The extended mixture distribution survival tree based analysis for clustering and patient pathway prognostication in a stroke care unit

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Abstract- **In our previous work we proposed a special class of survival distribution called Mixture distribution survival trees, which are constructed by approximating different nodes in the tree by distinct types of mixture distributions to achieve more improvement in the likelihood function and thus the improved within node homogeneity. We proposed its applications in modelling hospital length of stay and clustering patients into clinically meaningful patient groups, where partitioning was based on covariates representing patient characteristics such as gender, age at the time of admission, and primary diagnosis code. This paper proposes extended Mixture distribution survival trees and demonstrates its applications to patient pathway prognostication and to examine the relationship between hospital length of stay and/or treatment outcome. 5 year retrospective data of patients admitted to Belfast City Hospital with a diagnosis of stroke is used to illustrate the approach.**
Keywords- **Stochastic modeling, Survival tree, Length of stay modelling, Prognostication, Clustering, Gaussian mixture distributions, Phase type distributions**

I. INTRODUCTION

Mixture distribution survival trees [1] are special type of survival trees, which are constructed by approximating different nodes in the tree by distinct types of mixture distributions to achieve more improvement in the likelihood function and thus the improved within node homogeneity. Survival trees can be used as a powerful method for partitioning survival data into clinically meaningful patient groups for prognostication, i.e., for determining importance, effects of various input covariates (such as a patient's characteristics) and their influence on output measures such as patients' survival, their expected length of stay, discharge destination, or treatment outcome [2] [3]. In our previous work [1], we proposed a mixture distribution survival tree based method where tree nodes were approximated using Gaussian mixture distributions and phase type distributions, for into homogeneous groups with respect to their length of stay

(LOS) where partitioning was based on covariates representing patient characteristics such as gender, age at the time of admission and primary diagnosis code. This paper extends this approach to patient pathway prognostication i.e. for determining importance and effects of various input covariates such as gender, age at the time of admission and primary diagnosis code on patients' hospital length of stay and to examine the relationship between length of stay in hospital and treatment outcome.

An application of the approach to patient pathway prognostication is illustrated using 5 years' retrospective data [4] for 1985 patients admitted between January 2003 and December 2007 to the Belfast City Hospital with a diagnosis of stroke (hemorrhagic stroke, cerebral infarction, transient ischaemic attack TIA, and stroke unspecified). All patients were discharged between January 9th, 2003 and March 11th 2008. No information that identified individual patients was supplied. Patients were aged between 24 years and 101 years. Patient's lengths of stay range from is 0 days (admitted and discharge on the same day) to 1425 days, mean LOS 29.01 days with 52.84 days standard deviation [4].

II. MIXTURE DISTRIBUTION SURVIVAL TREE CONSTRUCTION

A survival tree can be constructed by recursively splitting nodes into daughter nodes by one of the covariates based on some splitting criteria either maximizing either within node homogeneity or between node separation [3]. Each daughter node is approximated by both GMD and C-PhD with different set of components. We used splitting criteria to maximize within node homogeneity expressed in terms of Akaike Information criterion (AIC) [5].

AIC = -2*Log likelihood+2*df.

Where df is the number of free parameters to be estimated. For nodes modeled by n component (phase) Coxian phase type distribution (C-PhD), $df = 2*n-1$ and for a node modeled by m component Gaussian mixture distribution (GMD), $df = 2*m-1$.

A split with minimum value of AIC is selected. If at a node, there is no split providing positive improvement in the AIC, the node is designated as a terminal node.

We used three covariates gender, age at the time of admission and type of stroke diagnosed. The covariate 'age' has value 'old' for those aged 70 or over and it has value 'young' for those aged below 70 years. Based on the primary ICD-10 diagnosis code [6], patients can have any of the four values (hemorrhagic stroke, cerebral infarction, transient ischaemic attack TIA, and other strokes) for the covariate 'stroke diagnosed'.

