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# Definition of age-dependent reference values for the diameter of the common bile duct and pancreatic duct on MRCP: a population-based, cross-sectional cohort study

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## ABSTRACT

**Objective** Changes of the pancreaticobiliary ducts herald disease. Magnetic resonance cholangiopancreatography (MRCP) allows accurate duct visualisation. Data on reliable upper reference ranges are missing.

**Design** Cross-sectional whole body MRI data from the population-based Study of Health in Pomerania were analysed. The width of the common bile duct (CBD) and the pancreatic duct (PD) was determined. We aimed to describe the distribution of physiological duct diameters on MRCP in a population of healthy subjects and to identify factors influencing duct size.

**Results** After excluding pre-existing pancreaticobiliary conditions, CBD and PD diameters from 938 and 774 healthy individuals, respectively, showed a significant increase with age ( $p < 0.0001$ ) and exceeded the conventional upper reference limit of normal in 10.9% and 18.2%, respectively. Age-dependent upper reference limits of duct diameters were delineated with non-parametric quantile regression, defined as 95th percentile: for CBD up to 8 mm in subjects <65 years and up to 11 mm in subjects  $\geq 65$  years. For the PD reference diameters were up to 3 mm in subjects <65 years and up to 4 mm in subjects  $\geq 65$  years.

**Conclusions** This is the first population-based study delineating age-adjusted upper reference limits of CBD and PD on MRCP. We showed that up to 18.2% of healthy volunteers would have needed diagnostic workup, if the conventional reference values were used. The utilisation of the adapted reference levels may help to avoid unnecessary investigations and thus to reduce healthcare expenditure and test-related adverse events.

## INTRODUCTION

Changes in the diameters of the pancreaticobiliary ducts point to disease ranging from benign conditions like chronic pancreatitis or bile duct stones to worrisome mucinous cystic neoplasms and pancreaticobiliary cancers. Magnetic resonance cholangiopancreatography (MRCP) is the first-line, non-invasive imaging modality for full duct visualisation, with broad availability and ever-increasing accuracy.<sup>1</sup> However, reference ranges of duct diameters in asymptomatic individuals and their change with age

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ An increasing diameter of the common bile duct (CBD) or pancreatic duct (PD) heralds disease.
- ⇒ Previous reference levels for CBD and PD rely on transabdominal ultrasound and endoscopic retrograde pancreatography (ERP) and are mainly derived from patients' cohorts. Modern imaging technology with increasing sensitivity and specificity warrants adaptation of previous reference levels.
- ⇒ Systematic evaluation of CBD and PD diameters employing modern non-invasive imaging technology such as MRCP (magnetic resonance cholangiopancreatography) in population-based cohorts corrected for age and relevant confounders are lacking.

## WHAT THIS STUDY ADDS

- ⇒ Employing conventional reference levels for the diameters of CBD and PD would have resulted in additional diagnostic workup to exclude potentially life-threatening disease in up to 18.2% of healthy volunteers.
- ⇒ In a population-based and thus relevant setting, we established and quantified age dependency of CBD and PD diameters resulting in novel evidence-based reference levels for subjects below and above the age of 65 years as well as after gallbladder surgery. Follow-up and sensitivity analysis excluded relevant pathologies missed at first imaging.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Adaptation of reference values to modern imaging technology in a population-based setting is being suggested.
- ⇒ Our study will set new reference levels to improve standard of care and thus may avoid unnecessary investigations, reduce health care expenditure and test related adverse events.

and after medical procedures have only been studied in small cohorts with short follow-up and population-based data are missing.<sup>2,3</sup>

