Retinal detachment following cataract phacoemulsification - a review of the literature

Running title: Retinal detachment following phacoemulsification

M Hamza Qureshi, MB BChir, MA[1,2]
David HW Steel, MBBS, MD, FRCOphth[1,3]

[1]Institute of Genetic Medicine, Newcastle University, Newcastle Upon Tyne, UK
[2]Royal Victoria Infirmary, Queen Victoria Road, Newcastle Upon Tyne, UK
[3]Sunderland Eye Infirmary, Queen Alexandra Road, Sunderland, UK

Correspondence to:
Mr. DH Steel
Sunderland Eye Infirmary
Queen Alexandra Road
Sunderland
UK
David.steel@ncl.ac.uk
Telephone +44 (191) 5699065
Fax: +44 (191) 5699060

The authors have no conflict of interest to declare.

Retinal detachment following cataract phacoemulsification - a review of the literature

Abstract

A link between cataract surgery and rhegmatogenous retinal detachment (RRD) has long been considered. Indeed, pseudophakic retinal detachment (PPRD) forms a substantial and increasing proportion of RRD. We reviewed the literature to answer the following questions: What is the incidence of PPRD in eyes following phacoemulsification cataract surgery and how does its risk change over time following surgery? We also sought to assess how the risk is modified by intraoperative factors (operative complications, surgeon grade, subsequent laser capsulotomy), intrinsic eye-related factors (laterality, myopia, previous RRD, previous trauma, previous PVD) and patient factors (sex, age, ethnicity, affluence, systemic comorbidities). Secondarily we asked how the incidence of PPRD after phacoemulsification compares to the RRD incidence in the general population and how identified risk factors contribute to the pathophysiology of PPRD.

A search of the Medline and Ovid databases was conducted for relevant publications from 1990 onwards using defined search terms with pre planned inclusion and exclusion criteria.

The 10-year PPRD incidence after phacoemulsification was identified as being between 0.36-2.9%. This decreases over time to 0.1-0.2% annually but remains above the general population. The PPRD risk is further elevated by (in order of decreasing effect) intraoperative vitreous loss, increasing axial length, younger age, male sex and trainee operating surgeons.

The PPRD risk after phacoemulsification is approximately ten times the general population's RRD risk. This risk is modified by the interplay of a hierarchy of risk factors, of which intraoperative vitreous loss, myopia, age and sex have the biggest effect.

Retinal detachment following cataract phacoemulsification - a review of the literature

Introduction

Rhegmatogenous retinal detachment (RRD) refers to the separation of the neurosensory retina from the underlying retinal pigment epithelium related to a break in the retina. RRD following cataract surgery (pseudophakic retinal detachment, or PPRD) forms a substantial and increasing proportion of RRD (1), with estimates varying from 21.6% (2) to 37.2% (3) of RRDs in the developed world being PPRDs. Cataract extraction is one of the most commonly performed surgical procedures globally with approximately 330,000 cataracts removed each year in England alone (4). This figure is likely to increase further with an ageing population. It is important to understand the relationship between cataract extraction and PPRD as it is a serious, vision-threatening event with approximately half of all patients not recovering better than driving vision (visual acuity 6/12) (5).

The risk of PPRD varies with the method of cataract extraction. Conventional extracapsular cataract extraction (ECCE) carries a lower risk of PPRD by approximately one third compared to its predecessor, intracapsular cataract extraction (ICCE) (6). ECCE has in turn been replaced almost entirely by phacoemulsification in the developed world, starting in the early 1990s (7, 8). The early literature on phacoemulsification suggested an intermediate PPRD risk, between that of ICCE and ECCE (6). However, these estimates may not reflect the true PPRD risk given refinements and greater familiarity and training in phacoemulsification since its early popularisation. This seems to be borne out by long-term studies reporting declining overall PPRD rates (9) and more recent studies finding equivalent (10) or lower (11) rates of PPRD after phacoemulsification as compared to ECCE.

The risk of PPRD after phacoemulsification is estimated variously at between 0.036% (12) to 0.656% (13) at 12 months. In comparison the incidence of primary RRD in the general population is between 0.0104% (14) to 0.0207% (3), implying that phacoemulsification increases risk of RRD by at least a factor of 1.7. This risk of PPRD is proposed to be further altered by a variety of demographic and intraoperative factors including age, sex, myopia and intraoperative complications etc.

Quantifying the risk of PPRD and the effect of these additional risk factors is important for clinicians and patients to make an informed decision before proceeding with cataract extraction. Previous reviews of the literature cannot directly answer this question as they date back to before the near-universal spread of phacoemulsification as the main surgical technique or make no distinction between phacoemulsification and other techniques (including refractive lens exchange which may confound results due to a predominantly young, myopic population with consequently higher native RRD risk).

In this review we attempt to draw together the findings of studies available from 1990 onwards examining the effect of phacoemulsification cataract surgery on the risk of retinal detachment and additional factors that modify this risk.

Baseline Risk of RRD in the general population

The incidence of RRD in the general population is between 0.01-0.02% and is associated with greater socioeconomic prosperity and male sex (men are at approximately double risk). Right eyes are affected more often than left and the peak incidence of RRD is around the sixth decade of life (15). RRD risk varies with ethnicity; Caucasians are estimated to be at ten-fold higher risk than African populations (16). Asian populations have younger age of onset (17, 18)

but incidence varies; East Asians are at similar risk to Caucasians (14) whereas South Asians have lower risk of RRD, estimated to be threefold less than Caucasians (19, 20). Myopia, fellow eye RRD and proliferative diabetic retinopathy, myopia and fellow eye RRD are significantly associated with higher RRD risk (21, 22). Nd:YAG laser capsulotomy has previously been considered a risk factor for RRD - this has more recently been challenged (23).

In 80-90% of RRDs the precipitating event is a retinal break associated with a posterior vitreous detachment (PVD) (24). PVD is a natural, age-related result of progressive vitreous liquefaction and increases rapidly around age 60-70 years. It has been estimated that, in between 8-15% of people affected, this is associated with retinal break formation (25, 26). It has also been suggested that established and complete PVD without RRD at presentation is protective against RRD when cataract surgery is performed (22, 27).

Methodology and Search Strategy

We conducted a search of the Medline and Ovid databases for all publications from 1990 using the search terms:

(retinal detachment) AND (pseudophak* OR phacoemulsification OR (Cataract AND (surgery OR operation OR extraction OR removal)))

This yielded 2634 results which were supplemented by manual searches primarily using additional references from key articles. Inclusion criteria included: prospective or retrospective studies of RRD incidence in a predominantly post-phacoemulsification population and English language. Papers which met our criteria were analysed for PPRD incidence overall and by risk factor. Any papers whose eligibility was not clear from the abstract were retrieved and read to ascertain whether they merited inclusion. Exclusion criteria were: population size of <1000

pseudophakic eyes, inclusion of phacoemulsification performed pre-1990, inclusion of refractive (clear) lens exchange phacoemulsification, populations with >40% ICCE or ECCE, solely paediatric population and incomplete data.

A summary of the findings of the 16 papers that met these criteria is provided in Table 1 and discussed below. In summary, the population sizes ranged from 1793 to 2,680,167 with an estimated total of 3,211,671 pseudophakic eyes. Four papers were by the same Taiwanese group (Sheu and colleagues) following a fixed population over multiple years of follow up (10, 28-30). In addition to these four, a fifth study by a different group was also based in Taiwan (31), a sixth in Singapore (32) and a seventh in New Zealand (33). All other studies investigated phacoemulsification in European centres. Minimum study follow up durations from the time of cataract surgery ranged from no defined minimum duration (11, 31) (i.e. PPRD incidence calculated over the same time periods as phacoemulsification) to 10 years post-phacoemulsification (33). Three studies retrospectively calculated the frequency of individual risk factors present in PPRD eyes compared with the frequency in unaffected pseudophakic eyes (32, 34, 35). All other studies stratified the pseudophakic population by presence or absence of risk factors and prospectively calculated the incidence of PPRD.

Overall incidence in pseudophakic population

The reported incidence of PPRD varied considerably between studies and also with the length of follow up. The lowest reported cumulative incidence of PPRD was 0.36% over 10 years (12), equating to an annual incidence of 0.036% (by Szijártó and colleagues in Hungary) while Sheu et al. reported 2.31% over 8 years in their final published follow up (10), equating to 0.289% per annum which is the highest value in our review. In general however, studies with longer follow up report a greater cumulative incidence of PPRD with an approximately linear relationship corresponding to an incidence of 0.1-0.2% for each addition year after phacoemulsification (see

Figure 1). This is supported by evidence that the risk of RRD in pseudophakic eyes remains significantly elevated for over a decade after the operation (36).