Figure 1 is the schematic representation of the final mixture distribution survival tree for the length of stay data on stroke patients from the Belfast City Hospital. The resulting tree has 12 terminal nodes. A node with 'P' is modeled by C-PhD while a node with 'G' is modeled by GMD, i.e., node 9, node 17 and node 19 are modeled by GMDs and all other nodes root node (node 1), node 2, node 3, node 4, node 5, node 6, node 7, node 8, node 10, node 11, node 12, node 13, node 14,

node 15, node 16, node 18, node 20 and node 21 are modeled by C-PhDs. Nodes of the tree and possible splits of these nodes are listed in Table 1. Bold faced covariates were selected for splitting the parent node. Nodes which are better fitted by GMD are having AIC shaded yellow. The AIC of root node was 16825.6 and new total AIC of all the terminal nodes of the survival tree is 16397.92 with 427.68 total improvement in AIC.
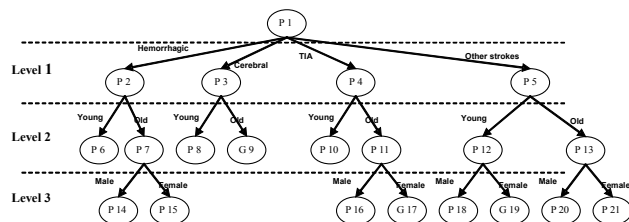

Fig. 1. Mixture distribution survival tree for the length of stay data on stroke patients from the Belfast City Hospital

TABLE I
MIXTURE DISTRIBUTION SURVIVAL TREE CONSTRUCTION (NODES AND POSSIBLE SPLITS)

