts. These comments and responses will be posted on the NICE website when the guideline is published.
GRP = Guidelines Review Panel member. These are added to this table for convenience but will not be posted on the web.
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Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Pulmonary Fibrosis Yahoo Group and The Crackle Fund	1		General		We welcome this document.	Thank you for your comment.
SH	Pulmonary Fibrosis Yahoo Group and The Crackle Fund	2		3.1		Statistics published are out of date and too general	Thank you for your comment. These have been revised post consultation.
SH	Pulmonary Fibrosis Yahoo Group and The Crackle Fund	3		4.3.1.c		Some drugs on the list are used fro Pulmonary Hypertension and not for IPF.	The listed drugs are not licensed for IPF, but they are occasionally used in clinical practice and they have been subjected to clinical trials in IPF.
SH	R.C.G.P.	4		General		This is an excellent and unexceptional document. No changes would result in improvement. The authors are to be congratulated on a crystal clear, useful and practical paper.	Thank you for your comment.
SH SH	Association for Respiratory Technology and Physiology (ARTP)	5		4.2		We recommend that tertiary care is also included, as many tertiary centres operate specialist clinics looking after patients with IPF or see lots of these patients	Thank you for your comment. We have now revised this to "all settings"
SH	Association for Respiratory Technology and Physiology (ARTP)	6		4.3.1 (a)		Pulmonary Function tests should go into this section too, as together with imaging, these tests are key to accurate diagnosis of IPF	Thank your for your comment. This has been added.
SH	Association for Respiratory Technology and Physiology (ARTP)	7		4.3.1(b)		In pulmonary function tests, you mention spirometry and gas transfer measurement. We also recommend that measurement of lung volumes and its subdivisions (plethysmography or gas dilution) is	Thank you for your comment. The guideline will address the value of different lung function measurements in diagnosing diagnose IPF and will focus on those parameters which are relevant for clinical practice in

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						included. Lung volumes are essential (especially on initial presentation)l in determining if there is a restrictive defect, which might not be apparent during spirometry testing and may also aid in differentiating between chest wall or neuromuscular diseases, gas trapping or hyperinflation.	determining disease progression.
SH	Association for Respiratory Technology and Physiology (ARTP)	8		4.3.1(b)		We would also include simple exercise testing such as 6 minute walk test/shuttle walk test, to assess exercise tolerance and to monitor oxygenation during exercise	Thank you for your comment. This has been revised to now say "such as the 6 minute walk test"
SH	Association for Respiratory Technology and Physiology (ARTP)	9		4.3.1 (d)		Non invasive ventilation (NIV) may be used in some cases of IPF	Thank you for your comment. We agree and have added this to the scope.
SH	Association for Respiratory Technology and Physiology (ARTP)	10	7	4.4a		Would recommend using spirometric indices (FEV1, FVC, VC, FEV1/FVC, FEV1/VC). FEV/FVC ratios are useful in differentiating between obstructive and restrictive disorders. Shape of flow-volume curves are also recommended Also lung volume measurement (i.e Total lung capacity (TLC) may be a better measurement of assessing lung capacity, as discussed above	Thank you for this helpful information. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.
SH	Association for Respiratory Technology and Physiology (ARTP)	11		4.4b		We recommend that TLco, is standardised for the patients [Hb] where possible , especially if the [Hb] is abnormal In addition to TLco, Kco is an important measurement in patients with IPF, In early IPF, Kco may be preserved.	Thank you for this helpful information. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.
SH	Association for Respiratory Technology and Physiology (ARTP)	12		4.2		All pulmonary function labs performing tests should have qualified competent staffing and also have a quality control/assurance programme in place to ensure accurate and reproducible results are obtained.	Thank you for your comment.
SH	The British Lung Foundation	13		General		The British Lung Foundation welcome the development of a clinical practice guideline for	Thank you for your comment.