PPRD risk over time following phacoemulsification

Nine studies investigated how the PPRD incidence evolves with time from phacoemulsification. Three found no period of increased incidence (11, 33, 37) while one found a late increase in incidence after 4 years for myopic males only (10). A further three reported a higher PPRD incidence in the first 6-24 months post-phacoemulsification (28, 34, 38). An eighth study found a significantly shorter median time from phacoemulsification to PPRD (44 days compared to 6.3 months) if the eye suffered intraoperative posterior capsule rupture (PCR) or if the operator was a trainee surgeon independently of whether PCR occurred (figures not given) (39). Notwithstanding the short follow up in this study (minimum three months) the implication is that the early postoperative period carries higher risk of PPRD. Moreover this finding is corroborated by a ninth study which found the first year after phacoemulsification to have the greatest risk of PPRD and that the median time to PPRD was shortened from 31 months to 10 months in eyes which suffered PCR with vitreous loss (12).

The five studies reporting increased PRPD risk in the early postoperative period do not necessarily negate an additional long-term increase in PPRD risk. Indeed Bjerrum and colleagues note that the while the highest PPRD risk is during the first six months (Hazard Ratio, HR of 9 relative to the un-operated fellow eye) and then decreases, the PPRD risk plateaus at two years (HR 3) and remains higher than the fellow eye for a decade (38).

While the case for an early increased PPRD risk is compelling given the link with intraoperative complications, it may also in part reflect greater surveillance in the early postoperative period, especially in complicated cases, and increasing patients lost to follow up with time.

PPRD risk after phacoemulsification in comparison to ECCE

As earlier estimates may have overestimated the PPRD risk after phacoemulsification due to the technique's unfamiliarity, we selected studies in which phacoemulsification was the predominant cataract extraction method. Nevertheless, six studies which included some ECCE cases compared the PPRD incidence in ECCE and phacoemulsification cases.

Daien et al. found a higher PPRD incidence after ECCE cases (HR 3.11) (11). All other studies reported no significant difference (28-31) with the exception of Sheu et al. who in their final follow up found phacoemulsification was associated with a higher PPRD incidence (Relative Risk, RR of 1.78). Interestingly in their previous follow up papers (2005-2007) this difference did not reach significance in the overall population. Moreover, they note that in their final study that the increased risk after phacoemulsification was attributable to cases from the first year of their operative period (c.1999). This period corresponded to a changeover from ECCE to phacoemulsification and the two techniques had no significant difference in PPRD incidence when only considering cases from the following year (10).

Unifying the results of these studies it would appear that phacoemulsification is as safe or safer than ECCE once the technique is familiar. For centres transitioning from ECCE to phacoemulsification, the newer technique may well have a greater PPRD risk and previous studies which found a higher PPRD risk after phacoemulsification than ECCE should be viewed as overestimates in light of this. Conversely, we note (as did Daien and colleagues), that current estimates of higher PPRD risk after ECCE than phacoemulsification may be confounded by the fact that in centres where phacoemulsification is the dominant technique, ECCE is now reserved for more challenging cases such as cataracts with denser crystalline lenses not amenable to phacoemulsification.

Intraoperative complications

All groups who examined the effect of intraoperative complications (vitreous loss or PCR), found a significant association with increased PPRD except Sheu et al. and Boberg-Ans and colleagues in their first study (34). The estimated increase in risk varied from approximately fourfold at four years (11) to as high as 42 times higher risk of retinal detachment surgery within 3 months following PCR (4). The latter figure is from Day et al. who found this higher initial PPRD risk following PCR decreased over time (OR 23.98 and 18.28 at 6 and 12 months respectively). As previously mentioned, the same group also found in a different study that PCR was associated with a shorter time to PPRD (39).

In the only other study to examine the effect of intraoperative complications on the time from phacoemulsification to PPRD, Szijártó et al. likewise found PCR associated with shorter time to PPRD but only if accompanied by vitreous loss (12). This point is also borne out by the observation that among the nine studies which found higher incidence of PPRD in eyes suffering intraoperative complications, five considered intraoperative complications collectively (i.e. without distinguishing the presence or absence of vitreous loss) (4, 12, 31, 32, 39) while four specified PCR with vitreous loss as being associated with higher PPRD risk (11, 33, 35, 40). Of these, Russell et al. and Petousis et al. specifically compared the PPRD risk in eyes suffering PCR with and without vitreous loss and found increased PPRD only in cases of PCR with vitreous loss, with no significant increase in PPRD risk in eyes suffering PCR without vitreous loss. The implication of this would be that intraoperative complications per se are not associated with higher PPRD risk, rather vitreous loss is. This may be to do with the pathophysiology of PPRD, as explored below, but has significance in terms of detection, management and training of PCR intraoperatively.

Surgeon grade

One study meeting our inclusion criteria examined the effect of surgeon grade on PPRD by classifying operators into trainee, independent non-consultant and consultant surgeons. They found a shorter time from phacoemulsification to RRD in eyes operated on by more junior surgeons (39). The authors did not comment on whether the overall rate was higher after cataract extraction by junior surgeons but in light of this finding this is likely to be the case at least in the immediate post-operative period. Given the short follow up time of this study it is unclear whether this only reflects a higher early incidence and whether over longer post-operative follow up the PPRD incidence is significantly different if operated on by consultants.

Intraoperative complications are more likely at the hands of a trainee surgeon (4) and surgeon grade is a variable in the current PCR risk calculator (41). However, this study finds the lower surgeon grade increases PPRD risk independently of PCR. If this is the case it could be hypothesised that the increased risk also relates to greater anterior chamber fluctuations, more prolonged surgery and infusion volumes into the eye.

More generally, familiarity of surgical teams with phacoemulsification decreases PPRD risk as demonstrated by Sheu and colleagues who showed that a transition from ECCE to phacoemulsification was marked by initially higher PPRD incidence following phacoemulsification. This became non-significant one year after transition away from ECCE as the predominant cataract extraction technique (10).

Nd:YAG capsulotomy

Nd:YAG capsulotomy has previously been associated with increased post-cataract extraction RRD risk (42, 43) but all seven studies meeting our criteria found no significant link with increased PPRD overall in their post-phacoemulsification population. However in a sub-group

analysis, Lin et al. found that high myopes had an increased PPRD risk if they underwent Nd:YAG capsulotomy (31). Similarly Sheu et al. in their first follow up found an association in their sub-group of patients aged under 50 years but none in their overall pseudophakic population (28). Unfortunately, although Sheu and colleagues' subsequent follow up studies confirmed that capsulotomy is not significant overall, they did not revisit whether this remained significant in younger eyes over a longer period of follow up.

Unlike studies focusing only on post-capsulotomy PPRD risk (none of which met our inclusion criteria), the studies in our review were all primarily concerned with post-phacoemulsification risk with Nd:YAG capsulotomy considered secondarily. Because of this, their results may be confounded by follow-up times that were calculated from phacoemulsification rather than from capsulotomy. None of the included studies gave data on time lags between phacoemulsification and capsulotomy, introducing an uncontrolled variable. Moreover, given that this may have occurred as much as 2 years after phacoemulsification this shortens the time during which post-capsulotomy PPRDs can occur and would be expected to underestimate the effect of laser capsulotomy when incidence is calculated from the time of phacoemulsification.

This uncertain significance of laser capsulotomy on PPRD risk in our selected studies is in keeping with more recent studies (44), including a review of the literature which suggests that there is no convincing association between Nd:YAG capsulotomy and PPRD (23), though, like Lin et al., the authors note that a significant association may exist for myopic eyes undergoing capsulotomy.

These observations may be reconciled with findings to the contrary, especially by older studies, in light of a study by Olsen and Olson which considered 1099 ECCE and 1418 phacoemulsification cases, with approximately one third of each group going on to have laser

capsulotomy. They found that whilst Nd:YAG capsulotomy was significantly associated with PPRD after ECCE, it had little impact on PPRD risk in the context of phacoemulsification (45), perhaps relating to consistent intracapsular IOL fixation and more assured 'separation' of the anterior and posterior segments.

Axial length and Myopia

As with phakic RRD, myopia was strongly associated with increased PPRD risk in all 11 studies that considered it. All studies used axial length rather than refractive error and the definition of myopia varied between the various groups from >23 mm to >25 mm. Estimates varied between a 2.74 (40) to 18.90 (31) times increased risk compared to non-myopes. Sheu and colleagues found female sex (30) and older age (28) were protective against the increased PPRD risk from myopia.

