SUPPLEMENTARY MATERIAL

Manuscript Title: Widespread Gaps in the Quality of Care for Primary Biliary Cholangitis in the United Kingdom

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KEYWORDS: Standards; Liver Cirrhosis, Biliary; Liver Diseases; Hepatitis, Autoimmune; Guideline; Ursodeoxycholic Acid.

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PBC AUDIT PROFORMA

The 2-page supporting proforma provided to hospitals for data collection.

PBC Audit

Patient # Age

M/F Weight kg Year of Diagnosis

Date patient last weighed / /

	Y	N
1. Clinical diagnosis:		
Accurate diagnosis with ≥ 2 of diagnostic criteria (ANA/AMA >1 in 40, cholestatic LFTs, consistent histology)?		
2. Treatment:		
a. Is there ongoing treatment with Ursodeoycholic Acid 13-15mg/kg/day? *[If YES go to question 'f', if NO go to question 'b']*		
b. Is there treatment with Ursodeoxycholic Acid at an alternative dose? *[If YES go to question 'f' if NO go to question 'c']*		
c. Is the patient on UDCA at an unspecified dose? *[If YES go to question 'f', if NO go to question 'd']*		
d. Has the patient had treatment with UDCA and discontinued? *[If YES please give the reason if known, if NO go to question 'e']*		
e. The patient has no recorded treatment with UDCA? *[If YES go to question 'f']*		

f. Is there a record of assessing response at 1 year? *(ALP <1.67 ULN)*	Full	Part	None	No record
3. In the past 12 months, record of presence/absence of:				
a. Pruritus?				
b. Fatigue?				

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PBC Audit

	Y	N
4. Bone density:		
a. Assesment within the last 5 years		
b. If abnormal (T ≤-score 2.5), record of appropriate action plan in notes?		
5. Is patient high risk? Defined as bilirubin > 50 µmol/L *OR* dropping albumin		
OR patient is decompensating (variceal bleed, ascites or encephalopathy?		
6. If high risk, has patient been considered for transplant in the past 3 months?		
7. If cirrhotic, record of screening for:		
a. HCC within the last year? (or offered and patient declined)		
b. Varices within the last year? (or offered and patient declined)		
c. If No: Is there record of varices screening in the last 2 years?		
8. If co-existing Autoimmune Hepatitis, record of diagnostic biopsy?		

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Supplementary Table 1. Summary of the performance in England, Wales and Scotland.

Standard	Target (%)	Number of patients treated according to guidelines/total number patients† (%)			*p*-value
		England	Wales	Scotland	
Prescription of the recommended UCDA dose of 13-15mg/kg daily	90	164/277 (59.2)	97/218 (44.5)	31/110 (28.2)	<0.0001
Assessment of biochemical response to UDCA following one year of treatment	80	243/277 (87.7)	86/218 (62.8)	83/110 (75.5)	<0.0001
Recorded symptom assessment of pruritus	90	108/293 (36.9)	66/181 (36.5)	35/118 (29.7)	0.3566
Recorded symptom assessment of fatigue	90	74/293 (25.3)	65/181 (35.9)	32/118 (27.1)	0.0406
Assessment of bone density within five years of diagnosis	80	217/326 (66.6)	79/178 (44.4)	62/117 (53.0)	<0.0001
Assessment of liver transplant eligibility in high risk patients	90	25/39 (64.1)	5/13 (38.5)	9/9 (100.0)	0.0127

Footnotes:

† Total number of patients where data was available.

Supplementary Table 2. Summary of the performance in hospitals with general gastroenterology clinics and hospitals with dedicated hepatology clinics.

Standard	Target (%)	Number of patients treated according to guidelines/total number of patients† (%)		*p*-value‡
		GGC Centres	DHC Centres	
Prescription of the recommended UCDA dose of 13-15mg/kg daily	90	17/45 (37.8)	275/560 (49.1)	0.1640
Assessment of biochemical response to UDCA following one year of treatment	80	38/45 (84.4)	374/479 (78.1)	0.4461
Recorded symptom assessment of pruritus	90	19/57 (33.3)	190/535 (35.5)	0.7731
Recorded symptom assessment of fatigue	90	37/139 (36.8)	176/535 (32.9)	0.5565
Assessment of bone density within five years of diagnosis	80	22/55 (40.0)	336/566 (59.4)	0.0065
Assessment of liver transplant eligibility in high risk patients	90	3/10 (30.0)	36/51 (70.6)	0.0272

Footnotes:

GGC: general gastroenterology clinic, DHC: dedicated hepatology clinic.