Discussions about the physiological upper limit of the diameter of the extrahepatic bile duct and the pancreatic duct (PD) have been ongoing in the medical literature ever since their first non-invasive visualisation, but surprisingly, no definitive answer to this seemingly simple question has been agreed on.<sup>4</sup> The studies defining the conventionally used upper reference limits of either 6 mm<sup>5</sup> or 7 mm<sup>6,7</sup> for the common bile duct (CBD) date back almost 40 years and were established by ultrasound at a time when simply finding the non-dilated bile duct was a challenge. For the PD, the standard of 3 mm was set by pancreatography studies in the 1970s<sup>8</sup> and is still in use, although it was later discovered that non-invasive imaging and endoscopic-retrograde pancreatography do not correlate well.<sup>9,10</sup> Thus, revisiting the question of what are the upper reference limits for both, the diameters of the PD as well as the CBD, and adopting it for increase in age has been suggested by a number of authors.<sup>11,12</sup> An increase in the duct diameters with advanced age has been discussed as early as 1983.<sup>7</sup> However, this has not been investigated in 'healthy individuals' beyond the age of 65 years. Moreover, the question whether the CBD diameter changes after cholecystectomy has been debated,<sup>5,13,14</sup> yet an MRI based and population-based study is not available. Therefore, we investigated the normal distribution of CBD and PD diameters in healthy volunteers from the general population who underwent MRCP. We aimed to describe the distribution of physiological diameters of pancreaticobiliary ducts on MRCP in a population of healthy subjects and to identify factors influencing duct size.

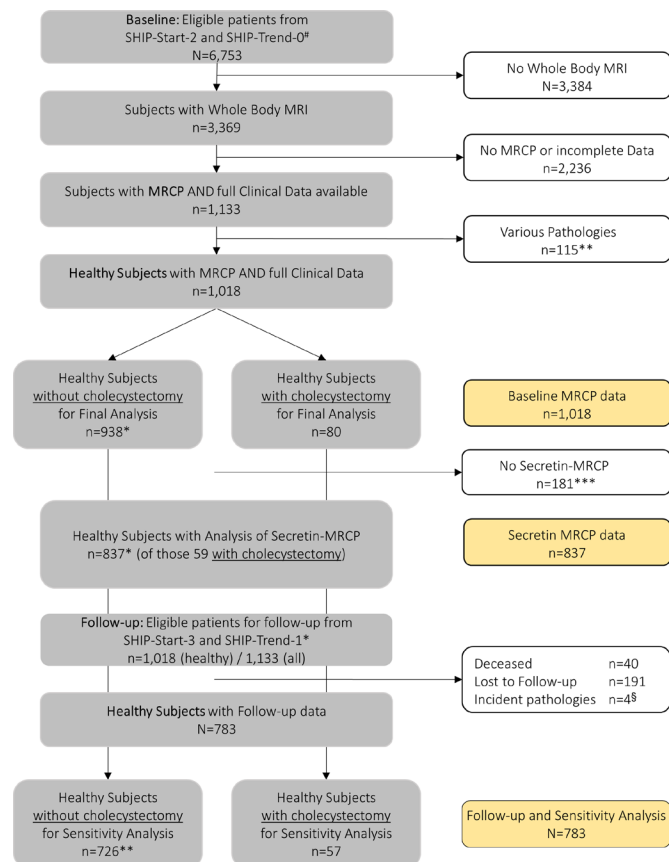
## METHODS

### Study population

Subjects were recruited from the Study of Health in Pomerania (SHIP).<sup>15,16</sup> SHIP is a prospective, population-based cohort project in Northeast Germany with the objective to study the prevalence and incidence of diseases, as well as to analyse associations between risk factors, subclinical disorders and manifest affliction. Representative samples of the 20–79 year old Caucasian inhabitants of the study region were drawn from local population registries. Further details on sampling methods and recruiting are given elsewhere.<sup>16,17</sup>

SHIP consists of two cohorts: SHIP-Start and SHIP-Trend. Timeline and recruitment are illustrated in online supplemental figure 1. The data for our study population, that is baseline analyses presented here, were derived from SHIP-Start-2 and SHIP-Trend-0, both acquired between 2008 and 2012. In these two study waves, whole body MRI including MRCP was first offered as part of the investigational protocol to all participants.<sup>18,19</sup> Follow-up periods were different for both subgroups, namely 2014–2016 for SHIP-Start and 2016–2019 for SHIP-Trend (online supplemental figure 1).