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						Idiopathic Pulmonary Fibrosis (IPF).	
SH	The British Lung Foundation	14		3.1 (b)		Consultation with our experts has revealed that the evidence that smoking is a risk factor for Idiopathic Pulmonary Fibrosis is weak and inconsistent. There are however, stronger links between geographic region and occupations history, along with diabetes and reflux.	Thank you for your comment. The potential risk factors for IPF are not specifically in the remit of the guideline. We have revised this section to state 'smoking is probably a risk factor'.
	The British Lung Foundation	15		3.1 (c)		With reference to the median age of presentation being 68 years, our experts have noted that the median age is nearer 70+ years rather than 68.	Thank you for your comment. We agree and have revised this in the scope.
SH	The British Lung Foundation	16		3.1 (d)		With reference to the incidence of IPF, the British Lung Foundation believe that it is important to stress that incidence is increasing rapidly over time. Up to date figures show that current incidence is 8-9 per 100,000 per annum.	Thank you for your comment. We agree and have revised this in the scope.
SH	The British Lung Foundation	17		3.2 (c)		Our experts have noted that the evidence underpinning N-acetyl cysteine has been under reported in the draft scope. The British Lung Foundation recommend that rather than stating that N-acetyl cysteine may be beneficial, there is the following: When N-acetyl was used in association with steroids and azathioprine, it was associated with a slower rate of decline in lung function. The British Lung Foundation recommend that the scope has more emphasis on the importance and effectiveness of N-acetyl cysteine.	Thank you for your comment. We have revised this section in the scope to state: 'Currently, there is no proven effective drug therapy for IPF. Corticosteroids and azathioprine are often used. A recent trial suggests the addition of N-acetylcysteine to prednisilone and azathioprine may slow the rate of disease progression more than prednisolone and azathioprine alone'.
SH	The British Lung Foundation	18		3.2 (e)		Following consultation with our experts, there is evidence to show that this statement is not correct; there has never been a trial of transplantation. In people diagnosed under 65 (the potential transplant population), median survival is greater than 5 years which is similar to post transplant figures. Further, more research and help is required to transplant rapid decliners.	Thank you for your comment. This section has been revised to indicate that lung transplantation is a valuable resource for selected patients.
SH	The British Lung Foundation	19		3.2 (f)		Regarding pulmonary rehabilitation services, the service would be improved by the development of	Thank you for your comment.

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						multi-disciplinary teams.	
SH	The British Lung Foundation	20		4.3.1		The British Lung Foundation recommend that within this section, there is a section on co-morbidity; people with IPF have a ten-fold increase in the risk of lung cancer and a three-fold risks of acute coronary syndromes. There are important aspects of care.	Thank you for your comment. Patients with IPF are treated in a similar way to patients with background COPD or emphysema, weighing up the risks and benefits with the patient of chemotherapy, radiotherapy or surgery. Given this, we do not consider it to be a high priority for inclusion in the IPF guideline. Please refer to the recently published NICE update guideline on lung cancer available on http://guidance.nice.org.uk/CG24.
SH	The British Lung Foundation	21		4.3.1		The British Lung Foundation also recommend that the development of a national trial network is a priority.	Thank you for your comment. The development of a national trial network is outside of the remit of the guideline**.** Recommendations on how care should be delivered will be developed
SH	The British Lung Foundation	22		4.3.1		The British Lung Foundation recommend that there is an exploration of the role of interstitial lung disease nurses in supporting patients with IPF.	Thank you for your comment. A specific question on the role of interstitial lung disease nurses in supporting patients with IPF will not be addressed in the guideline. evidence will be reviewed on how care should be delivered and this may include the specialist nurse as part of a multidisciplinary team.
SH	Royal College of Nursing	23		General		The Royal College of Nursing welcomes proposals to develop this guideline. It is timely.	Thank you for your comment.
SH	Royal College of Nursing	24		4.3.1a		It needs to be made clear that there will be some patients for whom the diagnosis may not be clear, even when discussed at an MDT, with a biopsy/CT.	Thank you for your comment. The GDG will consider this when reviewing the evidence and developing recommendations.
SH	Royal College of Nursing	25		4.3.1c		Related to comment 2 above, other treatments not due to be considered in this guideline i.e. cyclphosphamide may have a place, especially as some people with connective tissue disease may represent with a UIP pattern in the absence of other manifestations of joint disease.	Thank you for your comment. People with IPF as a complication of connective tissue disease will not be covered as part of the scope of this guideline, and cyclophosphamide has not been considered a high priority treatment option for IPF.
SH	Royal College of Nursing	26		4.3.1c		Given the poor prognosis of this condition and the lack of a really effective treatment, other treatment options may be considered by the treating clinician and patient weighing up potential risks and benefits.	Thank you for your comment.
SH	Royal College of Nursing	27		4.3.1c		Given comments 2-4 above, research/ trial participation into all aspects of this condition are encouraged.	Thank you for your comment. The development of a national trial network is outside of the remit of the guideline**.** Recommendations on how care should be delivered will be developed

