



Published in final edited form as:

*Am J Transplant.* 2012 June ; 12(6): 1603–1609. doi:10.1111/j.1600-6143.2011.03969.x.

## Lack of Standardization in Exception Points for Patients with Primary Sclerosing Cholangitis and Bacterial Cholangitis

D Goldberg, MD, MSCE<sup>1,2</sup>, T Bittermann, MD<sup>3</sup>, and G Makar, MD, MSCE<sup>1</sup>

<sup>1</sup>Department of Medicine, Division of Gastroenterology, University of Pennsylvania

<sup>2</sup>Clinical Center for Epidemiology and Biostatistics, University of Pennsylvania School of Medicine

<sup>3</sup>Department of Medicine, University of Pennsylvania

### Abstract

For conditions that the Model for End-Stage Liver Disease (MELD) score does not accurately predict waitlist mortality, transplant centers may apply to regional review boards for exception points. For patients with primary sclerosing cholangitis (PSC) suffering from bacterial cholangitis, consensus recommendations published in 12/2006 are to grant exception points for recurrent cholangitis with 2 episodes of bacteremia or 1 episode septic complications. Using data provided by the United Network for Organ Sharing, we evaluated PSC patients who applied for exception points due to bacterial cholangitis from 2/27/02 to 3/14/11. Prior to publication of the recommendations, 66.0% of applications were accepted, compared with 80.1% after ( $P < 0.001$ ). Focusing on applications after publication of the recommendations, 311 (74.6%) did not meet the recommended criteria, and 250 (80.4%) of these were approved. Of patients with approved applications, those not meeting consensus criteria were more likely to be transplanted, (77.4% vs. 62.8%,  $P = 0.043$ ), while those with denied applications for approved indications were more likely to die/be removed (44.4% vs. 9.5%,  $P = 0.49$ ). While data are needed to properly identify those patients at highest risk for waitlist mortality, standardized criteria or a centralized review board should be adopted to ensure consistency in the granting of exception points.

### Keywords

Exception points; primary sclerosing cholangitis; bacterial cholangitis; regional review boards

### Introduction

While the Model for End-Stage Liver Disease (MELD) score accurately predicts 90-day mortality of patients on the liver transplant waitlist, there are conditions for which the score does not accurately predict this risk. In these cases, transplant centers may apply to regional review boards (RRB) for exceptions points, with the RRB granting exceptions based on pre-specified systematic criteria for recognized exceptional diagnoses [REDs such as hepatocellular carcinoma (HCC)] or on a case-by-case basis

Excluding patients transplanted with exception points for HCC, according to Organ Procurement and Transplantation Network (OPTN) data as of 3/14/2011, 12.2% of transplant recipients with primary sclerosing cholangitis (PSC) received exception points, as

---

Corresponding Author: David Goldberg, Hospital of the University of Pennsylvania, 3400 Civic Center Boulevard, 9 Penn Tower, Philadelphia, PA 19104, Phone: 646-242-6349, Fax: 215-349-5915, david.goldberg@uphs.upenn.edu.

### Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

opposed to 8.9% of all other patients. There are no standardized criteria for the granting of exception points for patients specifically with PSC.(1)

In 2006, an OPTN-sponsored consensus conference concluded that exception points should be granted based on the risk of waitlist mortality, waitlist removal, or non-liver related disease potential. (2) Concurrently, first-time consensus recommendations (CR) were published on the granting of exception points for patients with PSC and bacterial cholangitis, stating that exception points be granted for either: a) 2 episodes of culture-proven bacteremia within a 6-month period or b) septic complications of cholangitis; with those episodes being non-iatrogenic, in the absence of a biliary tube or stent, with documentation the patient was on suppressive antibiotic therapy, had positive blood cultures, without a correctable structural lesion. (3)

Since the publication of these CR, there has not been a systematic evaluation of their impact and the compliance of the RRBs with them. The objectives of this manuscript were: a) characterize the reasons for application for exception points for PSC and bacterial cholangitis; b) determine the compliance with the published recommendations for these applications; and c) determine the patient outcomes of those applying for these exception points.

