ClinicalEvidence

Retinal detachment

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ABSTRACT

INTRODUCTION: Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment, where a retinal "break" allows the ingress of fluid from the vitreous cavity to the subretinal space, resulting in retinal separation. It occurs in about 1 in 10,000 people a year. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of interventions to prevent progression from retinal breaks or lattice degeneration to retinal detachment? What are the effects of different surgical interventions in people with rhegmatogenous retinal detachment? What are the effects of interventions to treat proliferative vitreoretinopathy occurring as a complication of retinal detachment or previous treatment for retinal detachment? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2009 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 20 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: corticosteroids; cryotherapy; daunorubicin; fluorouracil plus low-molecular-weight heparin; laser photocoagulation; pneumatic retinopexy; scleral buckling; short-acting or long-acting gas tamponade; silicone oil tamponade; and vitrectomy.

QUESTIONS

What are the effects of interventions to prevent progression from retinal breaks or lattice degeneration to retinal detachment? . . . 4

What are the effects of different surgical interventions in people with rhegmatogenous retinal detachment? . . . 5

What are the effects of interventions to treat proliferative vitreoretinopathy occurring as a complication of retinal detachment or previous treatment for retinal detachment? . . . 8

INTERVENTIONS

PREVENTING RETINAL DETACHMENT

Likely to be beneficial

Cryotherapy* . . . 4

Laser photocoagulation* . . . 4

DIFFERENT SURGICAL INTERVENTIONS FOR RHEGMATOGENOUS RETINAL DETACHMENT

Unknown effectiveness

Scleral buckling versus pneumatic retinopexy (there is consensus that both surgical techniques are effective: insufficient evidence to compare effects of scleral buckling versus pneumatic retinopexy) . . . 5

Scleral buckling versus primary vitrectomy (there is consensus that both surgical techniques are effective but effects of scleral buckling compared with vitrectomy are unclear: in pseudophakic or aphakic RRD, rate of retinal re-attachment after one operation may be lower post-scleral buckling compared with post-vitrectomy, but scleral buckling may be associated with a lower rate of development or progression of cataract in phakic RRD) . . . 6

TREATING PROLIFERATIVE VITREORETINOPATHY

Likely to be beneficial

Silicone oil or long-acting gas tamponade (silicone oil and long-acting gas equally effective in people receiving vitrectomy for rhegmatogenous retinal detachment with severe proliferative vitreoretinopathy; silicone oil is more effective than short-acting gas at increasing re-attachment rates) . . . 8

Unknown effectiveness

Corticosteroid injection during vitrectomy surgery New . . . 10

Daunorubicin infusion during vitrectomy surgery New . . . 10

Fluorouracil plus low-molecular-weight heparin added to infusion solution during vitrectomy surgery . . . 11

To be covered in future updates

Preventing proliferative vitreoretinopathy

Footnote

*Based on consensus; no RCT evidence available.

Key points

- Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment, where a retinal "break" allows the ingress of fluid from the vitreous cavity to the subretinal space, resulting in retinal separation. It occurs in about 1 in 10,000 people a year.

  This review considers only acute progressive RRD.
- Cryotherapy and photocoagulation are widely used for preventing progression from retinal breaks or lattice degeneration to RRD, and there is consensus that they are effective, particularly in people with symptomatic flap tears and retinal dialysis.

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- There is consensus that scleral buckling, pneumatic retinopexy, and vitrectomy are all effective for treating RRD.

  We found insufficient evidence to assess effects of scleral buckling compared with pneumatic retinopexy.

  The effects of scleral buckling compared with primary vitrectomy are unclear. There is limited evidence that, in phakic RRD, scleral buckling improves visual acuity at 1 year, and is associated with a reduced risk of development or progression of cataract. However, in pseudophakic and aphakic RRD, rates of retinal re-attachment after one operation are lower post-scleral buckling compared with post-vitrectomy.
- In people undergoing vitrectomy for RRD with severe proliferative vitreoretinopathy (occurring as a complication of retinal detachment or previous treatment for retinal detachment), silicone oil and long-acting gas are equally effective for increasing re-attachment rates and improving visual acuity; silicone oil is better than short-acting gas.
- We found insufficient evidence assessing the effects of fluorouracil plus heparin, corticosteroid, or daunorubicin given during vitrectomy surgery for proliferative vitreoretinopathy.