An overview over the selection of the study participants for the cross-sectional analysis is given in figure 1. In detail, among the 6753 SHIP-Start-2 and SHIP-Trend-0 participants, 3369 agreed to whole-body MRI. In 1133 subjects, MRCPs as well as full clinical data were available. These cases were subsequently screened for eligibility in the present analyses. One hundred and fifteen subjects were excluded for presence of pathologies of the pancreaticobiliary system detected either on MRI, in other study related examinations, or according to self-reported medical history. To define pancreaticobiliary health at baseline of our study, the following items were taken into consideration. MRI-related: cholelithiasis (gallbladder or duct), acute or chronic cholecystitis, parenchymal or ductal signs of acute or chronic pancreatitis, cystic pancreatic lesions, intrahepatic cholestasis,



# see suppl. Figure 1, \*at least one measurement taken, \*\* excluded were: cholelithiasis, choledocholithiasis, chronic pancreatitis, pancreatic fluid collections or cystic lesions including pseudocysts, cholestatic liver disease, liver cirrhosis, previous acute or chronic hepatitis, primary or metastatic malignancy of the abdomen. For details see suppl. Table 1, \*\*\*includes 5 cases with unreadable secretin-MRCP, § see text.

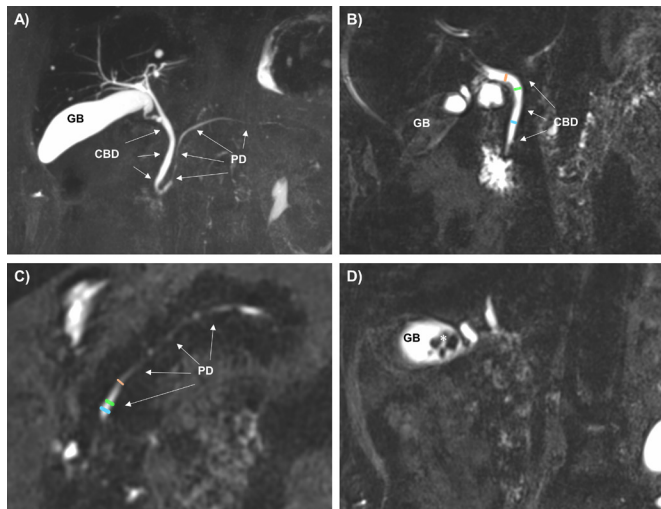
**Figure 1** Flow chart representing the selection of the study populations. MRCP, magnetic resonance cholangiopancreatography.

cirrhosis, previous pancreatic or liver resection, tumours of upper abdomen and previous cholecystectomy. Furthermore, the following reported illnesses were screened: acute or chronic pancreatitis, pancreatic cancer, liver cancer or other cancers, gallstones or gallstone-related symptoms, cirrhosis and acute or chronic hepatitis.

Of the remaining 1018 subjects who fulfilled all inclusion criteria (figure 1), 80 had undergone cholecystectomy and were analysed as a separate subgroup. In a secondary analysis, all patients with secretin MRCP were analysed (n=837, 778 without and 59 with cholecystectomy) and compared with the baseline group previously. For this analysis, 176 without secretin-MRCP and 5 unreadable cases had to be excluded (figure 1).

A morbidity and mortality follow-up was attempted in 1018 individuals (938 healthy+80 with cholecystectomy) as part of SHIP-Start-3 and SHIP-Trend-1 as outlined previously (figure 1 and online supplemental figure 1). The median follow-up period was 65.2 months,  $\pm 5.6$  months.

Follow-up data analysed included newly diagnosed pancreaticobiliary disease detected in study related examinations (including whole body MRI, liver ultrasound and blood examination) or according to self-reported medical history, as reported elsewhere.<sup>17</sup> Medical records not related to SHIP were not available as the identity of the subjects was kept confidential. All subjects who died, were lost to follow-up or had incident pathologies (ie, pancreatic cancer or newly diagnosed liver disease) during follow-up and were excluded secondarily from



**Figure 2** Representative pictures from magnetic resonance cholangiopancreatography (MRCP) of study subjects. (A) Maximum intensity projection in the coronal orientation for orientation of the reader. (B) Single section of coronal MRCP for identification of the largest diameter of the CBD. The gallbladder is partially displayed. (C) Single section of coronal MRCP for identification of the largest diameter of the PD. (D) Single section of coronal MRCP for analysis of the gallbladder. It contains round structures with no T2-signal indicating gallstone disease (asterisk). CBD, common bile duct; GB, gallbladder; PD, pancreatic duct.

the group of ‘healthy’ subjects for a sensitivity analysis, leaving a sample sizes of 783 of which 57 had cholecystectomy. (figure 1).