## Methods

### Study Population

All analyses were based on OPTN data from 2/27/02-3/14/11. 2/27/02 was chosen as the start date, as it was the first date patients could apply for exception points under the newly instituted MELD allocation system. We included all patients listed with a primary diagnosis of PSC based on UNOS diagnostic codes.

We included patients listed for either primary transplantation or retransplantation (if the narrative and UNOS coding documented recurrent PSC in the absence of hepatic artery thrombosis, donation after cardiac death donor, or other anatomic causes of biliary strictures). 34/337 (10.1%) of applicants were listed for retransplantation.

We analyzed a UNOS Standard Transplant Analysis and Research (STAR) file that included the requested exception score, the reason for exception point application (based on 11 possible codes), the entire narrative submitted by the transplant center, and the result of the application. We included only patients whose reason for application was categorized as "other," excluding patients who applied for exception points for REDs (i.e. HCC).

We selected only those patients whose primary reason for applying for exception points was bacterial cholangitis. Among those with two stated reasons for applying, bacterial cholangitis was chosen as the primary reason, unless the other stated reason was cholangiocarcinoma, for which the patient would need to be placed in a pre-specified neoadjuvant chemotherapy protocol. The reasons for application for exception points were coded based on the categories listed in table 1. These categories were chosen to allow for categorization of applications that met CR for granting of exception points, while still allowing for an analysis of the varying reasons for applications.

### Outcome

The primary outcome was the result of the application for exception points. The application had five potential outcomes based on the decision by the RRB: request approved, request denied, withdrawn, indeterminate, or not approved 21 days. We dichotomized the results of applications to either approved vs. denied (which included all other possible outcomes).

## Statistical Analysis

Wilcoxon rank-sum and Kruskal-Wallis tests were used for continuous variables, and chi-square tests for categorical variables, given the non-normal distribution of the data. Logistic regression analysis was used to determine the odds of having an exception point application accepted pre vs. post-1/1/07.

As the CR for the granting of exception points for bacterial cholangitis in patients with PSC was published in December of 2006, we coded exception point applications on or after January 1, 2007, as post-recommendation applications.

The primary analysis focused on applications after 1/1/07, as this represented the first time that RRBs had CR for granting exception points for PSC and bacterial cholangitis. We performed a pre- vs. post-1/1/07 comparison to determine if the publication of the CR impacted the decision-making of the RRBs, and of those applying for exception points.

The PSC cholangitis CR concluded that to obtain exception points, specific documentation was needed, however only 15/655 (2.3%) applications met these specified criteria (including lack of documentation on whether episodes were non-iatrogenic, if a biliary tube or stent was present, if patient was on suppressive antibiotics, or if a correctable stricture was present). We defined meeting CR if patients met the minimal clinical criteria needed to receive exception points—either 2 episodes of bacteremia or evidence of septic complications/sepsis (table 1).

The requested MELD was adjusted for the median match MELD at transplantation (defined as the MELD score used for allocation) within that region for that pre-specified time period. (4) The median MELD was chosen due to the non-normal regional distribution of MELD scores at transplantation. The median match MELD from 2/27/02-12/31/06 and 1/1/07-3/14/11 was calculated, and we divided the requested MELD score by the respective median match MELD score, to calculate the “adjusted” MELD.

## Results

Since 2/27/02, there were 44,258 exception point applications, among 22,042 applicants, with 13,340 applications for “other” reasons, among 6,143 applicants. Among the 6,143 “other” applicants, 337 (5.5%) applied due to PSC and bacterial cholangitis, with 188 after 1/1/07. There were 3,788 patients with PSC on the waitlist during this time.

There were 655 exception point applications, with a mean of  $1.56 \pm 0.84$  and  $2.37 \pm 1.94$  applications per patient before and after 1/1/07, respectively. Table 2 displays the patient demographics pre- vs. post-1/1/07. The two groups were similar with respect to age, gender, race/ethnicity, insurance status, blood-type, and initial MELD score at listing. However, applicants after 1/1/07 waited 150 fewer days prior to the first application for exception points. Patients who applied for exception points were younger (44.6 vs. 47.0,  $P=0.002$ ) than the total cohort of patients with PSC listed for transplantation.(5)

## Regional variation

Nearly one-half (45.2%) of applicants were from regions 9 and 10 (table 3), even though only 18.2% of all waitlisted PSC patients were in those regions. The greatest proportion of waitlisted PSC transplant candidates are from regions 5 (13.8%), 7 (12.6%), 10 (11.3%), 2 (10.9%), and 3 (10.4%), yet with the exception of region 10, a substantially smaller proportion of PSC exception point applicants were from these regions (table 3).