Six studies grouped their patients by axial length and demonstrated a dose-dependent relationship between axial length and PPRD risk. Lin et al, who found the most pronounced effect, found eyes with axial length 23-26 mm had a non-significant adjusted relative risk of 3.92 compared to eyes with axial length <23mm while eyes with axial length >26 mm had a significantly increased relative risk of 18.90. (31). Importantly they also found a significant, dose-dependent protective effect of being non-myopic against the effects of young age and intraoperative complications (see Table 2).

Previous RRD in operated eye

Previous RRD is a strong risk factor for phakic re-detachment in the same eye. On this basis it might be expected that after phacoemulsification such eyes would likewise show a higher PPRD incidence. Forsell and colleagues recently demonstrated a low rate of PPRD in a small group of patients with previous RRD in the operated eye (46). Unfortunately, this study did not meet our

criteria and the majority of those that did excluded eyes with previous RRD. The only study in our review to investigate the effect of previous RRD on PPRD risk in the same eye found no significant difference, unsurprisingly given the small numbers concerned (2 PPRDs in a population of 11 eyes with RRD preceding phacoemulsification) (33).

Previous RRD in fellow eye

A previous RRD in the fellow eye is known to be a strong risk factor for phakic RRD in the contralateral eye. However only two studies examined the significance of fellow eye RRD on PPRD on the contralateral side. Russell et al. found a minimally significant increased risk if the fellow eye had suffered a RRD (33), while Sheu et al. found such eyes at much higher risk of PPRD risk (crude RR 17.34) (10). The latter study had a much larger population size (9388 pseudophakic eyes in Sheu et al. compared to 1793 in Russell et al.) though the number of operated eyes with a history of fellow eye RRD is small in both (6 in Sheu et al. and 4 in Russell et al.) and is more likely to account for the large difference in findings. We would also expect that the nature of the fellow eye RRD may alter the risk of PPRD differently depending on how long ago it occurred and whether the detachment was a primary rhegmatogenous RRD or secondary to trauma or an intraocular tumour. The dearth of available data addressing this is likely due to the comparatively small number of eyes in this category making further subdivision of fellow eye RRD unfeasible.

Ocular trauma

Ocular trauma is a known risk factor for RRD. The incidence of RRD following trauma is estimated at around 5% over 6 months (47). In our review of PPRD risk factors, many studies excluded eyes with a history of trauma. Of the ten that did not, only three examined the effect on PPRD incidence. In two retrospective studies, Boberg-Ans et al. and Olsen et al. found that

eyes that had suffered PPRD had no significantly higher chance of having had a history of ocular trauma (34, 35). Both studies were comparatively small, especially when considering their sub-population of eyes which had previously suffered trauma (Boberg-Ans et al. found 1 eye with previous trauma out of 22 PPRDs in a total population of 6521 pseudophakic eyes and Olsen et al. found 7 eyes with previous trauma out of 48 PPRDs in a total population of 12,222 pseudophakic eyes).

In contrast, in a much larger study (203 eyes with previous trauma out of 11,424 PPRDs in a total population of 2,680,167 pseudophakic eyes) Daien et al. found eyes with a history of trauma were at significantly increased PPRD risk (HR 3.98) (11). This finding is more in keeping with the known increased RRD risk in the general population after ocular trauma and so the findings of the earlier two studies may be the result of smaller population sizes.

It is also conceivable that the risk of PPRD in such eyes varies with the nature and severity of the trauma, how long ago it occurred, whether it disrupted the vitreous or retina and what, if any, treatment was given. Given these additional factors, ocular trauma per se may not be as helpful a variable in calculating PPRD risk as defined injuries to specific anatomical structures. Realistically however it may be difficult to recruit populations of sufficient size to be able to further subdivide eyes in such a way.

Gender

In the general population, RRD is more common in men than women, with the sex ratio estimated at between 1.5:1 (48) and 2:1 (1). Of the 14 studies investigating the effect of sex on PPRD risk after phacoemulsification, 10 found a significantly greater incidence of PPRD in men, with the increased risk between 1.72 (10) to 3.39 (33) times that of women. Of the remaining four, two are the 2005 and 2006 studies by Sheu et al. who went on to demonstrate in their

312 subsequent studies of the same population that with increasing follow up men did have a higher
313 PPRD risk than women (10, 30).
314
315 This raises the question of whether the increased PPRD incidence in men is genuinely
316 attributable to phacoemulsification or whether over such long follow up the increased incidence
317 reflects the higher background RRD risk for men. Exploring this, Bjerrum and colleagues
318 compared PPRD incidence in the operated eye to RRD in the un-operated fellow eye, finding
319 that, when adjusted for the higher PPRD incidence in male un-operated fellow eyes, the
320 attributable increase in PRPD risk of male operated eyes was not significantly more than
321 women, i.e. phacoemulsification increases the risk of RRD uniformly irrespective of sex and the
322 higher incidence of PPRD in males is due to a higher pre-operative risk (38).
323
324 If this is true, men are still at greater risk of PPRD than women following phacoemulsification but
325 to understand why this is the case pre-operative risk factors for RRD are more significant. Olsen
326 and colleagues suggest the answer lies in male eyes being longer than female eyes (i.e. a
327 higher incidence of myopia in men) which is a known risk factor for RRD (35). While this is true
328 of the Danish population studied by Olsen et al. (49) and has been invoked to explain the male
329 preponderance of RRD in a Scottish population (50), the global picture is more unclear. While
330 women show higher incidence of hyperopia (Odds ratio, OR 1.28), myopia shows similar
331 prevalence in men and women globally when adjusted for age and race. Moreover in some
332 populations women have significantly higher rates of high myopia than men, (e.g. OR 1.61 in
333 white Australians) (51). It has also been suggested that posterior migration of the posterior
334 border of the vitreous base contributes to the higher incidence of RRD in men (50, 52).
335
336 Furthermore, the higher PPRD risk in men seems to be independent of the effect of age, axial
337 length and previous ocular trauma. In a population excluding eyes with a history of trauma,

Sheu and colleagues found female sex mitigates the additional risk from young age and myopia, strengthening the case for a different explanation which they suggest may be a greater incidence of unreported ocular trauma in males than females (30).

Age

All papers examining age as a risk factor found young age significantly associated with PPRD, contrary to the wider population's increased risk or RRD with age up to around 60. Those studies which grouped their study population into age brackets all found a dose-dependent relationship between increasing age and lower PPRD risk. The most modest increase is reported by Sheu et al. who, in their final follow up study, found a relative risk of 2.69 for patients aged under 50 compared to those aged over 60 years (10). The largest age-dependent risk modification is reported by Petousis et al. who found those aged under 60 at approximately 40-fold greater risk of PPRD than those aged over 80 years (40). This lower PPRD risk in older patients appears to be independent of sex and also mitigates the additional PPRD risk in myopic eyes (28).

Bjerrum et al. note that above the age of 50 PPRD risk drops exponentially by just over half for each decade (38), a relationship which also approximates to the results of several other studies in this review, although due to differences in age bracketing this is difficult to quantify. This observation is also in line with an older estimate of change in PPRD risk following ECCE by a Swedish group who found PPRD risk changed by a factor of 0.94 for each additional year of age, which when raised to the tenth power corresponds to a factor of 0.54 over a decade (53).

However, Bjerrum and colleagues found this increased risk also applied to RRD in fellow un-operated eyes, i.e. phacoemulsification increases the risk of RRD uniformly irrespective of age. This would suggest that higher incidence of PPRD in younger patients is due to a higher pre-

operative risk (38). Given younger eyes in the general population have a lower native RRD risk, the higher risk in these patients may presumably be attributed to pathological processes which predispose both to early cataracts and easily detached retinas.

Systemic diseases

Of the studies considering the impact of systemic diseases (primarily hypertension and diabetes), all found no significant effect (10, 29-31) other than Daien and colleagues who found an increased PPRD risk in diabetics (HR 1.18) (11). If so, this may be the result of traction on the retina from proliferative diabetic retinopathy which is a known risk factor for RRD in the general population and was implicated in a British study which found a rise in RRD attributable to an increased prevalence of diabetes (54).

Ethnicity

Comparisons of RRD incidence in the general population have found differences depending on ethnicity with Caucasian, Asian and African populations associated respectively with higher, intermediate and lower RRD risk. Quek et al's study of a Singaporean population is the only one in our review to examine the risk of PPRD as affected by ethnicity, finding no significant effect (32). This study is limited by its short follow up duration (minimum 6 months) and consequently low number of PPRDs (total 39) making underestimation of risk more likely. The authors also did not specify which ethnicities they compared in their population. This is especially important as the literature on the effect of race on phakic RRD incidence suggests a tendency among East Asian authors to compare within Asian sub-populations (Chinese, Indian, Malay etc.) whereas Western authors tend to compare more broadly between Caucasian, Asian or African populations. This methodological difference may significantly alter whether or not a particular study finds differences in RRD or PPRD incidence

Other risk factors

In the general population right eyes are at greater risk of RRD than left eyes. No studies that met our criteria examined the effect of laterality on PPRD risk, although it has been postulated in phakic eyes that it may be related to ocular dominance and myopia. Likewise, while some studies have linked affluence with increased RRD risk, there is currently no literature investigating this as a risk factor for PPRD specifically. Similarly, although PVD is known to be associated with RRD, we found no studies meeting our criteria which considered the effect of PVD on PPRD incidence.