### Reading of MRCP imaging and assessment of duct diameters

Duct diameters were measured by a single trained investigator (FK) blinded to any other individual data on MRCP coronal sequence using OsiriX software for Mac.<sup>20</sup> Training was overseen by J-PK, who has more than 10 years of professional experience in abdominal cross-sectional imaging. PT, who has more than 3 years of professional experience in diagnostic imaging, validated a subset of reads (see further). At first, the presence or absence of the gallbladder and any evidence of gallstones was recorded (figure 2A,D). Next, all abnormalities or pathological signs of the CBD and PD were recorded, including obstructing stones, strictures, irregularities or masses. The CBD was assessed at the largest diameter distal to the cystic duct, and the PD was assessed at its largest diameter in the pancreatic head. The diameters of CBD and PD were measured perpendicular to the long axis (figure 2B,C). Median differences of 1 mm and more

were deemed of clinical relevance when interpreting the data, with regard to known limits of spatial resolution of MRCP and common practice in clinical decision making.<sup>21–23</sup>

Further information on MR technique, study medication and protocol for incidental findings, laboratory analyses and statistical analysis can be found in the online supplemental methods section.

## RESULTS

### Study cohort

An overview on the selection of the study participants for the cross-sectional analysis is shown in figure 1 and is outlined in detail in Methods and in the online supplemental appendix 1.

### Characteristics of healthy subjects and those with cholecystectomy

Among the 938 healthy subjects eligible for the study with MRCP and clinical information available, men were slightly over-represented, accounting for 52.7% of the study population (table 1). In contrast, among the subjects with cholecystectomy, women were over-represented with 57.5%. Healthy subjects had a median age of 51 years, while cholecystectomy subjects were older with a median age of 62 years. Median body mass index (BMI) was in the overweight range (27 kg/m<sup>2</sup>) in healthy and in the cholecystectomy subjects (29 kg/m<sup>2</sup>). Moreover, median ALAT, ASAT and GGT activities were in the normal range of healthy and cholecystectomy subjects. There were no differences between the primary group and the subgroups with secretin MRCP and the subgroup with available follow-up (table 1). Characteristics of excluded subjects can be found in online supplemental table 1.

### Findings and upper reference limits for duct diameters estimated by quantile regression

In the group of healthy subjects with clinical data and MRCP (n=938), the diameters of the CBD and PD increased with age. For instance, subjects in the third decade of their life had a median (IQR) native CBD diameter of 4.5 mm (1.30 mm) compared with 6.1 mm (3.05 mm) in subjects aged 70 years or older. Similarly, for the PD, subjects aged 20–29 years had median (IQR) native diameter of 1.4 mm (0.37 mm). The median native PD diameter increased to 2.6 mm (1.32 mm) in subjects aged 70 years or older. Full data are presented in table 2. In the entire cohort of healthy subjects, 18.2% of native CBD measurements exceeded the mark of 7 mm and 11.0% of native PD measurements exceeded 3 mm. These findings indicate that a large proportion of asymptomatic, healthy volunteers recruited from the general population exceeds the conventional upper reference limits for

**Table 1** Characteristics of the selected healthy participants and those with cholecystectomy

Characteristics	Healthy			Cholecystectomy		
	Native (n=938)	Secretin (n=778)	With follow-up (n=726)	Native (n=80)	Secretin (n=59)	With follow-up (n=57)
Male, %	52.7	56.6	52.9	42.5	37.3	45.6
Age, years	51.0 (41.0–62.0)	50.0 (40.0–61.0)	50.0 (41.0–61.0)	62.5 (55.0–70.5)	62.0 (55.0–69.0)	62.0 (54.0–68.0)
BMI, kg/m <sup>2</sup>	27.0 (24.5–30.2)	26.9 (24.3–30.0)	27.0 (24.5–30.0)	29.3 (25.6–32.3)	30.0 (25.6–32.2)	29.0 (25.6–32.3)
ALAT, $\mu$ kat/L	0.37 (0.27–0.52)	0.38 (0.27–0.52)	0.38 (0.27–0.53)	0.34 (0.28–0.51)	0.34 (0.28–0.54)	0.33 (0.28–0.51)
ASAT, $\mu$ kat/L	0.30 (0.24–0.37)	0.29 (0.24–0.37)	0.30 (0.24–0.37)	0.29 (0.24–0.38)	0.30 (0.25–0.39)	0.30 (0.25–0.39)
GGT, $\mu$ kat/L	0.49 (0.38–0.70)	0.49 (0.38–0.71)	0.49 (0.38–0.70)	0.48 (0.36–0.69)	0.46 (0.36–0.73)	0.49 (0.36–0.68)

Data are proportions or median (first to third quartile).