47.0% of transplants for exception cases of PSC and bacterial cholangitis were from regions 9 and 10. The only other exceptions with a similarly disproportionate distribution of exceptions were portopulmonary hypertension and familial amyloidosis, with 53.6% and 43.0% of transplants for each of these exceptional indications from regions 5 and 7, respectively.

There was substantial regional variability in the number of exception points requested, even after adjusting for median match MELD at transplantation (table 3). There were significant differences in the acceptance rate of applications across regions, with regions 3, 9, 10, and 11 all accepting greater than 80% of exception point applications (table 3)

### Reasons for exception point applications

Table 4 characterizes the reasons for exception point applications. The overwhelming majority of applications were for patients with recurrent bacterial cholangitis without documented bacteremia or sepsis. A minority met the clinical criteria laid out in the 2006 CR, with 106 (25.4%) applications either for 2 episodes of bacteremia or 1 episode of sepsis or hepatic abscesses.

### Pre vs. Post-1/1/07

The majority (65.4%) of applicants had all of their applications for exception points accepted (table 5), however 16.0% had all of their application denied. A significantly greater proportion of exception point applications were accepted after 1/1/07, 80.1% vs. 66.0%, respectively, ( $P < 0.001$ ), regardless of whether the applicant met CR. Among those applications accepted, the number of MELD exception and adjusted exception points granted were statistically higher prior to 1/1/07. However, even after adjusting for the patient's adjusted MELD request score, the odds of having an exception point application approved were 1.7 times higher after 1/1/07 (OR=1.73, 95% CI: 1.19–2.53,  $P = 0.004$ ).

### Applications after 1/1/07

After 1/1/07, there was no difference in the proportion of accepted applications for patients meeting vs. not meeting clinical criteria for exception points (79.3% vs. 80.4%,  $P = 0.78$ ) (table 6). Analyzed by year, there were a similar number of applications over time, a similar proportion of those meeting vs. not meeting CR, and a similar proportion accepted over time (data not shown). Among those applicants for whom all of their applications were accepted, 74.8% were transplanted, while 3.0% died or were removed due to being too sick. Among applicants with at least one accepted application and at least one denial, 68.6% of were transplanted, while 4.7% died or were removed. The proportion transplanted and died/removed between these two groups were similar ( $P = 0.38$ ), and they were combined for future analyses. Compared to patients who had at least 1 application accepted, those with all of their applications denied had a significantly lower proportion transplanted (43.3% vs. 73.4%,  $P = 0.002$ ), and a greater proportion died/removed from the list (20.0% vs. 1.3%  $P < 0.001$ ).

When subdivided into patients whose applications were accepted (at least 1) or entirely denied, those with accepted applications for unapproved indications were significantly more likely to be transplanted than those accepted for approved indications (77.4% vs. 62.8%,  $P = 0.043$ ), with no difference in the risk of death (2.3% vs. 0.9%  $P = 0.54$ ). Applicants with applications that were denied for approved indications were more likely to die/be removed than those for non-approved indications (44.4% vs. 9.5%,  $P = 0.049$ ), without a difference in the odds of transplantation (33.3% vs. 47.6%,  $P = 0.38$ ; table 7). The data were similar for primary vs. re-transplant PSC candidates, and the results were unchanged when we restricted the analysis to only patients listed for primary transplantation.

## Discussion

This study is the first to characterize patients with PSC applying for MELD exception points due to bacterial cholangitis. We found that since the publication of CR in December of 2006, there has been an increase in the number of exception point applications for PSC and bacterial cholangitis, with a concomitant increase in the proportion of exception point applications accepted. Despite the publication of CR, the overwhelming majority of applications were accepted for clinical conditions not meeting the pre-specified criteria by the consensus conference. PSC candidates with approved exception point applications for bacterial cholangitis were more likely to be transplanted than those whose applications were denied. Notably, those candidates granted exception points for clinical conditions not meeting the CR had a greater odds of being transplanted. Furthermore, among those candidates meeting CR, yet denied exception points, there was a significantly increased risk of waitlist removal for death or clinical deterioration, signifying that the CR may appropriately identify those at greater risk of waitlist dropout.