Node	Covariate	Covariate value	Number of patients	Mean LoS	Standard deviation (LoS)	Coxian-phase type distribution			Gaussian mixture distribution			Improvement in AIC
						Loglikelihood (L_{max})	Number of phases	AIC	Loglikelihood	Number of phases	AIC	
All	**Complete dataset**	**Root node**	**1985**	**29.0106**	**52.8382**	**-8407.8007**	**3**	**16825.60**	**-8481.625**	10	**17021.25**	-
Level 1												
1 (Root node)	Gender	Male	933	26.5938	44.0575	-3859.8125	2	7725.625	-3897.236	7	7834.47	10.2825
		Female	1052	31.154	59.4698	-4539.8469	3	9089.694	-4569.59	9	9191.18	
	Age	Young	624	19.2564	39.1523	-2316.974	2	4639.948	-2342.454	7	4724.9	127.159
		Old	1361	33.4827	57.4932	-6024.2472	3	12058.49	-6047.846	9	12147.7	
	Diagnosis	**Hemorrhagic**	**154**	**33.6039**	**56.4456**	**-659.05019**	**3**	**1328.1**	**-665.5723**	**6**	**1365.14**	306.1832
		Cerebral	**655**	**36.6611**	**47.6753**	**-2973.8941**	**4**	**5961.788**	**-2980.867**	**6**	**5995.73**	
		TIA	**425**	**9.31294**	**19.9516**	**-1298.6262**	**2**	**2603.252**	**-1316.503**	**6**	**2667**	
		Other	**751**	**32.5433**	**65.0453**	**-3310.1386**	**2**	**6626.277**	**-3297.443**	**8**	**6640.89**	
Level 2												
2 Hemorrhagic	Gender	Male	80	28.2	52.09832	-317.63202	4	649.2640	-328.0819	4	678.1638	12.50299
		Female	74	39.4459	60.254	-328.16667	3	666.3333	-329.4363	6	692.873	
	Age	**Young**	**50**	**24.56**	**55.117**	**-173.39875**	**4**	**360.7975**	**-187.3508**	**3**	**390.702**	15.65113
		Old	**104**	**37.9519**	**56.561**	**-468.82587**	**4**	**951.6517**	**-477.7462**	**4**	**977.492**	
3 Cerebral	Gender	Male	302	33.70860	49.8833	-1334.898	4	2683.796	-1339.464	5	2706.93	-2.395836
		Female	353	39.18697	45.5501	-1635.194	3	3280.388	-1639.346	5	3306.69	
	Age	**Young**	**194**	**24.0670**	**42.4506**	**-785.3629**	**3**	**1580.726**	**-793.676**	**5**	**1615.35**	35.8404
		Old	**461**	**41.961**	**48.787**	**-2173.9068**	**2**	**4353.814**	**-2158.611**	**5**	**4345.22**	
4 TIA	Gender	Male	207	8.7005	22.6817	-607.9547	2	1221.909	-637.5377	4	1297.08	-1.20391
		Female	218	9.8945	16.9366	-686.27346	3	1382.547	-690.5091	5	1409.02	
	Age	**Young**	**176**	**5.83523**	**11.1641**	**-455.8639**	**2**	**917.7278**	**-465.3673**	**4**	**952.735**	24.78144
		Old	**249**	**11.7711**	**24.0154**	**-827.3716**	**2**	**1660.743**	**-823.7194**	**8**	**1693.44**	
5 Other strokes	Gender	Male	344	30.7413	43.4091	-1490.577	4	2995.154	-1490.229	6	3014.46	8.886526
		Female	407	34.0663	78.7981	-1808.118	2	3622.237	-1864.211	3	3744.42	
	Age	**Young**	**204**	**24.9608**	**43.76126**	**-818.1347**	**4**	**1650.269**	**-819.1983**	**6**	**1672.4**	36.23604
		Old	**547**	**35.3711**	**71.1697**	**-2466.8858**	**2**	**4939.772**	**-2543.835**	**3**	**5103.67**	
Level 3												
6 Hemorrhagic Young	Gender	Male	29	30.5172	69.1114	-108.83289	2	223.6658	-105.682	4	233.364	-9.21382
		Female	21	16.3333	22.8126	-70.172765	2	146.3455	-74.17359	3	164.347	
7 **Hemorrhagic Old**	**Gender**	**Male**	**51**	**26.8823**	**39.2027**	**-211.39224**	**4**	**436.7845**	**-211.0736**	**4**	**444.147**	2.30463
		Female	**53**	**48.6038**	**67.5821**	**-253.2813**	**2**	**512.5626**	**-245.9886**	**7**	**531.977**	
8 Cerebral Young	Gender	Male	104	24.6731	49.2715	-420.88798	2	847.776	-427.2601	4	876.52	-3.15333
		Female	90	23.36667	32.9415	-361.0516	4	736.1032	-364.2716	4	750.543	
9 Cerebral Old	Gender	Male	198	38.4545	49.6696	-903.58419	4	1821.168	-903.381	4	1828.76	-0.62756
		Female	263	44.6008	47.9429	-1259.34	2	2524.681	-1251.528	6	2537.06	
10 TIA Young	Gender	Male	88	5.7386	11.3263	-224.74588	2	455.4918	-232.5108	3	481.022	-5.52344
		Female	88	5.9318	10.9988	-230.8797	2	467.7595	-231.1457	4	484.291	
11 **TIA Old**	**Gender**	**Male**	**119**	**10.8908**	**28.0847**	**-377.7327**	**2**	**761.4654**	**-401.7215**	**3**	**819.443**	2.615394
		Female	**130**	**12.5769**	**19.5270**	**-444.56883**	**4**	**903.1377**	**-437.3312**	**4**	**896.662**	
12 **Other strokes Young**	**Gender**	**Male**	**119**	**30.1092**	**52.7719**	**-493.3325**	**3**	**996.665**	**-486.2055**	**6**	**1006.41**	0.265422
		Female	**85**	**17.7529**	**24.6624**	**-322.7928**	**3**	**655.5857**	**-318.6695**	**3**	**653.339**	
13 **Other strokes Old**	**Gender**	**Male**	**225**	**31.0756**	**37.52**	**-987.5257**	**4**	**1989.051**	**-991.5326**	**4**	**2005.07**	3.802914
		Female	**322**	**38.3727**	**87.1713**	**-1470.4587**	**2**	**2946.917**	**-1517.217**	**3**	**3050.43**	

At level 2, for all nodes, the covariate 'age' provided the most significant split while the covariate 'gender' did not provide significant splits for the group of patients with diagnosis cerebral infarction and for the group of patients with diagnosis TIA. For example, among patients with TIA, young patients were most likely to have a shorter length of stay (mean LOS 5.84) while old patients were likely to have relatively longer length of stay (mean LOS 11.77).