Subgroup with secretin scans is displayed separately.

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; CBD, common bile duct; PD, pancreatic duct.



**Table 2** Median duct diameters in healthy individuals

	Healthy native	Healthy secretin	Cholecystectomy native	Cholecystectomy secretin
<b>CBD</b>				
Median (IQR), mm	5.3 (1.13)	5.2 (2.15)	8.2 (4.21)	8.0 (3.48)
>7 mm, %	18.2	15.9	63.8	69.5
<b>PD</b>				
Median (IQR), mm	1.8 (0.96)	2.0 (1.09)	2.1 (1.09)	2.3 (1.46)
>3 mm, %	11.0	17.3	22.4	32.8

Data are proportions or median (IQR).  
CBD, common bile duct; PD, pancreatic duct.

the diameter of the proximal CBD and the PD. In multivariable adjusted quantile regression models age demonstrated consistent and highly significant (all models  $p < 0.001$ ) positive associations with CBD and PD diameters (online supplemental table 2).

Therefore, an adaption of the upper reference limits is indicated to guide clinical decision making in the future. We applied quantile regression analysis to determine age-dependent upper reference limits of duct diameters. We found that the median as well as the 95th percentile of CBD and PD diameters increased with age. Yet, the slope of the regression curve was steeper for the 95th percentile than for the median (figure 3). In the following, we derived upper reference limits for the whole cohort and distinct age groups (<65 years and  $\geq 65$  years) as displayed in table 3. In summary, for subjects younger than 65 years, a CBD diameter up to 8 mm and a PD diameter up to 3 mm can be considered within the reference range, whereas in subjects aged 65 years or older, a CBD diameter up to 11 mm and a PD diameter up to 4 mm is within the upper reference limit. We further observed that cholecystectomy leads to an enlarged CBD diameter, and upper reference limits according to quantile regression analysis are included in table 3. A online supplemental table 3 summarises upper reference limits of CBD and PD diameters in healthy subjects according to age decade of subjects.

### Effect of cholecystectomy

These data refer to 80 subjects with cholecystectomy and available MRCP at baseline (without and with secretin). In subjects aged 50 years and above who had their gallbladder removed but had no evidence of remaining pancreaticobiliary pathology, the native CBD diameter was enlarged compared with healthy subjects ( $p < 0.001$  for all comparisons, online supplemental

figure 2). Median native PD diameters were similar between healthy individuals and those with cholecystectomy.

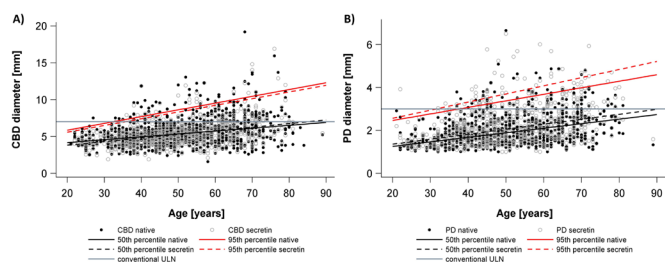
In cholecystectomised subjects, CBDs exceeded the upper reference limit of 7 mm in more than 60% of cases (table 2). The effect of cholecystectomy on duct diameters was considered when determining new upper reference limits (table 3).

### Effect of secretin administration

Secretin data were available from 837 subjects, 59 of those with cholecystectomy (table 1 and figure 1). Application of secretin led to an increase in the median PD diameter from 1.8 mm (IQR 0.96 mm) to 2.0 mm (IQR 1.09 mm) ( $p < 0.01$ ) and to a decrease in the CBD diameter (median (IQR) native 5.3 (2.12) and with secretin 5.2 (2.15),  $p < 0.01$ ) (table 2). The effect of secretin on duct diameters was taken into account and corrected for when determining new upper reference limits (table 3 and online supplemental table 3).