For certain conditions such as HCC within Milan criteria, standardized, accepted medical criteria exist for allocating exception points. For others, such as PSC and bacterial cholangitis, we must rely on expert medical opinion and CR to guide decisions, as data are lacking on the risk of waitlist mortality for patients with PSC and bacterial cholangitis. However, the publication of CR did not change the acceptance practices of RRBs, and there continues to be acceptance of exception point applications for conditions for which there is no proven increased risk of waitlist mortality. It appears that other guidelines published at the same time were taken into account by RRBs, as an increased proportion of applications were accepted for familial amyloid polyneuropathy (data not shown), for which the guidelines recommended automatic exception points.(2)

There have only been two reviews of the RRB exception point allocation process published to date, with limited follow-up.(6, 7) Since these publications though, there have been over 600 new applications for PSC and bacterial cholangitis.

Over time, as MELD scores at the time of transplantation have increased, there have been an increasing number of applications for exception points (data not shown). Given the limited organ supply, it is critical that exception points are allocated to patients whose risk of waitlist mortality is in fact higher than their native MELD score indicates. Despite recommendations for proper documentation of culture-proven and non-iatrogenic bacteremia, use of suppressive antibiotic therapy, and evidence that a structural lesion is not correctable, the overwhelming majority of narratives submitted to RRBs for review lack such data, or even data documenting episodes of bacteremia or sepsis.

Even in region 9, where there are pre-specified criteria for exception points, applications were accepted with the narrative solely asking for 25 points for a patient with PSC due to region 9 consensus, without any mention of hospitalization, bacteremia, or antibiotics (the exact wording/quotation was not used to protect anonymity). Since 1/1/07, all (16/16) applications meeting CR, (among 9 patients) were approved at a mean MELD score of  $26 \pm 2.6$ , with 7 (77.8%) patients transplanted and none having died to date. However, of 68 applications among 29 patients for conditions not recognized by the CR, 52 (76.5%) were accepted at a mean MELD score of  $25.7 \pm 1.3$ , with 18 (62.1%) patients transplanted, and only 1 (3.5%) having died.

Notably, nine of these patients remain waitlisted despite having bacterial cholangitis dating back to October 2007, with 7 having repeated episodes. None had documented bacteremia or sepsis, supporting the CR that repeated bacteremia and/or sepsis are associated with a higher risk of waitlist mortality. Also, among those applicants denied exception points, the risk of

death or removal was higher among those meeting the 2006 CR. The sample size for these observations is small, and requires further validation.

We found there to be significant variability in the utilization of exception point applications in different regions. For example, in regions 1 and 9 (traditionally thought of as “high-MELD” regions), since 1/1/07, there was one applicant from region 1 vs. 38 from region 9, despite 91 PSC candidates (4.3% of total) in region 1, as opposed to 150 (8.2%) in region 9 during this time. Additionally, nearly half the applications were from two regions (9 and 10), despite the broad distribution of waitlisted PSC candidates, with significantly different rates of acceptance of exception point applications across regions (table 4). This data suggests that the current process by which RRBs review and grant exception points falls short of meeting the U.S. Department of Health and Human Services’ Final Rule stating that organ allocation, “shall not be based on the candidate’s place of residence or place of listing.” (9) The nature of the data does not provide insight into the regional variation in the approval of exception point applications, and future research will be conducted to gain insight into the decision making process by RRBs.