Phacoemulsification-attributable risk

Bjerrum and colleagues highlighted a largely neglected consideration which is that the increased rate of RRD in the pseudophakic population is not necessarily attributable to cataract extraction. Cataract-prone eyes may have an increased native risk of RRD and a small study of 64 patients has previously demonstrated increased risk of RRD in the un-operated fellow eyes of PPRD patients (55). As such the most appropriate control, rather than being the general population, is the fellow eyes of the same patients. With this in mind they still find a significant attributable risk to phacoemulsification (1.36 PPRDs per 1000 person-years in the operated eye compared to 0.32 in the fellow eye). Interestingly however, while they found young age and male sex significantly associated with PPRD, this became insignificant when compared to the comparably increased fellow eye RRD risk in these patients. The implication of this would be that while young males with cataracts are at higher risk of RRD, the phacoemulsification procedure increases the risk uniformly (by a factor of 4.2 in this study) irrespective of age or sex.

As this study remains the only one to present data on fellow eye RRD incidence and only investigated age and sex, we are unable to comment definitively on how this would modify the

attributable risk of PPRD as calculated by other groups and how this would vary with other risk factors, but we would expect it to be lower than previous calculations comparing to the wider, cataract-free population. Nevertheless, even with this analysis, the additional PPRD risk following phacoemulsification will precipitate more PPRDs in populations whose native RRD risk is high.

This methodological approach is hampered however by the typically short duration between phacoemulsification of one eye and its fellow. Furthermore, if a cataractous eye has a higher native risk of RRD, the fellow eye may have a reduced native RRD risk if it does not develop a cataract till later in life making it no better a control than the general population – Bjerrum and colleagues note however that their study period was marked by many patients who developed cataracts simultaneously but had long waiting times between cataract extractions which may mitigate this to some degree. Perhaps most conspicuously, this study excluded eyes that suffered intraoperative complications, a risk factor unambiguously related to the phacoemulsification procedure and not shared with the fellow eye.

Finally, this approach underemphasises the potential effect of a small additional risk on eyes with an already high baseline RRD risk. From a patient perspective, overall PPRD risk is the key concern – even if the proportion of this risk attributable to phacoemulsification is small, this is more likely to precipitate RRD in populations at higher baseline risk.

Pathophysiology of PPRD

In an effort to establish a causative link between cataract extraction and PPRD, Mahroo and colleagues analysed the clinical features of phakic RRDs and PPRDs in 500 eyes and found differing patterns in position and size of breaks between the two groups (56). In comparison to phakic RRDs, PPRDs presented less frequently with vitreous haemorrhage and more frequently

with multiple breaks, breaks smaller than 0.5-disc diameter and with breaks in the inferonasal quadrant and at the more surgically challenging 5 o'clock to 7 o'clock position. To further dissect whether the difference in pathophysiology of phakic RRDs and PPRDS is purely due to phacoemulsification or the cataractous eye itself, the authors further compared between phakic eyes with cataract and pseudophakic eyes, finding a similar pattern of differing clinical features between the RRDs of both groups as they did between pseudophakic eyes compared to all phakic eyes. If replicable, this study's results would strongly support the phacoemulsification procedure as contributing a distinct additional risk.

It has been suggested that the mechanism of PPRD involves vitreous changes during and after phacoemulsification (57). This draws on the fact that RRD in phakic eyes is typically preceded by PVD (24) although only a small proportion of PVDs are associated with RRD. The age-related liquefaction of the vitreous that naturally results in PVD progresses most rapidly in the sixth decade of life, explaining the peak incidence of RRD. The increased RRD risk with PVD is in the acute setting, after which established (chronic) PVD is believed to be protective against subsequent RRD (22, 27).

A similar process may occur as a result of acute vitreous traction caused by movement of the lens capsule during phacoemulsification. This would also explain why PCR and specifically vitreous loss so dramatically increases the risk of PPRD in the studies we reviewed, and why this increased risk seems to become less marked over time. This mechanism would also explain the higher incidence of PPRD after ICCE.

Changes in vitreous tractional forces may also underpin the longterm increased rate of PPRD beyond the early postoperative period. The protuberance of the posterior surface of the native

lens is thought to reduce vitreous traction on the peripheral retina (58). This protective effect may be reduced in pseudophakia and lost in aphakia.

Changes in the composition of the vitreous may also be implicated. A post-mortem study of three pseudophakic and seven phakic eyes found changes in the protein composition and structure of the vitreous humour after phacoemulsification that were not present in the phakic eyes which included two un-operated fellow eyes. The authors noted in particular the presence of crystallins (which are absent in phakic eyes) in the anterior vitreous and lower viscosity in the anterior than the posterior vitreous (which represents a reversal of the viscosity gradient in phakic eyes). The authors conclude that the vitreous' normal protein processing and clearance mechanisms are altered in pseudophakic eyes (59). These alterations may destabilise the vitreous body and by disrupting the native clearance mechanisms may go on to cause further changes which underpin the long-term increase in PPRD risk, perhaps by accelerating the process of liquefaction and syneresis that results in PVD.

Finally, this model is further supported by studies suggesting a high incidence of PVD after phacoemulsification. A small study of 49 eyes by Ivastinovic and colleagues found 59.2% had new PVD at 1 month after phacoemulsification and 71.4% at 3 months (60). A larger study of 188 eyes found 78.7% of eyes without pre-existing PVD developed one by 26 months after phacoemulsification. Interestingly, the incidence was higher (87.23%) if the eye had pre-operative lattice degeneration (retinal thinning with separation and liquefaction of overlying vitreous) (61).

We note that Daien et al. have built on this model to suggest an explanation for the higher PPRD risk in younger eyes (in contrast to the lower phakic RRD risk in younger eyes, making age the only risk factor whose effect differs in phakic RRD and PPRD). They suggest that older

493 eyes are more likely to have an established pre-operative PVD which is therefore protective
494 against vitreous changes during and after phacoemulsification (11). However, in light of Bjerrum
495 and colleagues' work using the un-operated fellow eye as a control, we would expect this to be
496 reflected in a higher PPRD risk in younger eyes directly attributable to the procedure. In reality
497 Bjerrum at al. found no significant difference due to age on the risk directly attributable to the
498 procedure, instead finding the higher risk in younger eyes was entirely attributable to a higher
499 pre-operative risk in young patients (calculated using fellow eye incidence) (38). In fact
500 Ivastinovic et al. found a higher incidence of new PVD after phacoemulsification in those aged
501 over 70 (92.3% compared to 47.8%) (60), all of which suggests that the lower PPRD incidence
502 in older eyes is not entirely due to the protective effect of a pre-existing PVD.
503
504 **Limitations**
505 The available literature is also limited by small population sizes. Due to the relative rarity of
506 PPRD, even with our criteria including population >1000 the number of PPRDs occurring is low;
507 only 4 of our 16 studies had more than 50 PPRDs. The available literature also frequently
508 excluded eyes with previous RRD and some had very short follow up durations (4). In some
509 studies PPRD incidence was calculated over a fixed data collection period without adjusting for
510 the fact that the patients underwent phacoemulsification during the same time window (11, 31,
511 32, 39) which may lead to underestimation of the crude PPRD rate. Conversely studies with
512 long follow up times may overestimate the risk of PPRD attributable to phacoemulsification in
513 younger patients due to the natural history of RRD – without adjusting for age, over long follow-
514 up durations younger patients are more likely than older patients to have a RRD in later life
515 which is wrongly attributed to phacoemulsification even if the durations of follow up are equal.
516 This may explain why Szijarto and colleagues found that while younger patients had a higher
517 estimated PPRD incidence, the mean time between phacoemulsification and PPRD was longer
518 (12).

519

520 More broadly our survey of the literature was limited by methodological differences between the
521 different studies considered, particularly in how they quantified risk factors for PPRD, making
522 direct comparisons more challenging. The populations of some studies are also wholly or partly
523 subsumed in others (e.g. Olsen et al. examined phacoemulsification patients at a single Danish
524 centre from 2000 to 2005 (35) all of whom should also be included in the Danish National
525 Patient Registry which was used by Bjerrum et al. to examine all Danish patients from 2000 to
526 2010 (38)).