At level 3, for all but one group of young patients (young patients with diagnosis of other strokes), the covariate gender did not provide prognostically significant splits. While at level 3, for groups of old patients with stroke diagnosis hemorrhagic stroke, TIA and other strokes (node 7, node 11 and node 13) the covariate gender provided prognostically significant splits). For the group of old patients with cerebral infarction (node 9) the covariate gender split is not prognostically significant.

III. THE EXTENDED MIXTURE DISTRIBUTION SURVIVAL TREE CONSTRUCTION

This mixture distribution survival tree method can be extended to examine the relationship between the treatment outcome and patients' length of stay distribution and their interrelationship with patient characteristics by further partitioning each group of patients (determined using mixture distribution survival tree method above) into subgroups with more homogeneous patient pathways by covariate 'treatment outcome'. Although the information about the treatment outcome is not available at the time of admission, we can assign the probability to each treatment outcome using cohort analysis. The covariate ' treatment outcome ' can have any of the two values death or discharge from the hospital.

TABLE II
EXTENDED MIXTURE DISTRIBUTION SURVIVAL TREE CONSTRUCTION (NODES AND POSSIBLE SPLITS)

Node	Covariate	Covariate value	Number of patients	Mean LoS	Standard deviation (LoS)	Coxian-phase type distribution			Gaussian mixture distribution			Improvement in AIC
						Loglikelihood (L_{max})	Number of phases	AIC	Loglikelihood	Number of phases	AIC	
All	Complete dataset	Root node	1985	29.0106	52.8382	-8407.8007	3	16825.60	-8481.625	10	17021.25	-
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		Old	1361	33.4827	57.4932	-6024.2472	3	12058.49	-6047.846	9	12147.7	
	Diagnosis	Hemorrhagic	154	33.6039	56.4456	-659.05019	3	1328.1	-665.5723	6	1365.14	306.1832
		Cerebral	655	36.6611	47.6753	-2973.8941	4	5961.788	-2980.867	6	5995.73	
		TIA	425	9.31294	19.9516	-1298.6262	2	2603.252	-1316.503	6	2667	
		Other	751	32.5433	65.0453	-3310.1386	2	6626.277	-3297.443	8	6640.89	
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2 Hemorrhagic	Gender	Male	80	28.2	52.09832	-317.63202	4	649.2640	-328.0819	4	678.1638	12.50299
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	Age	Young	50	24.56	55.117	-173.39875	4	360.7975	-187.3508	3	390.702	15.65113
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		Female	322	38.3727	87.1713	-1470.4587	2	2946.917	-1517.217	3	3050.43	

Each terminal node of the survival tree of Figure 1 is further partitioned into daughter nodes by the covariate 'treatment outcome'. We grow the tree if the split maximizes node homogeneity by minimizing the value of AIC and if at a node, there is no split providing significant improvement in AIC, the node is designated as a terminal node.