Our study had several limitations. We relied on data submitted to UNOS, and the narratives provided to UNOS by individual transplant centers. However, we do not have insight into the actual decision-making process of RRBs, and what factors beyond the narrative may impact the decision whether to grant exception points. We only included patients whose primary reason for applying for exception points was bacterial cholangitis, without accounting for other factors (i.e. complications of portal hypertension or quality of life) that may have impacted the decision to grant exception points. While we reviewed each narrative, including only those mentioning bacterial cholangitis, this complication may have been secondary to other complications of end-stage liver disease, despite our classification of the applications as a bacterial cholangitis case. However, even if such categorization caused us to include some patients for whom cholangitis was a secondary reason for application, the differences in applications for approved vs. non-approved conditions was so large that this would not have impacted our results. Lastly, the CR that we reference were based on expert opinion and not evidence-based. As such, our distinction between approved vs. non-approved applications may not truly represent whether an individual applicant has a condition for which his/her MELD score does not accurately capture the risk of waitlist mortality. Nevertheless, the data still demonstrates that the overwhelming majority of exception point applications are approved, despite lacking evidence that PSC and bacterial cholangitis in and of itself is associated with higher waitlist mortality. Lastly, we could not determine if all cases of “sepsis” represented sepsis alone or septic complications, although this represented only 2.6% of applications after 1/1/07, and would not have changed our results.

In conclusion, we demonstrate that the vast majority of exception point applications for patients with PSC and bacterial cholangitis are approved. Despite CR outlining clinical criteria for the granting of exception points, RRBs approved nearly 80% of applications for PSC and bacterial cholangitis, regardless of the indication. There was regional variability in the total number of exception point applications, and the percent of applications approved, which raises the concern for geographic disparities in access to exception points, and thus transplantation. While data is needed to properly identify those patients with PSC and bacterial cholangitis at highest risk for waitlist mortality, the lack of consistency in the granting of exception points for patients with PSC and bacterial cholangitis is concerning. Policy initiatives should be undertaken to either enforce uniform, standardized criteria that must be adopted by all RRBs (similar to what is done with HCC), or to create a national review board to oversee all exception point applications, to ensure equitable access to transplantation for patients with PSC and bacterial cholangitis.

## Acknowledgments

### Financial Support

1. NIH/NIDDK F32 1-F32-DK-089694-01 Grant (DG)
2. This work was supported in part by Health Resources and Services Administration contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

## List of Abbreviations

<b>MELD</b>	Model for End-Stage Liver Disease
<b>RRB</b>	Regional review board
<b>RED</b>	Recognized exceptional diagnosis
<b>HCC</b>	Hepatocellular carcinoma
<b>PSC</b>	Primary sclerosing cholangitis
<b>CR</b>	Consensus Recommendations
<b>OPTN</b>	Organ Procurement and Transplantation Network
<b>UNOS</b>	United Network for Organ Sharing

## References

1. [http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy\\_8.pdf](http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_8.pdf)
2. Freeman RB Jr, Gish RG, Harper A, Davis GL, Vierling J, Lieblein L, et al. Model for end-stage liver disease (MELD) exception guidelines: results and recommendations from the MELD Exception Study Group and Conference (MESSAGE) for the approval of patients who need liver transplantation with diseases not considered by the standard MELD formula. *Liver Transpl.* 2006; 12(12 Suppl 3):S128–36. Epub 2006/11/24. [PubMed: 17123284]
3. Gores GJ, Gish RG, Shrestha R, Wiesner RH. Model for end-stage liver disease (MELD) exception for bacterial cholangitis. *Liver Transpl.* 2006; 12(12 Suppl 3):S91–2. Epub 2006/11/24. [PubMed: 17123280]
4. Washburn K, Pomfret E, Roberts J. Liver allocation and distribution: Possible next steps. *Liver Transpl.* 2011; 17(9):1005–12. Epub 2011/06/03. [PubMed: 21634007]
5. Goldberg D, French B, Thomasson A, Reddy KR, Halpern SD. Waitlist survival of patients with primary sclerosing cholangitis in the model for end-stage liver disease era. *Liver Transpl.* 2011; 17(11):1355–63. Epub 2011/08/13. [PubMed: 21837735]
6. Voigt MD, Zimmerman B, Katz DA, Rayhill SC. New national liver transplant allocation policy: is the regional review board process fair? *Liver Transpl.* 2004; 10(5):666–74. Epub 2004/04/27. [PubMed: 15108259]
7. Rodriguez-Luna H, Vargas HE, Moss A, Reddy KS, Freeman RB, Mulligan D. Regional variations in peer reviewed liver allocation under the MELD system. *Am J Transplant.* 2005; 5(9):2244–7. Epub 2005/08/13. [PubMed: 16095504]
8. Thuluvath PJ, Guidinger MK, Fung JJ, Johnson LB, Rayhill SC, Pelletier SJ. Liver transplantation in the United States, 1999–2008. *Am J Transplant.* 2010; 10(4 Pt 2):1003–19. Epub 2010/04/28. [PubMed: 20420649]
9. <http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=289a22f3ef38f2e1b09a1a454be22daa&rgn=div8&view=text&node=42:1.0.1.11.78.0.3.9.8&idno=42>