527

528 **Conclusions**

529 In our survey of the recent literature, PPRD remains a rare but important adverse outcome
530 occurring in 0.36-2.9% of cases within 10 years of phacoemulsification. In line with more recent
531 studies, phacoemulsification in centres familiar with the technique has a similar or lower (62)
532 PPRD incidence than ECCE. Our survey found an initially high PPRD rate which drops to about
533 0.1-0.2% per year for several years, still approximately ten times greater than the RRD risk of
534 the general population.

535

536 Several patient, eye and operative factors are associated with increased PPRD risk, namely (in
537 order of decreasing effect) intraoperative vitreous loss, increasing axial length, younger age,
538 male sex and trainee operating surgeon. These are all the known risk factors for PPRD known
539 from older cataract extraction methods such as ECCE, with the exception of Nd:YAG laser
540 capsulotomy which appears not to pose a significant PPRD risk in the phacoemulsification
541 setting and trainee operating surgeon grade which does not seem to have been investigated in
542 the ECCE setting. Increasing age is protective, with an approximate halving of PPRD risk for
543 each decade above 50 years. Intraoperative complications and PCR with vitreous loss in
544 particular increase the PPRD risk more markedly in the initial postoperative phase and form the

single biggest risk factor for PPRD. These risks are likely to be multiplicative to existing risks meaning that for example in a young myopic male with a previous fellow eye RRD the risk in the operative eye can be higher than perhaps previously expected.

Long term complications of phacoemulsification such as PPRD can easily escape the notice of cataract surgeons due to increasing sub-specialisation (63). As such, closer monitoring for RRD postoperatively with prophylactic measures e.g. retinal tear photocoagulation may have a role in identifying and preventing RRD (64).

While we are getting a clearer picture of PPRD incidence, the exact risk of PPRD attributable to phacoemulsification remains elusive. For more effective counselling of patients who might be at higher risk, ideally a PPRD risk calculator is needed, based on data which accounts for the limitations of the currently available literature as outlined above.

Conflict of interest

The authors declare no conflict of interest.

Funding

No external funding was received in the course of this research.

References

1. Hajari JN, Bjerrum SS, Christensen U, Kiilgaard JF, Bek T, La Cour M. A nationwide study on the incidence of rhegmatogenous retinal detachment in denmark, with emphasis on the risk of the fellow eye. Retina. 2014;34(8):1658-65.

2. Mitry D, Charteris DG, Yorston D, Rehman Siddiqui MA, Campbell H, Murphy AL, et al. The epidemiology and socioeconomic associations of retinal detachment in Scotland: A two-

year prospective population-based study. Investigative Ophthalmology and Visual Science. 2010;51(10):4963-8.

3. Poulsen CD, Peto T, Grauslund J, Green A. Epidemiologic characteristics of retinal detachment surgery at a specialized unit in Denmark. Acta Ophthalmologica. 2016;94(6):548-55.

4. Day AC, Donachie PHJ, Sparrow JM, Johnston RL. The Royal College of Ophthalmologists' National Ophthalmology Database study of cataract surgery: Report 1, visual outcomes and complications. Eye (Basingstoke). 2015;29(4):552-60.

5. Tuft SJ, Gore DM, Bunce C, Sullivan PM, Minassian DC. Outcomes of pseudophakic retinal detachment. Acta Ophthalmologica. 2012;90(7):639-44.

6. Javitt JC, Vitale S, Canner JK, Krakauer H, McBean AM, Sommer A. National outcomes of cataract extraction I: Retinal detachment after inpatient surgery. Ophthalmology. 1991;98(6):895-902.

7. Courtney P. The National Cataract Surgery Survey: I. Method and descriptive features. Eye (Lond). 1992;6 (Pt 5):487-92.

8. Desai P, Reidy A, Minassian DC. Profile of patients presenting for cataract surgery in the UK: national data collection. Br J Ophthalmol. 1999;83(8):893-6.

9. Clark A, Morlet N, Ng JQ, Preen DB, Semmens JB. Whole population trends in complications of cataract surgery over 22 years in Western Australia. Ophthalmology. 2011;118(6):1055-61.

10. Sheu SJ, Ger LP, Ho WL. Late Increased Risk of Retinal Detachment After Cataract Extraction. American Journal of Ophthalmology. 2010;149(1):113-9.e1.

11. Daien V, Lepape A, Heve D, Carriere I, Villain M. Risks factors of retinal detachment following cataract surgery in a national population study between 2009 and 2012. Investigative Ophthalmology and Visual Science. 2015;56 (7):672.

12. Szijarto Z, Schvoller M, Poto L, Kuhn F, Kovacs B. Pseudophakic retinal detachment after phacoemulsification. Annals of Ophthalmology. 2007;39(2):134-9.

13. Alio JL, Ruiz-Moreno JM, Shabayek MH, Lugo FL, Abd El Rahman AM. The Risk of Retinal Detachment in High Myopia After Small Incision Coaxial Phacoemulsification. American Journal of Ophthalmology. 2007;144(1):93-8.e2.

14. Sasaki K, Ideta H, Yonemoto J, Tanaka S, Hirose A, Oka C. Epidemiologic characteristics of rhegmatogenous retinal detachment in Kumamoto, Japan. Graefes Archive for Clinical & Experimental Ophthalmology. 1995;233(12):772-6.

15. Mitry D CD, Yorston D, Siddiqui MA, Campbell H, Murphy AL, Fleck BW, Wright AF, Singh J; Scottish RD Study Group. The epidemiology and socioeconomic associations of retinal detachment in Scotland: a two-year prospective population-based study. Invest Ophthalmol Vis Sci. 2010;51(10).

16. Av-Shalom A, Berson D, Gombos GM, Michaelson IC, Zauberman H. Some Comments on the Incidence of Idiopathic Retinal Detachment Among Africans. American Journal of Ophthalmology. 1967;64(3):384-6.

17. Chandra A, Banerjee P, Davis D, Charteris D. Ethnic variation in rhegmatogenous retinal detachments. Eye. 2015;29(6):803-7.

18. Rosman M, Wong TY, Ong SG, Ang CL. Retinal detachment in Chinese, Malay and Indian residents in Singapore: a comparative study on risk factors, clinical presentation and surgical outcomes. Int Ophthalmol. 2001;24(2):101-6.

19. Mowatt L S-SG, Price N. Ethnic differences in the demand incidence of retinal detachments in two districts in the West Midlands. Eye. 2003;17:63-70.

20. Wong TT, JM; Schein, OD. Racial Difference in the Incidence of Retinal Detachment in Singapore. Epidemiology and Biostatistics. 1999;117(3):378-83.

21. Ghazi NG, Green WR. Pathology and pathogenesis of retinal detachment. Eye. 2002;16:411.

22. Steel DH. Retinal detachment. BMJ Clin Evidence. 2014;2014.
23. Grzybowski A KP. Does Nd:YAG Capsulotomy Increase the Risk of Retinal Detachment? Asia Pac J Ophthalmol (Phila). 2018;7(5):339-44.
24. Michels RG, Wilkinson CP, Rice TA. Michels retinal detachment. St. Louis: Mosby; 1997.
25. Kuhn F, Aylward B. Rhegmatogenous Retinal Detachment: A Reappraisal of Its Pathophysiology and Treatment. Ophthalmic Research. 2014;51(1):15-31.
26. Tanner V, Harle D, Tan J, Foote B, Williamson TH, Chignell AH. Acute posterior vitreous detachment: the predictive value of vitreous pigment and symptomatology. Br J Ophthalmol. 2000;84(11):1264-8.
27. Richardson PS, Benson MT, Kirkby GR. The posterior vitreous detachment clinic: do new retinal breaks develop in the six weeks following an isolated symptomatic posterior vitreous detachment? Eye (Lond). 1999;13 (Pt 2):237-40.
28. Sheu SJ, Ger LP, Chen JF. Risk factors for retinal detachment after cataract surgery in Southern Taiwan. Journal of the Chinese Medical Association. 2005;68(7):321-6.
29. Sheu SJ, Ger LP, Chen JF. Axial myopia is an extremely significant risk factor for young-aged pseudophakic retinal detachment in Taiwan. Retina. 2006;26(3):322-7.
30. Sheu SJ, Ger LP, Chen JF. Male Sex as a Risk Factor for Pseudophakic Retinal Detachment after Cataract Extraction in Taiwanese Adults. Ophthalmology. 2007;114(10):1898-903.e1.
31. Lin JY, Ho WL, Ger LP, Sheu SJ. Analysis of factors correlated with the development of pseudophakic retinal detachment - A long-term study in a single medical center. Graefe's Archive for Clinical and Experimental Ophthalmology. 2013;251(2):459-65.
32. Quek DT, Lee SY, Htoon HM, Ang CL. Pseudophakic rhegmatogenous retinal detachment in a large Asian tertiary eye centre: a cohort study. Clinical & Experimental Ophthalmology. 2012;40(1):e1-7.