### Effects of gender, liver function test and BMI on duct diameters in healthy subjects

Multivariable adjusted quantile regression models were used to analyse the relation between duct diameters, gender, liver function tests and BMI. MRCP data from subjects without cholecystectomy before ( $n = 938$ ) and after secretin ( $n = 837$ ) stimulation were analysed separately. It revealed associations between gender and CBD but not PD diameters (online supplemental table 2). The magnitude of the difference in CBD diameters between men and women was, however, marginal. Therefore, we decided not to pursue gender differences as part of this study. In further analyses, associations of alanine-aminotransferase (ALAT) activity



**Figure 3** Scatterplot of the largest perpendicular diameter of (A) the common bile duct (CBD) and (B) the pancreatic duct (PD) according to age in healthy subjects before and after secretin administration on magnetic resonance cholangiopancreatography. Red lines represent the 95th percentile and black lines represent the 50th percentile as estimated from quantile regression models. Solid lines represent results without secretin and the dashed lines results with secretin. The horizontal dotted lines represent the conventional upper limit of normal (ULN) of 7 mm and 3 mm for the respective duct.

**Table 3** Upper reference limits for common bile duct (CBD) and pancreatic duct (PD) diameters according to age, administration of secretin and cholecystectomy status

		Upper reference limits of normal		
		All ages	<65 years	$\geq 65$ years
<b>CBD</b>				
Native	Healthy	9.1	7.9	11.1
	Cholecystectomy	13.5	13.3	14.0
Secretin	Healthy	8.8	7.6	10.8
	Cholecystectomy	13.0	13.0	12.6
<b>PD</b>				
Native	Healthy	3.5	3.1	4.2
	Cholecystectomy	3.8	3.8	3.5
Secretin	Healthy	3.9	3.4	4.7
	Cholecystectomy	4.0	3.9	4.0

CBD, common bile duct; PD, pancreatic duct.

and BMI with duct diameters were assessed to exclude an influence of subclinical liver disease and obesity on the CBD or PD diameters. ALAT activity was neither associated with native or secretin-stimulated CBD diameter nor with secretin-stimulated PD diameter but with native PD diameter (online supplemental table 2 and online supplemental figure 3). Regarding BMI, we observed inverse associations with native CBD diameter as well as native and secretin-stimulated PD diameters (online supplemental table 2 and online supplemental figure 4). Again, due to the small effect sizes of the previous associations, a further evaluation of the effects was not pursued. Moreover, it demonstrated that an increase in CBD diameters is not associated with underlying liver or bile duct disease. This finding cannot be extended to the PD group since subjects with pre-existing hyperlipasaemia were excluded before secretin MRCP.

### Follow-up of study subjects

Among the 1018 included subjects with MRCP (938 healthy and 80 with cholecystectomy), 40 had died during follow-up, 191 were lost to follow-up and 4 developed incident pathologies after the index examination. The respective numbers are given in figure 1. The pathologies were: two cases of pancreatic ductal adenocarcinoma, one case with liver metastases of unknown primary and one case with cirrhosis, all of which were not evident at baseline examinations (for details see online supplemental file).

Reference limits for the CBD and PD diameters after exclusion of these subjects are presented in online supplemental table 4, thus representing a cohort of subjects with sustained health. Overall, differences in upper reference limits of CBD and PD diameters in the main and the sensitivity analysis were small and well below 1 mm and thus considered not clinically relevant.

### Reliability analysis

Certification of reader (FK) was achieved by randomly selecting 98 of the available 1018 (9.6%) readings for a second measurement by an independent expert reader (PT) blinded to previous results. Analysis showed excellent intraclass correlation (ICC)=0.912 (95% CI 0.846 to 0.950;  $p<0.0001$ ) for CBD and ICC=0.967 (95% CI 0.943 to 0.981;  $p<0.0001$ ) for PD. Cronbach's alpha was  $>0.8$  in all sets. Intrareader reliability was very good with ICC=0.884 (95% CI 0.805 to 0.933,  $p<0.0001$ ) and Cronbach's alpha  $>0.8$  on randomly selected 104 repeated reads from the available 894 MRCPs (10.2%). Full results can be found in online supplemental table 5.