DEFINITION

Retinal detachment can be defined as the separation of the neurosensory retina from the underlying retinal pigment epithelium (RPE). Direct apposition of the retina to the RPE is essential for normal retinal function, and retinal detachment involving the foveal centre leads to profound loss of vision in the affected eye. [1] [2] **Rhegmatogenous retinal detachment (RRD)** is the most common form of retinal detachment, where a retinal "break" allows the ingress of fluid from the vitreous cavity to the subretinal space, resulting in retinal separation. Retinal break refers to a full-thickness defect in the neurosensory retina. Retinal breaks that develop from a tear in the retina at the time of posterior vitreous detachment (PVD) are usually referred to as retinal tears. Lattice degeneration can lead to the formation of circular retinal holes, which are typically referred to as atrophic holes. Retinal breaks can also develop as a result of trauma to and inflammation of the eye: examples include retinal dialysis, which is typically secondary to blunt trauma, and tears associated with retinal necrosis, resulting from trauma or inflammation. Rarer causes of retinal detachment include: tractional retinal detachment secondary to fibrous tissue on the surface of the retina; exudative retinal detachment as a result of choroidal tumours that produce increased fluid flow through the subretinal space; [3] and ocular inflammatory conditions. Retinal detachments can also be a mixture of two or more of the above types. Asymptomatic and non-progressive chronic retinal detachment can also occur. This review considers only acute progressive RRD. **Diagnosis:** RRD is often, but not universally, associated with symptoms of flashes of light (retinal photopsia), visual floaters, and peripheral and usually progressive visual field loss. It is diagnosed by ophthalmoscopy. Acute RRD is seen as an oedematous folded retina with loss of the normal retinal transparency. The detachment can assume a bullous configuration that moves when the eye moves. There can be associated signs of PVD, as well as vitreous haemorrhage or RPE cells circulating in the vitreous cavity after retinal break formation. The presence of pigment cells in the anterior vitreous — visible on slit-lamp biomicroscopy (termed "Shafer's sign") — is a sensitive indicator of the presence of a retinal break in a person presenting with an acute PVD. [4] Chronic retinal detachments can be associated with retinal cyst formation and "tidemarks" demarcating the extent of the detachment, as well as subretinal fibrosis. [1] [2]

INCIDENCE/ PREVALENCE

RRD can occur at any age, but reaches peak prevalence in people aged 60 to 70 years. [5] [6] [7] It affects men more than women, and white people more than black people. Observational studies from the USA, Europe, and New Zealand found that non-traumatic, phakic (lens intact) RRD occurred in about 6 to 18/100,000 people a year (i.e., about 1/10,000). [5] [6] [7] [8] [9] [10] [11]

AETIOLOGY/ RISK FACTORS

The occurrence of retinal detachment is related to the interplay between predisposing retinal lesions and vitreoretinal traction, and occurs when fluid moves from the vitreous cavity through a retinal break into the subretinal space. [12] Most (80–90%) retinal detachments are associated with retinal-break formation at the time of PVD. [13] [14] PVD is a naturally occurring phenomenon, with a rapidly increasing prevalence in the 60 to 70-year-old age group. Most (70%) retinal breaks formed at the time of PVD are seen as tears in the retina, or as holes with a free-floating retinal operculum. Retinal breaks can occur in areas of previously abnormal retina — for example, lattice degeneration. [14] [15] Symptoms and signs of acute PVD are known to be associated with a higher risk of immediate progression to RRD in people with predisposing retinal lesions. However, people with established (chronic) PVD and predisposing retinal lesions who have not immediately progressed to RRD are at lower risk than those without a PVD. Symptomatic retinal tears with persistent vitreoretinal traction (not a complete PVD) have a high rate of progression to retinal detachment (>50% if left untreated). [16] The risk of retinal detachment is increased to a variable extent in people with asymptomatic pre-existing retinal disease or lesions, especially retinal-flap tears, operculated retinal holes after separation of a retinal flap, atrophic retinal holes, lattice degeneration (areas of retinal thinning with abnormal vitreoretinal adhesion), and retinal dialyses. Autopsy studies have shown that about 6% to 11% of people aged over 20 years have retinal breaks in one form or another. However, the chances of an RRD occurring in an asymptomatic eye with a retinal break and with no history of fellow-eye RRD is 0.5% over a follow-up period of 11 years. [17] [18] Similarly, 7% to

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8% of adults have areas of lattice degeneration, but only a small proportion of these lesions progress to RRD. [17] [19] [20] [21] Asymptomatic retinal dialysis is thought to have a high risk of progression to retinal detachment, especially after trauma. [22] [23] Increased risk of RRD is associated with several factors. There is a higher prevalence of RRD in short-sighted (myopic) people, [24] with around a 10-fold increased incidence in people with over 3 dioptres of myopia. [25] The fellow eye in people with an RRD is at a higher risk, with 2% to 10% of RRDs being bilateral. [26] [27] [28] [29] [30] Although some RRD occurring in a fellow eye will develop from pre-existing retinal lesions, most subsequent RRD (at least 50%, and possibly as high as 80–90%) in the fellow eye will occur from ophthalmoscopically normal areas of retina, [14] and so prophylaxis to visible abnormal areas may not completely reduce the incidence of fellow-eye RRD. There is also a higher incidence of RRD in people with a family history of retinal detachment, especially in conditions such as Stickler syndrome. People who have had previous cataract surgery also have a higher incidence of RRD. About 0.5% to 0.6% of people experience RRD after phacoemulsification surgery for cataracts, with the risk being increased by 15 to 20 times with rupture of the posterior capsule. [31] [32] About 10% of RRDs are associated with trauma. There are other conditions which, more rarely, increase the risk of RRD, including uveitis — especially CMV retinitis — and other degenerative retinal conditions, such as retinoschisis. Idiopathic macular holes may cause RRD in highly myopic eyes, but rarely in emmetropic or hypermetropic eyes.