33. Russell M, Gaskin B, Russell D, Polkinghorne PJ. Pseudophakic retinal detachment after phacoemulsification cataract surgery. Ten-year retrospective review. Journal of Cataract and Refractive Surgery. 2006;32(3):442-5.

34. Boberg-Ans G, Villumsen J, Henning V. Retinal detachment after phacoemulsification cataract extraction. Journal of Cataract and Refractive Surgery. 2003;29(7):1333-8.

35. Olsen T, Jeppesen P. The incidence of retinal detachment after cataract surgery. Open Ophthalmology Journal. 2012;6:79-82.

36. Hermann MM, Kirchhof B, Fauser S. Temporal occurrence of retinal detachments after cataract surgery. Acta Ophthalmologica. 2012;90(8):e594-e6.

37. Boberg-ans G, Henning V, Villumsen J, La Cour M. Longterm incidence of rhegmatogenous retinal detachment and survival in a defined population undergoing standardized phacoemulsification surgery. Acta Ophthalmologica Scandinavica. 2006;84(5):613-8.

38. Bjerrum So S, Mikkelsen KL, La Cour M. Risk of pseudophakic retinal detachment in 202 226 patients using the fellow nonoperated eye as reference. Ophthalmology. 2013;120(12):2573-9.

39. Day AC, Donachie PHJ, Sparrow JM, Johnston RL. United Kingdom National Ophthalmology Database Study of Cataract Surgery: Report 3: Pseudophakic Retinal Detachment. Ophthalmology. 2016;123(8):1711-5.

40. Petousis V, Sallam AA, Haynes RJ, Patel CK, Tyagi AK, Kirkpatrick JN, et al. Risk factors for retinal detachment following cataract surgery: The impact of posterior capsular rupture. British Journal of Ophthalmology. 2016;100(11):1461-5.

41. Narendran N, Jaycock P, Johnston RL, Taylor H, Adams M, Tole DM, et al. The Cataract National Dataset electronic multicentre audit of 55 567 operations: risk stratification for posterior capsule rupture and vitreous loss. Eye. 2008;23:31.

42. AMBLER JS, CONSTABLE IJ. RETINAL DETACHMENT FOLLOWING Nd: YAG CAPSULOTOMY. Australian and New Zealand Journal of Ophthalmology. 1988;16(4):337-41.

43. Tielsch JM, Legro MW, Cassard SD, Schein OD, Javitt JC, Singer AE, et al. Risk factors for retinal detachment after cataract surgery: A population-based case-control study. Ophthalmology. 1996;103(10):1537-45.

44. Tuft SJ, Minassian D, Sullivan P. Risk Factors for Retinal Detachment after Cataract Surgery. A Case-Control Study. Ophthalmology. 2006;113(4):650-6.

45. Olsen G, Olson RJ. Update on a long-term, prospective study of capsulotomy and retinal detachment rates after cataract surgery. Journal of Cataract and Refractive Surgery. 2000;26(7):1017-21.

46. Forsell S, Monestam E. Frequency of Retinal Redetachment after Cataract Surgery in Eyes with Previous Scleral Buckling Surgery. Ophthalmology Retina. 2018;2(1):4-9.

47. Johnston PB. Traumatic retinal detachment. Br J Ophthalmol. 1991;75(1):18-21.

48. Rowe JA, Erie JC, Baratz KH, Hodge DO, Gray DT, Butterfield L, et al. Retinal detachment in Olmsted County, Minnesota, 1976 through 1995. Ophthalmology. 1999;106(1):154-9.

49. Olsen T, Arnarsson A, Sasaki H, Sasaki K, Jonasson F. On the ocular refractive components: the Reykjavik Eye Study. Acta Ophthalmol Scand. 2007;85(4):361-6.

50. Mitry D, Tuft S, McLeod D, Charteris DG. Laterality and gender imbalances in retinal detachment. Graefe's Archive for Clinical and Experimental Ophthalmology. 2011;249(7):1109-10.

51. The Eye Diseases Prevalence Research G. The prevalence of refractive errors among adults in the united states,western europe, and australia. Archives of Ophthalmology. 2004;122(4):495-505.

52. Wang J, McLeod D, Henson DB, Bishop PN. Age-Dependent Changes in the Basal Retinovitreous Adhesion. Investigative Ophthalmology & Visual Science. 2003;44(5):1793-800.

53. Ninn-Pedersen K, Bauer B. Cataract patients in a defined swedish population, 1986 to 1990: V. postoperative retinal detachments. Archives of Ophthalmology. 1996;114(4):382-6.
54. Shah V, Hall N, Goldacre MJ. Retinal detachment in England: database studies of trends over time and geographical variation. British Journal of Ophthalmology. 2015;99(5):639-43.
55. Sharma MC, Chan P, Kim RU, Benson WE. Rhegmatogenous retinal detachment in the fellow phakic eyes of patients with pseudophakic rhegmatogenous retinal detachment. Retina. 2003;23(1):37-40.
56. Mahroo OA, Dybowski R, Wong R, Williamson TH. Characteristics of rhegmatogenous retinal detachment in pseudophakic and phakic eyes. Eye (Basingstoke). 2012;26(8):1114-21.
57. Coppe AM, Lapucci G. Posterior vitreous detachment and retinal detachment following cataract extraction. Current Opinion in Ophthalmology. 2008;19(3):239-42.
58. Lois N, Wong D. Pseudophakic retinal detachment. Survey of Ophthalmology. 2003;48(5):467-87.
59. Neal RE, Bettelheim FA, Lin C, Winn KC, Garland DL, Zigler Jr JS. Alterations in human vitreous humour following cataract extraction. Experimental Eye Research. 2005;80(3):337-47.
60. Ivastinovic D, Schwab C, Borkenstein A, Lackner EM, Wedrich A, Velikay-Parel M. Evolution of early changes at the vitreoretinal interface after cataract surgery determined by optical coherence tomography and ultrasonography. Am J Ophthalmol. 2012;153(4):705-9.
61. Ripandelli G, Coppe AM, Parisi V, Olzi D, Scassa C, Chiaravalloti A, et al. Posterior Vitreous Detachment and Retinal Detachment after Cataract Surgery. Ophthalmology. 2007;114(4):692-7.
62. Daien V, Le Pape A, Heve D, Carriere I, Villain M. Incidence, Risk Factors, and Impact of Age on Retinal Detachment after Cataract Surgery in France A National Population Study. Ophthalmology. 2015;122(11):2179-85.
63. Ducournau DH, Le Rouic JF. Is pseudophakic retinal detachment a thing of the past in the phacoemulsification era? Ophthalmology. 2004;111(6):1069-70.

64. Fan DSP, Lam DSC, Li KKW. Retinal complications after cataract extraction in patients with high myopia. Ophthalmology. 1999;106(4):688-91.

Titles and legends to figures

Table 1: Summary of studies meeting review criteria

Figure 1: Cumulative PPRD incidence as reported by the 16 studies included in this review