## DISCUSSION

### Justification of the study

MRCP is a commonly used non-invasive imaging modality in the evaluation of the pancreaticobiliary ductal system, and the availability and accuracy is increasing. Unfortunately, the physiological distribution of CBD and PD diameters among the general population as visualised on MRI has not been studied. Previous studies were restricted to patients who either had symptoms of or presented with already overt diseases of the pancreaticobiliary system.<sup>13 24 25</sup> Knowledge concerning the physiological diameter of CBD and PD is of clinical importance, since dilated ducts can indicate obstruction caused by inflammatory conditions, intraductal stones or tumours. The question whether conventional reference values for CBD and PD need updating has been raised by different authors. Some suggest an age dependency of the diameters with relevant physiological increase in duct diameters above the age of 50 years,<sup>11</sup> 65 years<sup>2 26</sup> or 70 years.<sup>24</sup>

### What is new?

Here we describe the age-dependent distribution of CBD and PD diameters in a large, prospectively recruited, extensively characterised, population-based cohort of volunteers undergoing standardised whole body MRI with MRCP. Age-dependent upper reference values were calculated using quantile regression analysis. When considering all ages, in 95% of healthy subjects the diameter of the CBD measured up to 9 mm and must therefore be considered physiological. However, since the CBD diameter increases significantly with age, an age-dependent adaptation is warranted. Quantile regression on the 95th quantile indicated that a CBD diameter of up to 11 mm is physiological in subjects aged 65 years or above. We conclude that the incidental finding of a CBD diameter of 8 mm in otherwise asymptomatic persons with no laboratory abnormalities should not be worrisome. In this study, we can also confirm that previous gallbladder removal leads to a postoperative CBD enlargement, leaving 95% of these subjects with a CBD diameter of 13 mm or less, not corrected for age or time interval since the operation.

Similarly, the PD diameter is increasing with age and exceeds the conventional upper reference value of 3 mm in a significant percentage of healthy subjects, even in those younger than 65 years. This effect is more pronounced when the duct diameter is assessed after secretin administration as previously described.<sup>27</sup> We therefore adapted the suggested reference values for MRCP with and without secretin stimulation.

The relevance and clinical importance of our findings are further supported by the fact that during the 5-year survival follow-up none of the subjects who exceeded the conventional reference values died of pancreaticobiliary malignancies.

### Comparison with other cohorts

Studies on the diameter of the CBD in the healthy population are contradictory in general and scarce when it comes to MRI. Early studies suggested that the CBD in persons with no overt biliary or pancreatic disease should not exceed 4–7 mm measured on ultrasound.<sup>5–7</sup> Later, with better instruments available, studies described a CBD of 8.5–10 mm on ultrasound to be physiological.<sup>28 29</sup> A recent MRCP-based study from China suggested an age-independent upper reference limit of 6 mm for asymptomatic hospital patients.<sup>30</sup> Despite methodological weaknesses and small study populations, a correlation between age and diameter was seen, with an increase of 0.04–0.07 mm per year.<sup>29 31</sup> Kaim *et al*<sup>12</sup> described an increase of the CBD in asymptomatic patients older than 75 years on ultrasound and suggested the upper reference limit of 10 mm. In patients who had undergone cholecystectomy, the mean diameter was further increased and an upper reference limit of 14 mm was suggested.<sup>12</sup> An age-dependent increase and additional effect of cholecystectomy was confirmed by studies from various countries including more than 10 000 patients using transabdominal ultrasound,<sup>13 14 29 32 33</sup> endoscopic ultrasound,<sup>24</sup> CT<sup>11 34</sup> and one small study with MRCP<sup>2</sup>; however, the validity for the general population and for MRCP remained unclear. This gap is closed by our data.

The 3 mm upper limit of normal for the PD was defined in an endoscopic retrograde cholangiopancreatography (ERCP) study from 1976<sup>8</sup> in 35 patients without pancreatic disease. In two studies, including a clinical MRCP cohort from China, the mean diameter rarely exceeded 3 mm as confirmed by us and others,<sup>35–37</sup> but the variation in asymptomatic individuals is significant and up to 10.9% of measurements are above the 3 mm limit. None of the studies provided upper reference limits. We therefore suggest new age-dependent upper limits based on

quantile regression in contrast to mean values. In patients >70 years of age undergoing ERCP, Hastier *et al*<sup>38</sup> showed the PD diameter increases in 44.8% of the patients. 21 of 136 subjects had a PD dilatation greater than two SD above the mean with a maximum of 6.9 mm and five subjects had a massive dilatation over 3 SD with a maximum diameter of 8 mm.<sup>38</sup> Similar findings were observed in an Indian cohort.<sup>39</sup> Recently, a MRI-based study from Japan debated these finding, but the study population was small and the span of the age groups covered was wide, which is why the effect was most likely missed.<sup>40</sup>