Figure 2 is the schematic representation of the extended mixture distribution survival tree for the length of stay data on stroke patients from the Belfast City Hospital. The resulting tree now has 19 terminal nodes. Only two terminal nodes (node 9 and node 26) are approximated by GMD and all other terminal nodes are approximated by C-PhD. Table 2 lists terminal nodes of the survival tree of figure 1, and possible splits of these nodes by the covariate 'treatment outcome'. Bold faced splits were selected for splitting the parent node. Parent nodes are represented by pale blue rows with treatment outcome "all". The column P/G specifies which distribution among C-PhD and GMD provides better fit. The total improvement in AIC is 115.655 and the new AIC of all the terminal nodes is 16282.27.
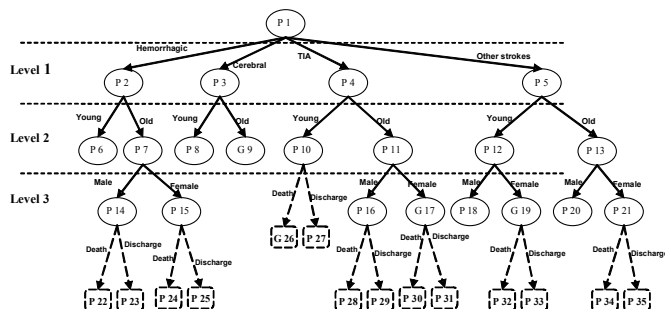
Fig. 2. Extended mixture distribution survival tree for the length of stay data on stroke patients from the Belfast City Hospital

IV. PATHWAY PROGNOSTICATION USING THE EXTENDED MIXTURE DISTRIBUTION SURVIVAL TREE

The extended mixture distribution survival tree method can effectively be used to examine the relationship between LOS and treatment outcome at discharge and their interrelation with patient characteristics such as age, gender and diagnosis.

The extended mixture distribution survival tree clusters the length of stay data into 19 clinically meaningful patient groups, each representing a distinct patient pathway within the system. We can see that in seven patient groups (i.e., the terminal nodes in Figure 1), the covariate 'treatment outcome' has prognostic significance, i.e., patients with different treatment outcomes follow different patient pathways, while, there is homogeneity among patient pathways followed by the other five patient groups. The treatment outcome is prognostically most significant among the group of old male patients diagnosed with Hemorrhagic stroke. This also reflects with the difference in mean LOS. Among this group of patients, those are expected to discharge are likely to have longer length of stay (mean LOS 31.9) than those die in the course of their treatment (mean LOS 10.9). The Treatment outcome has prognostic significance for all groups of female

patients while it has prognostic significance in only two groups of male patients (node 14 and node 16). All young patients with Hemorrhagic stroke followed homogeneous patient pathways. Treatment outcome does not have prognostic significance among all groups of patients diagnosed with cerebral infraction, while treatment outcome is prognostically significant in all groups of patients with TIA. Patients diagnosed with TIA and discharged from hospital are more likely to have shorter length of stay (mean LOS 5.24, 10.35, 11.16 respectively for node 27, node 29 and node 31) than those patients with TIA who died in the hospital (mean LOS 57.5, 21 and 48 respectively for node 26, node 28 and node 30).Prepare your paper in full-size format, on US letter paper 8 ½ by 11 inches). For A4 paper, use the A4 settings.

V. CONCLUSION

Mixture distribution survival tree have advantage of achieving the improved within node homogeneity. Therefore, mixture distribution survival tree based analysis is a more effective method for prognostication of survival data and for clustering survival data into groups of patients following homogeneous patient pathways. It is a powerful method for determining the relationship between input covariates and outcome measures and their interrelations. It provides better understanding of heterogeneity of patient pathways stratified by covariates representing patient characteristics such as age, gender, diagnosis and outcome measures such as treatment outcome, destination at discharge. We can also use the model to estimate the length of stay of a patient based on his/her characteristics (age, gender, diagnosis) available at the time of admission. We can extend this approach by further growing the tree by partitioning the terminal nodes into subgroups with more homogeneous patient pathways based on covariates representing outcome measures. Although the information about the treatment outcome is not available at the time of admission, we can assign the probability to each treatment outcome using cohort analysis. This information can be used for estimating bed requirements for each group of patients (following homogeneous patient pathways) and capacity planning for the whole care system. As future work we will also assess the use of other mixture distributions in order to achieve further improvement in within node homogeneity. Presently we are developing application of our model for capacity planning in a stroke care unit.

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