Table 2: Reproduced from Lin et al. 2013

	1	2	3	4	5	6	7	8	9
Lead Author	Boberg-Ans	Sheu	Boberg-Ans	Russell	Sheu	Sheu	Szijártó	Sheu	Olsen
Publication year	2003	2005	2006	2006	2006	2007	2007	2010	2012
Location	Denmark	Taiwan	Denmark	New Zealand	Taiwan	Taiwan	Hungary	Taiwan	Denmark
Method as described by authors	Retrospective review	Prospective cohort	Retrospective register based consecutive uncontrolled study	Retrospective review	Prospective cohort	Prospective cohort study	Retrospective series	Prospective cohort study	Retrospective cohort study
Size	6,521 PP eyes	9,398 PP eyes	6,352 PP eyes	1,793 PP eyes	9,398 PP eyes	9,398 PP eyes	11,098 PP eyes	9,388 PP eyes	12,222 PP eyes
Population age range/criteria	Feb-98	21-99	Feb-98	40-100	21-99	18-99	13-105	18-99	20-101
Study duration	1996-1998	1999-2001	1996-1998	1992-1993	1999-2001	1999-2001	1994-2004	1999-2001	2000-2005
Tumours excuded?	No	No	No	No	No	No	No	No	No
Trauma excluded?	No	Yes	No	Yes	Yes	Yes	No	Yes	No
CLE excluded?	Yes (inferred)	Yes (inferred)	Yes	Yes (inferred)	Yes (inferred)	Yes (inferred)	Yes (inferred)	Yes (inferred)	Yes (inferred)
ECCE excluded?	No (<1%)	No (37.8%)	Yes	Yes	No (37.8%)	No (37.8%)	Yes	No (37.8%)	Yes
Min. potential FU	15 months	1 yr	5 yrs	10 yrs	2 yrs	4 yrs	6 wks	6 yrs	2 yrs
Total PPRDs	22	(unquantified)	44	21	(unquantified)	(unquantified)	40	(unquantified)	48
Overall PPRD rate	0.41% 4.33 yr cumulative PPRD risk	0.4% 3 yr cumulative PPRD risk	0.93% 8 yr cumulative PPRD incidence vs.	1.17% cumulative 10yr PPRD rate	0.76% cumulative 4 yr PPRD rate	1.16 cumulative 6 yr PPRD rate	0.36% cumulative 10 yr PPRD rate	2.31% cumulative 8 yr PPRD rate	0.39% cumulative 4 yr PPRD rate
Inferred annual PPRD incidence	0.09%	0.13%	0.12%	0.12%	0.19%	0.19%	0.04%	0.29%	0.10%
Time from phaco to RD surgery	Highest in 1st yr post op	Highest in 1st 2 yrs, stable after 3	No sig. period of higher risk. Remains sig. above general population 6 yrs post op	No sig. period of higher risk, median 39 months	-	-	Highest in first year. Shorter if vitreous loss (not if just PCR) longer if younger - 31 months vs 10 months	No sig. period of higher risk overall. Males with mod. and high myopia (AL >23 mm) have sig. late increase (4 yrs) in PPRD risk	-
ECCE vs Phaco	(all PPRDs post phaco)	not sig.	EXCLUDED	EXCLUDED	not sig.	not sig.	EXCLUDED	Higher risk for Phaco vs ECCE (8 yr PPRD rate 2.91 vs 1.66%, RR 1.78) only sig in 1st yr of phaco introduction	EXCLUDED
Intraoperative complications vs not	not sig.	no sig. increase except if PCR in >60 yrs	-	Higher risk for ant. vitrectomy and for all complications combined, not sig. for PCR alone	not sig.	not sig.	Higher risk for all complications combined (RR 20.03. Complications were zonulolysis and PCR with and without vitreous loss)	not sig.	Higher risk for PCR with vitreous loss (PCR in 10.4% of PPRD pts vs 1.9% of general post-phaco population)
Surgeon grade	-	-	-	-	-	-	-	-	-
Nd:YAG capsulotomy vs not	not sig.	No sig. increased risk except in age <50 yrs	-	not sig.	-	not sig.	-	not sig.	not sig.

Myopic vs Nonmyopic	Higher risk for myopes (AL >25 mm, risk unquantified)	Dose-dependent higher risk for myopes (3 yr PPRD rate 0.25% 0.41% and 1.63% for AL <23, 23-26 and >26 mm) Effect not significant in >60 yr olds	-	4.87x higher risk for myopes (AL >24 mm)	Dose-dependent higher risk for myopes (4 yr PPRD rate 0.36%, 0.66% and 2.00% for AL <23, 23-26 and >26 mm)	Dose-dependent higher risk for myopes (RR vs AL <23 mm 2.38 and 6.12 for AL 23-26 and >26 mm)	Higher risk for myopes (RR 6.5 for AL >25 vs AL <25 mm)	Dose-dependent higher risk for myopes (crude RR vs AL <23 mm 1.78 and 4.61 for AL 23-26 and >26 mm)	Dose-dependent higher risk for myopes (4 yr PPRD rate 0.18% for AL <24 mm vs 2.8% for AL 27-28 mm)
Previous RD vs not	EXCLUDED	EXCLUDED	-	not sig.	EXCLUDED	EXCLUDED	EXCLUDED	EXCLUDED	-
Hx of fellow eye RD vs none	-	-	-	Minimally sig. higher risk	-	-	-	Higher risk (crude RR 17.34)	-
Ocular trauma Hx vs none	not sig.	EXCLUDED	-	EXCLUDED	EXCLUDED	EXCLUDED	-	EXCLUDED	not sig.
Male vs Female	Higher risk for men (unquantified)	not sig.	Higher risk for men (RR 2.5)	Higher risk for men (10 yr PPRD rate 2.1% vs 0.62%)	not sig.	Higher risk for men (RR 2.42)	not sig.	Higher risk for men (ARR 1.72)	Higher risk for men (58.3% males in PPRD population vs 34.9% in general post-phaco population)
Age	Higher risk for pts aged <65 yrs (unquantified)	Dose-dependent higher risk in younger pts (3 yr PPRD rate 1.01%, 0.67% and 0.29% for ages <50, 50-60 and >60 yrs)	Dose-dependent higher risk in younger pts (RR vs >80 years 10.2, 8.9 and 2.6 for ages <60, 60-69 and 70-79 yrs)	Higher risk for younger pts (10 yr PPRD rate 5.17% for <50 yrs vs 0.64% for >70 yrs)	Dose-dependent higher risk for younger pts (4 yr PPRD rate 1.41%, 0.72% and 0.50% for ages <50, 50-60 and >60 yrs)	Higher risk for younger (RR 3.00 for age <50 vs >60 yrs)	Higher risk for younger pts (RR 4.75 for age <65 vs >65 yrs)	Higher risk for younger pts (crude RR 2.69 for age <50 vs >60 yrs)	Higher risk for younger pts (mean age 60.5 yrs for PPRD pts vs 73.7 yrs for general post-phaco population)
Systemic disease vs not	-	-	-	-	not sig. for DM and hypertension	not sig. for DM and hypertension	-	not sig. for DM and hypertension	-
Ethnicity	-	-	-	-	-	-	-	-	-
Notes	NB. Retrospective risk factor analysis. Found PPRD risk in absence of preoperative risk factors similar to high estimate of general population RD incidence (0.12% 4 yr by Norregaard 1996).								Retrospective risk factor analysis for age, sex, myopia and operative complications. Also prospectively calculated PPRD incidence with varying axial length

10	11	12	13	14	15	16
Quek	Bjerrum	Lin	Daien	Day	Day et al	Petousis
2012	2013	2013	2015	2015	2016	2016
Singapore	Denmark	Taiwan	France	UK	UK	UK
Retrospective case-control study	Retrospective register based cohort study	Retrospective review	Population study	Prospective database study	Retrospective Case series	Single centre database study
24,846 PP eyes	202,226 PP eyes	9,184 PP eyes	2,680,167 PP eyes	180,114 PP eyes	61,907 PP eyes	18,065 PP eyes
(not specified)	40-104	18-96	40+	18+	18-104	(not specified)
2001-2003	2000-2010	2000-2010	2009-2012	2006-2010	2006	2005-2014
No	Yes	No	No	No	No	No
No	Yes	Yes	No	No	No	Yes
Yes (inferred)	Yes	Yes (inferred)	Yes	Yes (inferred)	Yes	Yes
No (18.5% ECCE or ICCE)	Yes	No (16.6%)	No (<1%)	Yes (inferred)	Yes	Yes
6 months	6 months	None (inferred)	None (included cataract ops till end)	1 year	3 months	3 months (inferred)
39	465	(unquantified)	11,424	108	131	36
0.16% cumulative 3.5 yr (inferred) PPRD rate	1.36 per 1000 person-years PPRD incidence rate (vs 0.32 fellow eye baseline)	0.84% cumulative 7 yr PPRD rate	0.99% 4 yr cumulative PPRD rate	0.03% cumulative 3 month PPRD risk	0.21% cumulative 4 yr (inferred) cumulative PPRD	0.30% 7 yr cumulative PPRD rate
0.05%	0.14%	0.12%	0.25%	0.12%	0.05%	0.04%
-	Highest 6 months post op (HR 9 vs fellow eye), levels off after 2 yrs and persists above fellow eye 10 yrs later (HR 3 vs fellow eye)	-	Linear increase in cumulative risk	-	Median 6.3 months if uncomplicated, 44 days if PCR	-
-	EXCLUDED	not sig.	Higher risk for ECCE (HR 3.11)	EXCLUDED	EXCLUDED	EXCLUDED
Higher risk for PCR (PCR in 23.1% of PPRD pts vs 1.0% of general post-phaco population)	EXCLUDED	Higher risk for all complications combined (ARR 6.09. Complications were PCR with and without vitreous loss. Complications not sig in non-myopes, AL <23 mm)	Higher risk for PCR with vitrectomy (HR 4.36)	Higher risk with PCR, decreases with time after phaco (OR 41.66, 23.98 and 18.28 at 3, 6 and 12 months)	Higher risk for PCR (4 yr PPRD rate 16.47% if PCR vs 1.83% without)	Higher risk for PCR only if with vitreous loss (HR 12.83)
-	-	-	-	(Lower intraoperative complication rate with consultants vs juniors)	Shorter time to PPRD with more junior operators independent of PCR	-
-	-	No sig. increased risk except in high myopes (AL >26 mm)	-	-	-	-