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SH	Royal College of Nursing	28		4.3.2c		To clarify the place in the management of IPF it would be beneficial for the developers to consider alternative drugs prescribed for IPF, such as, warfarin and cyclophosphamide	Thank you for your comment. We have added warfarin to the scope of the IPF guideline. Cyclophosphamide has not been considered a high priority treatment option for IPF.
SH	Royal College of Nursing	29		4.3.2e		Due to the unlicensed nature of all the medicines prescribed for IPF the SPC for individual drugs will not be helpful to inform prescribers' decisions for individual patients. N-acetylcysteine is not licensed for any indication in the UK and therefore there is not a SPC available. We would suggest the review of this statement.	Thank you for your comment. This statement is a standard statement included in NICE guidelines. However, if good evidence exists for unlicensed treatments these treatments will be included in the review of evidence.
SH	InterMune	30		3.2c		Will the guideline aim to differentiate which particular sub-groups of patients with IPF will benefit from a particular treatment or no specific therapy? See also comments for section 4.1.1b	Thank you for your comment. The GDG will consider which subgroups will benefit from particular therapies when developing the clinical questions to inform the evidence reviews.
SH	InterMune	31		3.2d		Pirfenidone is an emerging therapy for IPF and will be reviewed by NICE in an STA process. The timelines for publication of the STA is unknown at present but may be available before the publication for the Clinical Guideline (publication date May 2013). Will the results of the STA therefore be incorporated or will the CG group be considering the place of pirfenidone separately?	Thank you for your comment. The IPF guideline will incorporate the STA dependent on a technology appraisal consultation.
SH	InterMune	32		3.2 e		A positive benefit-risk of pirfenidone has been demonstrated in patients with IPF in three randomized, double-blind placebo controlled studies of IPF patients. The 12/17/10 positive CHMP Opinion and imminent MAA approval independently confirm this assessment. We ask the authors to consider this new information.	Thank you for your comment. The IPF guideline will incorporate the STA dependent on a technology appraisal consultation.
SH	InterMune	33		3.2f		Will the CG aim to identify or designate which centres within England Wales should be managing patients with IPF?	Thank you for your comment. This is not part of the remit for the IPF guideline.
SH	InterMune	34		4.1.1b		Does "no patient subgroups have been identified as needing specific consideration" relate to the fact that no attempt will be made to define which patients	Thank you for your comment. NICE has a duty to take reasonable action to avoid unlawful discrimination and promote equality of opportunities. For example, if a test is

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						with IPF will benefit most from therapy or will this be addressed during the development of the CG?	likely to be used to define eligibility for an intervention, we would have to point out how would the GDG consider whether all groups can complete the test. Any specific data on subgroups that is identified through relevant evidence will be addressed in the recommendations. The statement means that no relevant equality issues were identified during scoping,
SH	InterMune	35		4.3.1c		The pirfenidone MAA received a positive opinion from the CHMP (by consensus) on December 17, 2010 and MAA approval is expected imminently. When approved, pirfenidone will be the only drug licensed for IPF in the European Union. Given the timeframe of this CG process, pirfenidone should be added to the list of drugs to be reviewed as it will be the only drug licensed for IPF in the UK. (see also comment for section 3.2d above) None of the drugs listed in this Section are specifically licensed according to their SmPCs for IPF e.g. mycophenolate mofetil, N-acetyl cysteine, bosentan, ambrisentan, sildenafil (see comment on section 4.3.1e) as there has been little or no convincing evidence of a positive benefit-risk profile for these drugs in patients with IPF. *Note:* ambrisentan is spelt incorrectly in the scoping document.	Thank you for your comment. The IPF guideline will incorporate the STA dependent on a technology appraisal consultation. We have now corrected to ambrisentan.
SH	InterMune	36		4.3.1e		What level of evidence is required for unlicensed drugs for them to be recommended ahead of licensed medicines fro IPF from a risk management perspective?	Thank you for your comment. This statement is a standard statement included in NICE guidelines. However, if good evidence exists for unlicensed treatments these treatments will be included in the review of evidence.
SH	InterMune	37		4.4		The six minute walk test (6MWT) should be considered as an outcome measure as it is a clinically meaningful and according to the IPF medical literature, is a highly prognostic outcome	Thank you for your comment. This section has been revised to now say "and/or a measure of function such as the 6 minute walk test"