The effect on PD diameter and duodenal filling as well as safety of secretin for PD assessment on MRI is well described.<sup>27 41 42</sup> It is noteworthy, however, that there is a difference between ERCP and MRCP when assessing the PD. According to Tamura *et al*, ERCP measurements yield significantly higher diameters than MRCP (ratio 1.5) in patients with chronic pancreatitis,<sup>9</sup> which highlights the relevance of the data presented in the current study. In contrast, a study comparing measurements of the CBD diameter between ultrasound and MRI reported comparable results,<sup>3</sup> suggesting a generalisability of our findings to ultrasound of the extrahepatic bile duct as well.

A number of studies dispute the relation between age, gallbladder removal and CBD, but methodological aspects might explain these differences. The studies by Karamanos *et al* and Horrow *et al*,<sup>25 43</sup> for example, had non-representative age distribution especially among the elderly, since subjects were recruited in hospital. Another ultrasound and one MRI study were underpowered due to small number of subjects,<sup>3 44</sup> and in a further, study the follow-up period after cholecystectomy was too short.<sup>5</sup> Online supplemental table 6 gives an overview on previously published cohorts.

### Strengths and limitations

Due to the study design, our findings describe the upper reference limits for CBD and PD diameters. To test its prognostic accuracy and to define a clinical cut-off, a controlled study in patients with specific pancreaticobiliary conditions is needed. Concerning the CBD increase associated with previous cholecystectomy, it would be interesting to understand dynamics of this change with regard to time from surgery. Since information on the exact date of cholecystectomy in our study participants was not collected, we were unable to analyse this aspect in more detail. Ideally, this question should be answered in a prospective setting requiring long follow-up. Overall, the estimated upper reference limits for subjects analysed after gallbladder removal need to be interpreted with caution, as this subcohort was small. Although recruited from a distinct geographical area, due to the balanced composition and large size of the cohort, we are confident that the data are generalisable to Caucasian populations elsewhere; however, external validation studies, also including other ethnicities, are needed. The retrospective nature of the study leads to the fact that only a fraction of 34% of those undergoing MRI as part of SHIP were analysed. Thus, a selection bias cannot be excluded.

### CONCLUSIONS

This is, to our knowledge, the first population-based study investigating the diameter of pancreaticobiliary ducts on MRCP. We showed that up to 18.2% of healthy volunteers would have needed diagnostic workup for enlarged CBD or PD, if the conventional reference values were to be used. We therefore suggest a new set of age-adjusted upper reference limits for the proximal CBD and PD in asymptomatic persons with normal

liver function and lipase levels. Further validation and comparison with patients with proven pathology are needed. Our findings can help to avoid unnecessary investigations and thus reduce healthcare expenditure and test-related adverse events.

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**Contributors** GB and FK: study design, data acquisition and analysis, manuscript and figure preparation; AH and FK: statistical analysis, figures and tables; AA: study design and technical advice; PT: data acquisition and technical advice; HV: study design Study of Health in Pomerania (SHIP); PT: study design and methodological advice; MML: study design and manuscript preparation; J-PK: technical advice; JM: project supervision, study design, manuscript preparation and guarantor of this project.

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**Ethics approval** SHIP was approved by the institutional review board, and 'written informed consent was secured from each participant. In addition, the associated project 'CBD and PD duct diameter on MRCP' was approved by the SHIP scientific advisory board on 1 April 2015 (2015/48/D). The study was conducted in accordance with national legal requirements, the WMA's Declaration of Helsinki and all participating researchers followed Good Clinical Practice (ICH GCP) guidelines. All authors had access to the study data and reviewed and approved the final manuscript. Participants gave informed consent to participate in the study before taking part.

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**Data availability statement** Data are available on reasonable request. Data may be obtained from a third party and are not publicly available. The full list of available data from the SHIP studies can be found here: [https://www.fvcm.med.uni-greifswald.de/dd\\_service/data\\_use\\_explore.php?lang=ger](https://www.fvcm.med.uni-greifswald.de/dd_service/data_use_explore.php?lang=ger).

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