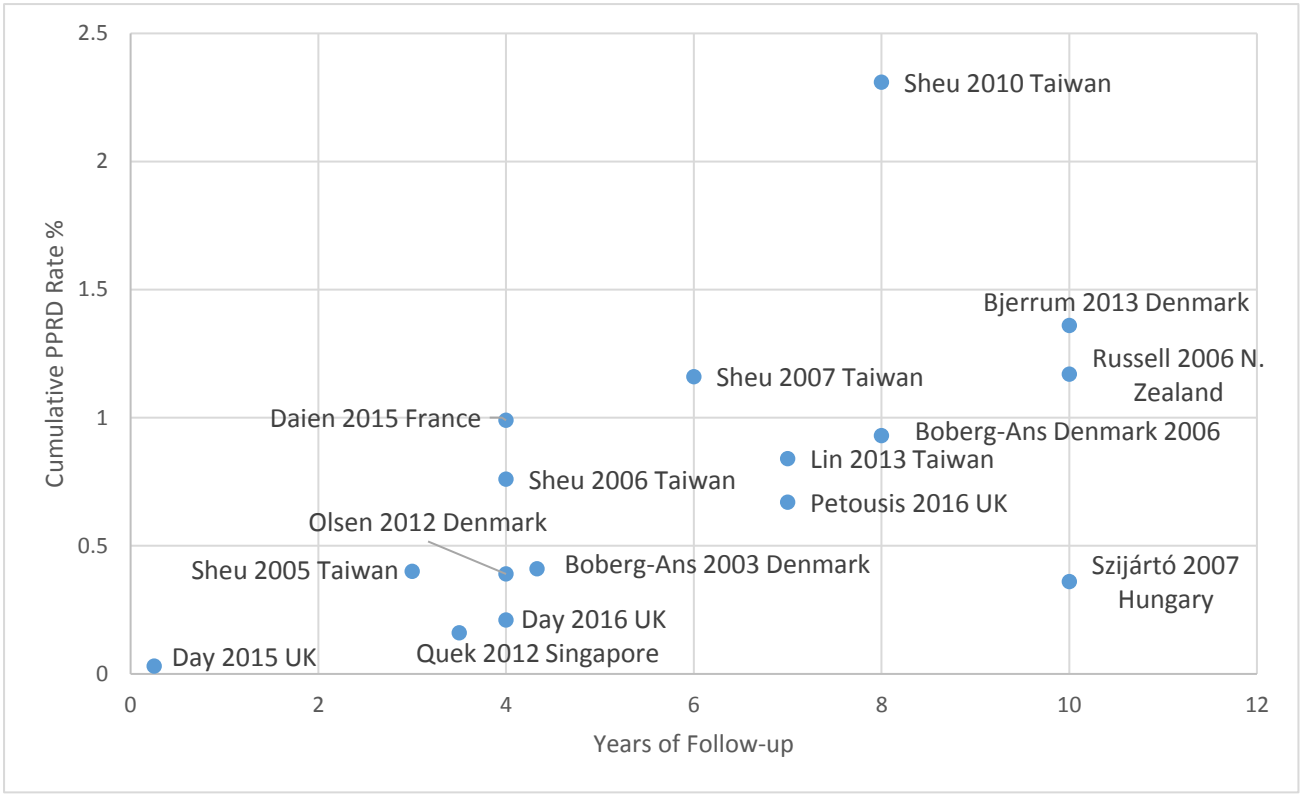
-	-	Dose-dependent higher risk for myopes (ARR vs AL <23 mm 3.92 and 18.90 for AL 23-26 mm and >26 mm)	Higher risk for high myopes (HR 6.12 for AL >26mm)	-	-	Higher risk for high myopes (HR vs AL 23-25 mm 3.98 for AL >25 mm) No sig. decreased risk for AL <23 mm
-	EXCLUDED	EXCLUDED	EXCLUDED	-	-	-
-	-	-	-	-	-	-
-	-	EXCLUDED	Higher risk with trauma Hx (HR 3.98)	-	-	-
Higher risk for men (76.9% males in PPRD population vs 54% in general post-phaco population)	Higher risk for men (HR 1.74) but phaco-attributable risk (relative to fellow eye) not sig. changed by sex	not sig.	Higher risk for men (HR 2.39)	-	-	Higher risk for men (HR 2.00)
Dose-dependent higher risk for younger pts (HR vs age >70 yrs 20.0 for age 31-40 and 3.5 for age 61-70 yrs)	Dose-dependent higher risk for younger pts (HR 14.8 for age 50-60 yrs vs >80 yrs) but phaco-attributable risk (relative to fellow eye) not sig. changed by age (except 40-49yr women who have sig. higher attributable risk vs 70-79 yr old women)	Dose-dependent higher risk for younger pts (ARR vs age >60 yrs 20.59 and 5.78 for <50 yrs and 50-60 yrs)	Dose-dependent higher risk for younger pts (HR vs age >75 yrs 5.22, 3.69 and 1.98 for age 40-54, 55-64 and 65-74 yrs)	-	-	Dose-dependent higher risk for younger pts (HR vs 60-80 yrs 5.12 and 0.16 for <60 and >80 yrs)
-	-	not sig. for DM and hypertension	Higher risk if diabetic (HR 1.18%)	-	-	-
not sig.	-	-	-	-	-	-
Retrospective risk factor analysis for age, sex, myopia and operative complications. Note PPRD incidence calculated over whole duration of study even for phacos performed partway through	Young and male cataract pts have a higher native risk of RD. Over 10 yrs the additional risk of PPRD attributable to the phaco per se was increased by a factor of 4.2 irrespective of sex and age.	Note PPRD incidence calculated over whole duration of study even for phacos performed partway through	Hierarchy of risk factors for PPRD: high myopia, young age, ECCE, PCR, eye trauma, male sex and diabetes. Note overall PPRD incidence calculated over whole duration of study even for phacos performed partway through.		Note PPRD incidence calculated over whole duration of study even for phacos performed partway through	

Variables	AL<23 mm (N=3240)		23mm≤AL<26 mm (N=5518)
	Adjusted Relative Risk (95%CI)	*P* Value	Adjusted Relative Risk (95%CI)
Age			
>60	1		1.75(0.18–16.81)
50<age≤60	0.04(0–7.182E+11)	0.84	13.78(1.25–151.99)
≤50	0.05(0–4.359E+27)	0.93	36.67(3.30–407.92)
Capsulotomy			
No	1		2.81(0.33–24.30)
Yes	0.03(0–54286105)	0.76	3.94(0.35–44.55)
Sex			
Female	1		0.02(0–136817.09)
Male	0.01(0–658818.80)	0.59	3.56(0.39–32.31)
Intraoperative complications			
No	1		3.44(0.41–28.89)
Yes	0.04(0–9.947E+18)	0.9	14.57(0.91–232.92)

CI = confidence interval, AL = axial length

* : P-Value was considered to be significant

	AL≥26mm (N=426)	
P Value	Adjusted Relative Risk (95%CI)	*P* Value
0.63	10.99(0.69□175.75)	0.09
0.03*	34.51(3.09□385.58)	0.004*
0.003*	151.80(15.63□1474.46)	<0.001*
0.35	7.25(0.57□92.44)	0.13
0.27	43.50(3.56□532.22)	0.003*
0.61	9.61(0.74□124.63)	0.08
0.26	8.57(0.87□84.78)	0.07
0.26	19.08(1.89□192.28)	0.01*
0.05*	46.73(1.71□1278.01)	0.02*


Cumulative PPRD Rate %
Years of Follow-up
2.5
2
1.5
1
0.5
0
0
2
4
6
8
10
12
Sheu 2010 Taiwan
Bjerrum 2013 Denmark
Russell 2006 N. Zealand
Sheu 2007 Taiwan
Daien 2015 France
Boberg-Ans Denmark 2006
Lin 2013 Taiwan
Sheu 2006 Taiwan
Petousis 2016 UK
Olsen 2012 Denmark
Sheu 2005 Taiwan
Boberg-Ans 2003 Denmark
Szijártó 2007 Hungary
Day 2016 UK
Quek 2012 Singapore
Day 2015 UK