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						measure in patients with IPF.	
SH	InterMune	38		4.4b		Measures of gas transfer such as DLCO and TLCO are inherently unreliable, not universally available to respiratory specialists/ pulmonologists and do not add independent incremental prognostic value to other measures such as FVC/VC, 6MWT or PFS.	Thank you for this helpful information. DLCO and TLCO are used and are clinically relevant. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.
SH	InterMune	39		4.4c		The St George Questionnaire is a health status instrument and is not technically a quality of life instrument. This instrument has not been rigorously validated in patients with IPF.	Thank you for this helpful information. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.
SH	InterMune	40		4.4e		Will mortality be considered in terms of overall survival and/ or progression free survival (PFS)? Given the technical challenges of conducting mortality studies in IPF patients, PFS is a useful and clinically meaningful outcome measure in patients with IPF.	Thank you for this helpful information. Mortality has been included in the list of outcomes in the IPF scope. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.
SH	InterMune	41		5.2		As stated above, how will the outcome of the STA for pirfenidone be incorporated into the CG development?	Thank you for your comment. The IPF guideline will incorporate the STA dependent on a technology appraisal consultation.
NICE	PPIP			General		Thank you for the chance to comment on this scope.	Thank you for your comment.
NICE	PPIP			3.2.b and 3.2e		The statement in 3.2.e that lung transplant is the only thing that affects outcomes seems to partially contradict the statement in 3.2.b that there is evidence that supportive treatment works, even if only in the early treatment of the condition. Does this mean that the supportive treatment only has a short term effect on outcomes, or that it only affects quality of life but not mortality or morbidity, or that lung transplant is the only thing proven to have an effect in the management of more advanced IPF?	Thank you for your comment. Section 3.2b has now been changed to say: 'To manage IPF, there is evidence to support a role for some types of best supportive care, such as smoking cessation, pulmonary rehabilitation, withdrawal of ineffective therapy, oxygen therapy and palliation of symptoms'.

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						Could this be clarified?	
NICE	PPIP			4.1.2b		Is there a risk that smoking could be viewed as an exogenous agent? Smoking is correlated with IPF, and it may help to clarify this issue.	Thank you for your comment. We disagree. We do not think the wording we have used can be misinterpreted
NICE	PPIP			4.3.1d		Thank you for including palliative care in this section.	Thank you for your comment.
NICE	PPIP			4.3.1		The PPIP team remain concerned that information and support for patients and carers is not specifically included in the draft scope. Please can this be re-considered. We know that IPF is a condition with a high likelihood of poor outcomes, and are concerned that the specific information, communication and support needs of patients and carers are able to be considered in developing this guideline. Although we are aware that there are separate NICE guidelines for medications adherence and for supportive and palliative care, we think it is important to be able to include specific recommendations for this condition This would be consistent with many other NICE guidelines. For example, the scope for advanced breast cancer included 'patient information and communication' and 'supportive and palliative care'.	Thank you for your comment. The specific information, communication and support needs of patients and carers will be captured whilst developing the recommendations on the delivery of care for patients with IPF.
NICE	PPIP			4.3.1e		The text "The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients." Could imply that doctors are deciding for the patient. Could this text be altered to say something like "…to inform the decisions they make with patients" or "to inform which drugs they decide to offer to patients"?	Thank your for your comment. This has now been revised to read "…to inform the decisions they make with patients".
NICE	PPIP			4.4.c		Can consideration be given to patient's quality of life on patient reported measures other than the EQ5, for example patient reported outcomes or more detailed functional tests that look at things other than walking (for example if someone is also unable to walk through other disability)?	Thank you for this helpful information. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.