**Table 1**

## Coding criteria for bacterial cholangitis narratives

Category	Coding criteria
Meeting recommendations	Recurrent bacterial cholangitis with 1 episode of sepsis <sup>*</sup>
	Recurrent bacterial cholangitis with 1 episode of hepatic abscesses
	Recurrent bacterial cholangitis with 2 episodes of sepsis <sup>*</sup>
	Recurrent bacterial cholangitis with 2 episodes of bacteremia <sup>**</sup>
Not meeting recommendations	1 episode bacterial cholangitis
	Recurrent bacterial cholangitis without bacteremia or sepsis <sup>***</sup>
	Recurrent bacterial cholangitis with 1 episode bacteremia <sup>**</sup>

<sup>\*</sup>Sepsis defined as any patient with documented sepsis, defined as use of the term “sepsis,” and/or documentation of severe inflammatory response syndrome (SIRS) criteria (fever/hypothermia, tachypnea, tachycardia, or leukopenia/leukocytosis) in the setting of cholangitis, or other septic complications other than hepatic abscesses. This group was categorized as meeting clinical criteria given the difficulty in determining whether patients had only sepsis or septic complications as specified in the consensus recommendations

<sup>\*\*</sup>Bacteremia code if the narrative used the term “bacteremia,” or cited positive blood cultures, with or without sepsis



**Table 2**

## Demographics of Exception Point Applicants with PSC and Bacterial Cholangitis

Variable	Pre-1/1/07, N=149	Post-1/1/07, N=188	P-Value
Age at listing, mean $\pm$ SD	44.5 $\pm$ 13.8	44.7 $\pm$ 15.4	0.56
Male gender, N (%)	102 (68.5)	121 (64.4)	0.43
Race/ethnicity, N (%) <sup>*</sup>			0.74
White	122 (81.9)	157 (83.5)	
Black	15 (10.1)	21 (11.2)	
Hispanic	5 (3.4)	6 (3.2)	
Asian	9 (2.7)	3 (1.6)	
Private insurance, N (%)	126 (84.6)	165 (87.8)	0.40
Bloodtype, N (%)			0.12
O	77 (51.7)	88 (46.8)	
A	56 (37.6)	63 (33.5)	
B	12 (8.1)	32 (17.0)	
AB	4 (2.7)	5 (2.7)	
Waitlist time (in days) prior to first exception point application, mean $\pm$ SD	398 $\pm$ 676	242 $\pm$ 563	0.038
MELD at time of first exception point application, mean $\pm$ SD	12.8 $\pm$ 5.8	12.6 $\pm$ 5.1	0.71

<sup>\*</sup> 1 patient pre-1/1/07 and 1 post-1/1/07 defined as American Indian/Alaskan Native, Native Hawaiian, or multiracial.

**Table 3**

Characteristics of Exception Point Applicants after 1/1/07, N=188

Region	Applicants, N (%)	Mean MELD application*	Adjusted MELD Application Score*	Acceptance Rate, N (%)**
1	1 (0.5)	20.0 ± 0	0.74 ± 0	0 (0.0)
2	16 (8.5)	26.1 ± 4.4	1.05 ± 0.18	27 (79.4)
3	25 (13.3)	17.5 ± 2.3	0.79 ± 0.10	64 (92.8)
4	14 (7.5)	20.9 ± 1.4	0.88 ± 0.06	41 (77.4)
5	12 (6.4)	26.1 ± 5.3	0.94 ± 0.19	12 (63.2)
6	2 (1.1)	21.5 ± 2.1	0.98 ± 0.10	2 (100.0)
7	7 (3.7)	17.8 ± 2.7	0.72 ± 0.11	9 (56.3)
8	18 (9.6)	23.5 ± 3.3	1.01 ± 0.14	33 (76.7)
9	38 (20.2)	26.1 ± 2.0	1.00 ± 0.08	68 (81.0)
10	47 (25.0)	20.8 ± 3.3	0.94 ± 0.16	65 (80.3)
11	8 (4.3)	18.8 ± 3.6	0.87 ± 0.16	13 (86.7)
		22.1 ± 4.4	0.93 ± 0.15	334 (80.1)