†Total number of patients where data was available.

‡Fisher's exact test was used to test independence between secondary and tertiary centres.

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SUPPLEMENTARY DATA COLLECTION

Methods

Supplementary data collection was optional and varied between hospitals according to the decision of the local audit lead. Additional data collection included the presence of steatosis, obeticholic acid (OCA) prescription, autoantibody status, biochemical profile at one year of UDCA treatment, transient elastography, and records of the following: oesophago-gastro-duodenoscopy (OGD) for varices screening and abdominal ultrasound for HCC screening. Supplementary data was used for further descriptive analysis and to assess UDCA response according to established criteria where possible.[1,2]

Sub-analyses were undertaken on supplementary data provided by York, London North West, Royal Free London and Imperial College NHS Trusts as they provided further data on the biochemical profile of patients. Determination of UDCA response status following one year of treatment was undertaken for each applicable patient according to the two sets of following criteria: Barcelona criteria, defined as decrease in ALP ≤40% and ALP ≥1 x upper limit of normal (ULN); and Toronto criteria, defined as ALP ≤1.67 x ULN.[1,3,4] Pearson's correlation coefficient (r) was calculated to assess the correlation between proportion of patients on correct UDCA dosing with the proportion of patients demonstrating a) UDCA response according to Barcelona criteria and b) UDCA response according to Toronto criteria.

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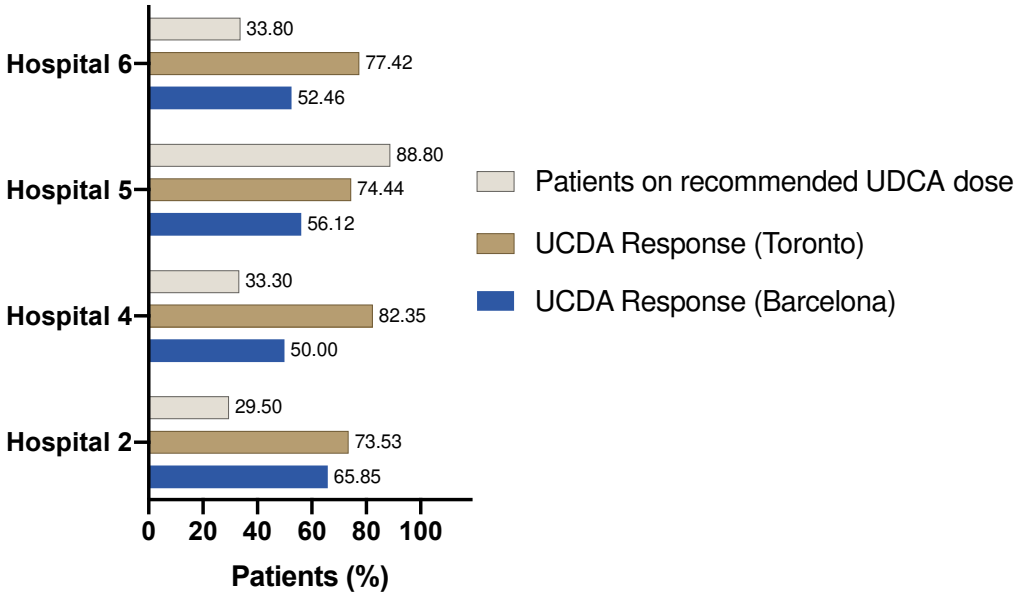
UDCA Treatment Response

The percentages of patients classified as demonstrating UDCA response according to the Barcelona criteria were 65.9% (Hospital 2), 50.0% (Hospital 4), 56.1% (Hospital 5) and 52.5% (Hospital 6). No significant correlation was observed between the percentage of patients prescribed the correct UDCA dose and the percentage of patients demonstrating UDCA response (p=0.4678) **(Supplementary Figure 1).**

In the same four sites, percentages of patients classified as demonstrating UDCA response according to the Toronto criteria were 75.5% (Hospital 2), 82.4% (Hospital 4), 74.4% (Hospital 5) and 77.4% (Hospital 6). No significant correlation was observed between the percentage of patients prescribed the correct UDCA dose and the percentage of patients demonstrating UDCA response (p=0.3147) **(Supplementary Figure 1).**



Supplementary Figure 1. Bar chart showing the percentages of PBC patients classified with UDCA treatment response according to Barcelona criteria and Toronto criteria. Percentages of patients on the recommended UDCA dose are shown for comparison. Four hospitals provided the necessary data on ALP profile for this analysis, as displayed on the y-axis.

