Hepatocellular carcinoma (HCC) is the 3rd most common cause of cancer death globally and effective systemic treatments for the disease are limited. HCC complicates chronic liver disease and its incidence is increasing dramatically in the UK. Sulfatase 2 (SULF2) is one of two extracellular heparan sulphate 6-O-endosulfatase and one of 17 human sulfatases. It reportedly modulates ligand activated FGF and Wnt signalling and is up-regulated in 57% of HCC. We aim to explore the potential of SULF2 as a therapeutic target for HCC treatment and have characterised its biology in HCC cell lines.

Methods Expression of SULF2 and its homologue SULF1 were assessed at RNA and protein levels in six HCC cell lines. The desulfating enzymatic activity of these cell lines were compared using the fluorogenic substrate 4-methylumbelliferyl sulphate (4-MUS). SULF2 was knocked down using short hairpin RNA lentiviral particles. SULF2 gene silencing effect on receptor tyrosine kinase signalling was investigated by phospho-ERK and phospho-AKT immunoblot and its effect on Wnt signalling by the TCF luciferase reporter assay. Cell growth was assessed by SRB assay.

Results 3 of the six tested HCC cell lines showed up-regulated SULF2 expression at the RNA and protein levels. HuH-7 cells had the highest sulfatase activity. SULF2 gene silencing in this cell line caused dramatic inhibition of Wnt5A-induced β-catenin-dependent transcriptional activity (twofold and p value = 0.03, Abstract PMO-094 figure 1), with relatively modest effects on the phosphorylation of ERK or AKT after stimulation with FGF-1, FGF-2 or IGF-I. SULF2 suppression significantly reduced cell number (twofold and p value <0.001, Abstract PMO-094 figure 2) and enzymatic activity (p value <0.0001, Abstract PMO-094 figure 3) of HuH-7 cells.

Conclusion SULF2 is over-expressed in the majority of HCCs and is catalytically active. SULF2 gene silencing in HuH-7 inhibits Wnt signalling and cell growth. These data support a key role for SULF2 in hepatocarcinogenesis, the inhibition of which offers a novel means of antagonising Wnt signalling in cancers.
Methods  
Between November 2005 and April 2009, 12 LPD following LPD and OPD. The aim of this study is to compare the adequacy of cancer resection and outcome following LPD and OPD.

Results  
R0 resection was achieved in 9 LPD vs 8 OPD (p=1.000). The T staging T2, T3, T4 were 6, 4, 2 for LPD vs 6, 5, 1 for OPD respectively (p=1.000). The mean tumour size was 19.8 for LPD vs 19.2 for OPD (p=0.870). The mean number of lymph node excised for LPD vs OPD (20.7 vs 18.5, p=0.554). Clavien grade I/II complications (5 vs 3), Clavien grade III/IV complications (2 vs 6) and pancreatic leak (2 vs 1) were statistically not significant (LPD vs OPD). The mean HDU stay was longer in OPD group (3.7 vs 1.4 days, p<0.000), but LOS was no different (14.9 vs 14.9 days, p=1.000). There were two recurrences each in LPD and OPD group (p=1.000). Overall mortality for LPD vs OPD (2 vs 6, p=0.193) and recurrence-related mortality (2 vs 2, p=1.000).

Conclusion  
Compared to open procedure, in patients with tumour size <2 cm, laparoscopic pancreaticoduodenectomy achieves similar rate of R0 resection, lymph node harvest and long-term recurrence. LPD patients have significantly shorter high-dependency stay and lesser post-operative complications. Though technically challenging, laparoscopic pancreaticoduodenectomy is safe and does not compromise oncological outcome for tumours <2 cm.