\*P=0.0001 for Kruskal-Wallis test of differences between groups

\*\*P<0.039 for chi-squared testing differences in acceptances between regions, excluding regions 1 and 6 due to only 1 and 2 applicants, respectively, in those regions

**Table 4**

Reasons for exception point applications among PSC patients applying for exception points due to bacterial cholangitis

Reasons for Application	Pre-1/1/07, N=238	Post-1/1/07, N=417
Recurrent cholangitis without bacteremia or sepsis *	177 (74.4)	279 (66.9)
1 episode cholangitis *	6 (2.5)	19 (4.6)
Recurrent cholangitis with 1 episode bacteremia *	0 (0.0)	13 (3.1)
Recurrent cholangitis with 2 episodes bacteremia †	13 (5.5)	43 (10.3)
Recurrent cholangitis with 2 episodes sepsis †	30 (12.6)	36 (8.6)
Recurrent cholangitis with 1 hepatic abscess †	7 (2.9)	16 (3.8)
Recurrent cholangitis with 1 episode sepsis †	5 (2.1)	11 (2.6)

\* Clinical criteria not meeting consensus recommendations

† Clinical criteria meeting consensus recommendations

**Table 5**

Outcome of application process for patients applying for applications after 1/1/07

<b>Outcome</b>	<b>Applicants, N=188*</b>
All applications accepted	123 (65.4)
All applications denied	30 (16.0)
Initial application approved, subsequent application denied higher score	16 (8.5)
Initial application denied, subsequent application accepted at lower score	8 (4.3)
Initial application approved and subsequent application denied for same or lower score	7 (3.7)
Initial application denied, subsequent application approved for same or higher score	4 (2.1)

\* Number of individual applicants for exception points after 1/1/07

**Table 6**

Characteristics of applications meeting vs. not meeting clinical criteria

Reason for application	Applicants	Applications	Accepted applications, N (%)	Mean accepted MELD score <sup>‡</sup>	Mean adjusted MELD accepted score <sup>‡</sup>
Recommended criteria <sup>*</sup>					
Pre-1/1/07	33	55	33 (60.0)	23.4 ± 4.6	1.00 ± 0.20
Post-1/1/07	52	106	84 (79.3)	22.0 ± 3.8	0.93 ± 0.15
P-value <sup>‡</sup>			0.02	0.09	0.04
Not recommended criteria <sup>*</sup>					
Pre-1/1/07	116	183	124 (67.8)	24.6 ± 4.8	1.04 ± 0.14
Post-1/1/07	136	311	250 (80.4)	21.5 ± 4.3	0.93 ± 0.16
P-value <sup>‡</sup>			0.002	<0.001	<0.001

<sup>\*</sup> Recommended criteria defined as recurrent cholangitis and either 2 episodes of bacteremia or 1 episode sepsis/abscess

<sup>‡</sup> P-value represents comparison of pre- vs. post-1/1/07

**Table 7**

Outcomes for patients applying for exception points after 1/1/07

	Transplanted, N (%)	Died/removed, N (%)
Accepted approved indication, N=43	27 (62.8) *	1 (2.3) <sup>‡</sup>
Accepted unapproved indication, N=115	89 (77.4) *	1 (0.9) <sup>‡</sup>
Denied approved indication, N=9	3 (33.3) <sup>†</sup>	4 (44.4) **
Denied unapproved indication, N=21	10 (47.6) <sup>†</sup>	2 (9.5) **

\* P=0.043 comparing odds of transplantation for approved vs. unapproved

<sup>‡</sup> P=0.54 comparing odds of death/removal for approved vs. unapproved

<sup>†</sup> P=0.38 comparing odds of transplantation for approved vs. unapproved

\*\* P=0.049 comparing odds of death/removal for approved vs. unapproved