Interpretation of UDCA Treatment Response

Although we expected to observe a significant relationship between the percentage of patients prescribed the appropriate UDCA dose and the percentage of patients exhibiting treatment response, as suggested by guidelines and existing literature[1,5,6] – we did not observe a statistically significant relationship. Our analysis of the UDCA treatment response was mostly based on ALP due to the limited collection of biochemical test results and our inability to use other criteria, such as Paris-I or Rotterdam.[1] Interestingly, the observed biochemical response, according to the Toronto criteria, was slightly higher than that measured using the Barcelona criteria. Prospective research is needed to validate the different biochemical response criteria in PBC patients.

Supplementary Table 3. Supplementary Patient Data

Additional descriptive data obtained from York, London North West, Royal Free and Imperial College NHS Trusts is presented.

Trust (number of PBC patients)	% of patients with positive antibody titre (number)			% of patients currently prescribed obeticholic acid (number)	% of patients who underwent liver elastography (number)	% of patients with steatosis (number)	Mean MELD of cirrhotic patients (SD)	Mean UKELD of cirrhotic patients (SD)
	AMA	PBC-specific ANA	ASMA					
Hospital 2 (75)	-	-	-	13.33% (10)	46.67% (35)	-	-	-
Hospital 4 (19)	100% (19)	42.11% (8)	5.26% (1)	0% (0)	73.68% (14)	31.58% (6)	7 (1)	48.33 (3.215)
Hospital 5 (166)	90% (149)	36.14% (60)	4.22% (7)	2.41% (4)	86.75% (144)	7.23% (12)	7.31 (1.545)	45.67 (3.617)
Hospital 6 (69)	78% (54)	30.43% (21)	-	1.45% (1)	-	-	-	-

Screening for Cirrhotic Complications

Data on cirrhotic patients was available from six hospitals. Across the six hospitals, 138 of 483 (28.6%) patients were diagnosed with cirrhosis. Variceal screening was undertaken on 63 of 138 (45.7%) patients. There was significant variation observed between hospitals in proportions of cirrhotic patients screened for varices, ranging from 0% (Hospital 4) to 80% (Hospital 7) ($p<0.0001$) **(Supplementary Figure 2A).**

Data on HCC screening was available in five hospitals, consisting of 93 cirrhotic patients. HCC screening was undertaken on 68 of 93 (73.1%) patients with no significant variation observed between hospitals. Proportions of cirrhotic patients screened for HCC ranged from 56% (Hospital 11) to 100% (multiple hospitals) ($p=0.1256$) **(Supplementary Figure 2B).**

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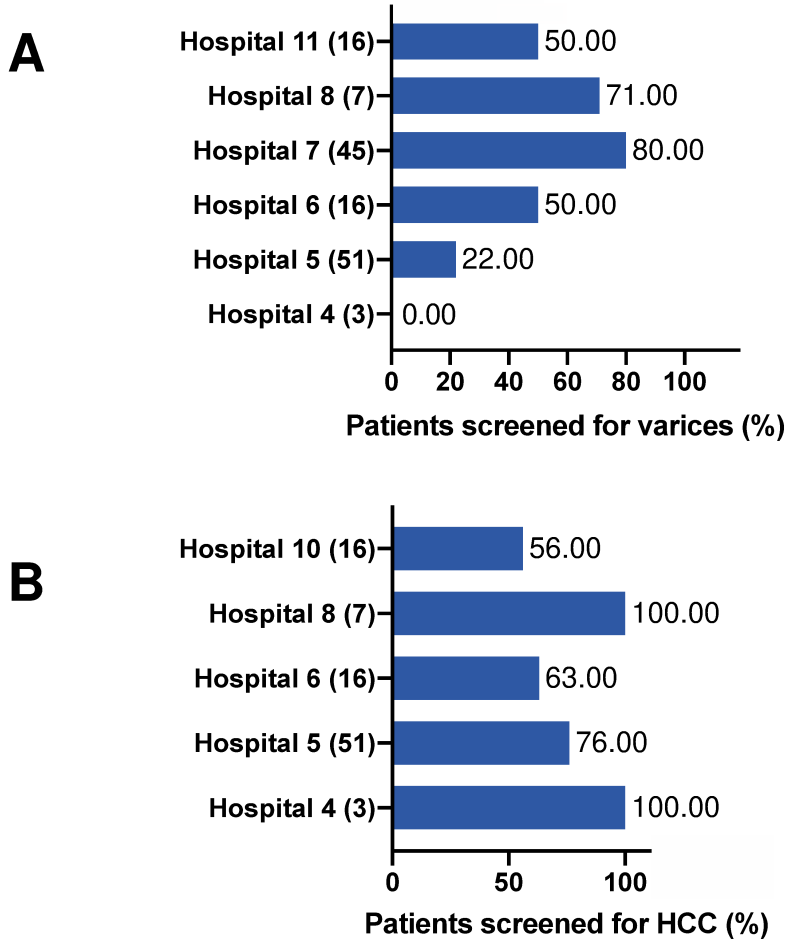