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SH	United Kingdom Clinical Pharmacy Association (UKCPA)			General		We have no comments to make at this time.	Thank you for your comment.
SH	British Thoracic Society			General		This is a very positive move for IPF and we strongly support it. The role of ILD nurses in supporting these patients should be explored. Other pressing issues include the development of a national trial network.	Thank you for your comment The development of a national trial network is outside of the remit of the guideline. A specific question on the role of interstitial lung disease nurses in supporting patients with IPF will not be addressed in the guideline. Evidence will be reviewed on how care should be delivered and this may include the specialist nurse as part of a multidisciplinary team.
SH	British Thoracic Society			3.1		The evidence that smoking is a risk factor for IPF is weak and consistent. There are stronger links with geographic region and occupational history – and also diabetes and reflux. So I think either all of the recognised factors should go in – or none so drop smoking. Certainly the association with smoking – even if true – is much smaller than that with COPD.	Thank you for your comment. The potential risk factors for IPF are not specifically in the remit of the guideline. We have revised this section to state 'smoking is believed to be a risk factor'.
SH	British Thoracic Society			3.1 section c		Median age of presentation is actually closer to 70+	Thank you for your comment. We agree and have revised this.
SH	British Thoracic Society			3.1 d		Incidence is increasing rapidly over time – this needs stressing. Current incidence is 8-9 per 100,000 per annum (Navaratnam Thorax in press)	Thank you for your comment. We agree and have included a statement that IPF is becoming more common
SH	British Thoracic Society			3.2 section c		I think that the evidence underpinning N-acetyl cysteine is under reported here. Rather than saying it may be beneficial I would have a sentence saying that when use in association with steroids and azathioprine it was associated with a slower rate of decline in lung function. As currently written this rather undermines what was a really important trial.	Thank you for your comment. We have revised this section in the scope to state: 'Currently, there is no proven effective drug therapy for IPF. Corticosteroids and azathioprine are often used. A recent trial suggests the addition of N-acetylcysteine to prednisilone and azathioprine may slow the rate of disease progression more than prednisolone and azathioprine alone'.

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SH	British Thoracic Society			3.2 section e		Actually this is not true – there has never been a trial of transplantation. In people diagnosed under 65 (the potential transplant population) median survival is great than 5 years which is similar to post transplant figures. The issue I think is that we should be transplanting rapid decliners and we need help and research in indentifying these. I'm sure that we do not need to do a trial– but work on patient selection is needed. As written however the scope has rather too much emphasis on transplant and not enough on N-acetyl cysteine.	Thank you for your comment. We have revised this section.
SH	British Thoracic Society			3.2 section f		This would be helped by the development of MDTs and a hub and spoke system similar to the cancer networks	Thank you for your comment. The guideline development group will be reviewing the evidence around appropriate care of IPF patients and will make recommendations as appropriate.
SH	British Thoracic Society			4.3.1		I think we need a section on co-morbidity. People with IPF have a 10 fold increase in the risk of lung cancer and a 3 fold increase risk of acute coronary syndromes. These are important aspects of care.	Thank you for your comment. Patients with IPF are treated in a similar way to patients with background COPD or emphysema, weighing up the risks and benefits with the patient of chemotherapy, radiotherapy or surgery. Given this, we do not consider it to be a high priority for inclusion in the IPF guideline. Please refer to the recently published NICE update guideline on lung cancer available on http://guidance.nice.org.uk/CG24.
SH	Royal College of Radiologists, British Society of Thoracic Imaging			4.3.1 a.		Diagnosis will inevitably include investigations to exclude secondary causes of a UIP pattern	Thank you for your comment. Thank you for your comment. We do not think this addition is appropriate in this section. However, this is likely to be part of the care pathway**.**

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SH	Royal College of Radiologists, British Society of Thoracic Imaging			4.3.1		A section on routine follow-up investigations and their periodicity – functional and, imaging etc would be helpful	Thank you for your comment. Thank you for your comment. We agree and have added a section on patient review and follow-up to the scope.
SH	Royal College of Radiologists, British Society of Thoracic Imaging			4.4		Functional, and clinical outcomes have limitations in IPF but remain the reference standard. Considerations should be given to including imaging outcomes such as the composite physiologic index (Wells et al) or even mentioning functional imaging using PET-CT	Thank you for this helpful information. Composite physiologic index or functional imaging using PET-CT are not commonly used and not frequently reported in trials. The outcomes listed are examples suggested for questions that we expect the guideline to answer. The list is not exhaustive and will be tailored to each evidence review. The guideline development group will finalise the list and we will include these in the options that we will consider.