Supplementary Figure 2. Screening for Cirrhotic Complications

(A) Bar chart showing the percentages of cirrhotic patients undergoing screening for varices. Data was available from six hospitals, as displayed on the y-axis. The number of patients with cirrhosis are shown in brackets for individual hospitals.

(B) Bar chart showing the percentages of cirrhotic patients undergoing screening for HCC. Data was available from five hospitals, as displayed on the y-axis. The number of patients with cirrhosis are shown in brackets for individual hospitals.

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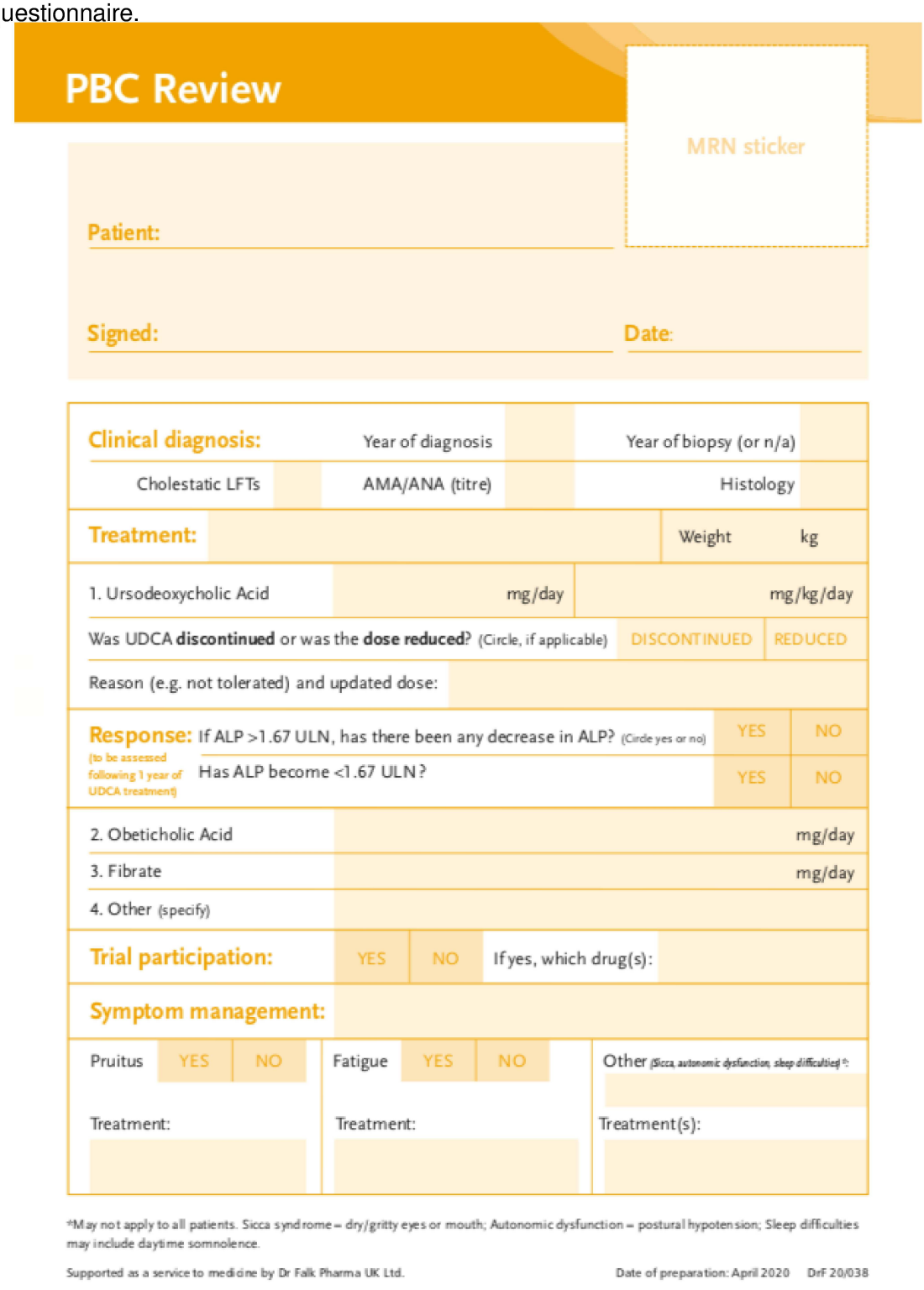
PBC REVIEW TOOL

The proposed 3-page PBC Review tool. Pages 1 and 2 contain questions based on EASL and BSG/UK-PBC guidelines. Page 3 contains the PBC-10 screening questionnaire.



PBC Review

MRN sticker

Patient:

Signed: Date:

Clinical diagnosis:	Year of diagnosis		Year of biopsy (or n/a)
Cholestatic LFTs	AMA/ANA (titre)		Histology
Treatment:			Weight kg
1. Ursodeoxycholic Acid	mg/day		mg/kg/day
Was UDCA **discontinued** or was the **dose reduced**? (Circle, if applicable)	DISCONTINUED	REDUCED	
Reason (e.g. not tolerated) and updated dose:			
Response: If ALP >1.67 ULN, has there been any decrease in ALP? (Circle yes or no)	YES	NO	
(to be assessed following 1 year of UDCA treatment) Has ALP become <1.67 ULN?	YES	NO	
2. Obeticholic Acid	mg/day		
3. Fibrate	mg/day		
4. Other (specify)			
Trial participation:	YES	NO	If yes, which drug(s):
Symptom management:			

Pruritus	YES	NO	Fatigue	YES	NO	Other (Sicca, autonomic dysfunction, sleep difficulties)*:	
Treatment:			Treatment:			Treatment(s):	

*May not apply to all patients. Sicca syndrome = dry/gritty eyes or mouth; Autonomic dysfunction = postural hypotension; Sleep difficulties may include daytime somnolence.

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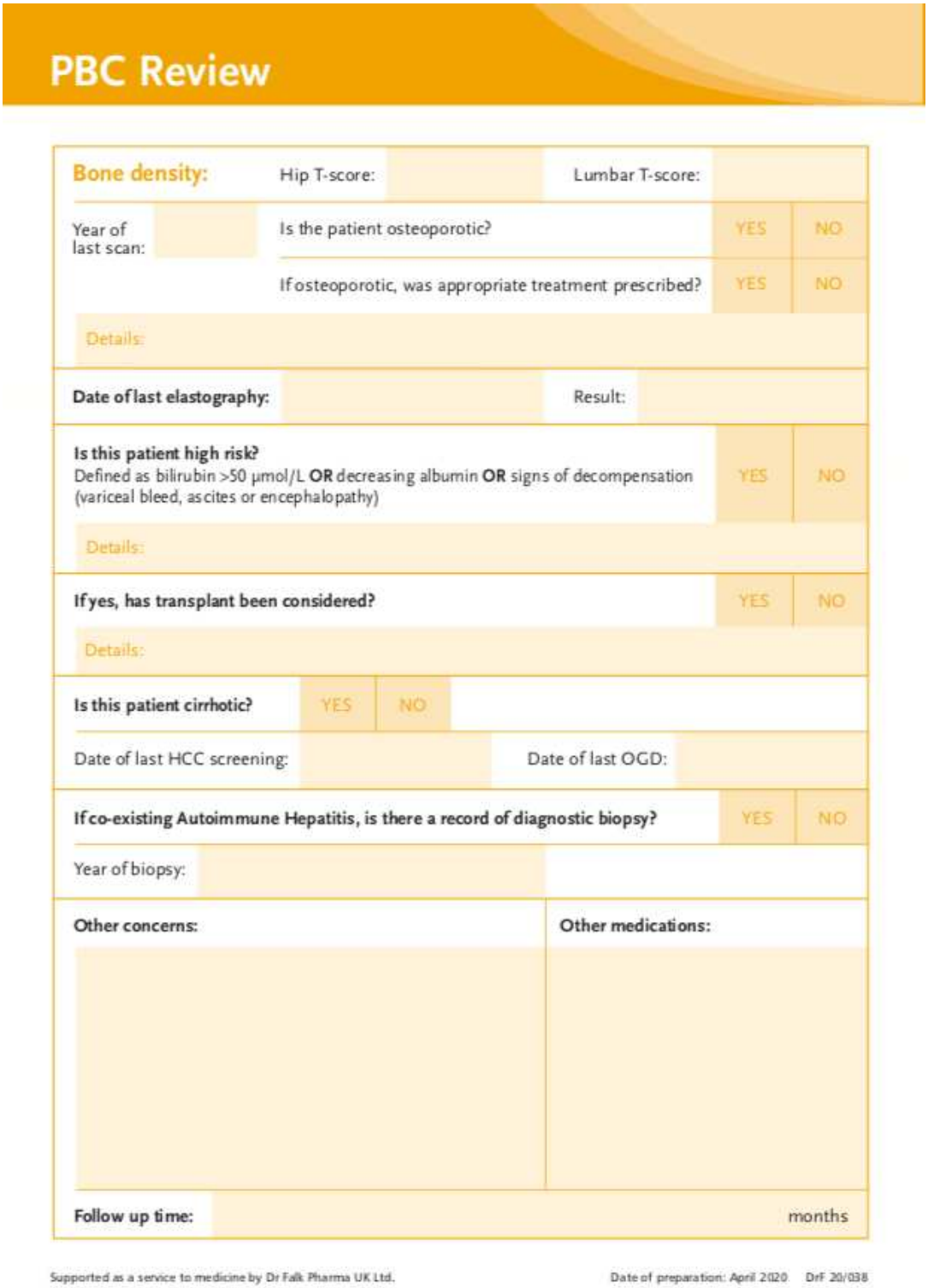

PBC Review

Bone density: Hip T-score: Lumbar T-score:

Year of last scan:

Is the patient osteoporotic? YES NO

If osteoporotic, was appropriate treatment prescribed? YES NO

Details:

Date of last elastography: Result:

Is this patient high risk?
Defined as bilirubin >50 µmol/L **OR** decreasing albumin **OR** signs of decompensation (variceal bleed, ascites or encephalopathy) YES NO

Details:

If yes, has transplant been considered? YES NO

Details:

Is this patient cirrhotic? YES NO

Date of last HCC screening: Date of last OGD:

If co-existing Autoimmune Hepatitis, is there a record of diagnostic biopsy? YES NO

Year of biopsy:

Other concerns:

Other medications:

Follow up time: months

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PBC Review

PBC-10 QUESTONNAIRE (circle the appropriate answer for all questions 1-10)

IN THE LAST FOUR WEEKS, how often did you experience any of the following?						
1. I have felt embarrassed because of the itching	Never	Rarely	Sometimes	Most of the time	Always	Not applicable
2. If I eat or drink a small amount, I still feel bloated	Never	Rarely	Sometimes	Most of the time	Always	
3. My mouth was very dry	Never	Rarely	Sometimes	Most of the time	Always	
4. Fatigue interfered with my daily routine	Never	Rarely	Sometimes	Most of the time	Always	Not applicable
5. I had to force myself to do the things I needed to do	Never	Rarely	Sometimes	Most of the time	Always	
6. If I was busy one day, I needed at least another day to recover	Never	Rarely	Sometimes	Most of the time	Always	
7. Because of PBC, I found it difficult to concentrate on anything	Never	Rarely	Sometimes	Most of the time	Always	
Now some more general statements about how PBC may be affecting you as a person. How much does the following statement apply to you?						
8. I feel guilty that I can't do what I used to be able to do because of having PBC	Not at all	A little	Somewhat	Quite a bit	Very much	Not applicable
These statements relate to the possible effects of PBC on your social life and your life overall. Thinking of your own situation, how much do you agree or disagree with them?						
9. My social life has almost stopped	Strongley agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	
10. PBC has reduced the quality of my life	Strongley agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	

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