PROGNOSIS

On presentation, retinal detachment is usually divided into "macula on", when the fovea is still attached, and "macula off", where the retina is detached centrally. [33] People with macula-on retinal detachments typically have good initial visual acuity, and a better prognosis with successful surgery. Rapidly progressive cases are therefore treated as a matter of urgency. Macula-off retinal detachments have worse initial visual acuity, and have a worse prognosis even with successful re-attachment of the retina. Overall, about 95% of people have anatomically successful repair of RRD, with 70% to 90% achieving this in one operation. In 90% of successfully repaired macula-on retinal detachments, vision is 6/12 or better. However, in those with macula-off retinal detachments, only 50% of eyes achieve a visual acuity of 6/15, and, if the macula has been detached for 1 week or more, this level of visual acuity is rarely achieved. [33] Reasons for anatomical failure of surgery include new or missed retinal breaks, and proliferative vitreoretinopathy (PVR). PVR is classified based on extent, position, and type of PVR: the American Retina Society proposed the first classification of PVR in 1983, [34] and, although updated in 1991 following The Silicone Oil Study, [35] this classification system continues to be widely used. Causes of poor visual acuity after successful repair include macular epiretinal membranes (fibrosis), cystoid macular oedema, and foveal photoreceptor degeneration in macula-off retinal detachments. [36]

AIMS OF INTERVENTION

To prevent progression from retinal breaks or lattice degeneration to RRD; to achieve retinal re-attachment in people with RRD; to achieve retinal re-attachment in people with PVR occurring as a complication of RRD or previous treatment for RRD; to achieve these aims with minimal re-operation rates and adverse effects of treatment.

OUTCOMES

Prevention: Rates of progression from retinal breaks or lattice degeneration to retinal detachment, complications (loss of visual acuity or adverse effects of treatment). **Treatment:** Anatomical re-attachment rate (after one operation and final rate), re-operation rate, visual acuity. **Treatment of eyes with proliferative vitreoretinopathy:** Rate of retinal re-attachment (after one operation and final rate), re-operation rate, visual acuity. **Adverse effects:** Axial length and refractive change, cataract, endophthalmitis, extraocular muscle dysfunction and diplopia, glaucoma, macular oedema, macular pucker, raised intraocular pressure, redetachment, subretinal and choroidal haemorrhage, PVR associated with initial treatment.

METHODS

Clinical Evidence search and appraisal March 2009. The following databases were used to identify studies for this review: Medline 1966 to March 2009, Embase 1980 to March 2009, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials, 2009, Issue 1 (1966 to date of issue). An additional search was carried out of the NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributors for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs, and RCTs in any language that were at least single blinded and contained more than 20 individuals, of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open label", or not blinded, unless blinding was impossible. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied, applying the same study design criteria for inclusion as we did for benefits. In addition, we

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use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. Scleral buckling surgery has been the mainstay of treatment for RRD for many years, and there is consensus that it is effective in cases where it is possible to close the retinal breaks with scleral indentation. We have therefore compared scleral buckling versus other surgical techniques (pneumatic retinopexy and vitrectomy). Various visual acuity scales have been used by the RCTs in the review; results for visual acuity are reported as cited in the original studies. See table 1, p 16 for an illustration of how the scales compare. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 21).

QUESTION **What are the effects of interventions to prevent progression from retinal breaks or lattice degeneration to retinal detachment?**

OPTION CRYOTHERAPY (CRYOPEXY)

We found no direct information from RCTs about cryotherapy for preventing progression from retinal breaks or lattice degeneration to rhegmatogenous retinal detachment. However, cryotherapy is widely used, and there is consensus that it is effective, particularly in people with symptomatic flap tears and retinal dialysis.

For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits: We found one systematic review (search date 2006), which identified no RCTs assessing cryotherapy for preventing progression from asymptomatic retinal breaks or lattice degeneration to rhegmatogenous retinal detachment (RRD). [37]

Harms: We found no RCTs.

Comment: **Clinical guide:**
Transclerally applied cryotherapy and transpupillary laser photocoagulation are widely used to treat predisposing retinal lesions in an attempt to prevent progression to RRD. We found one systematic review (search date not reported), which made consensus recommendations supported primarily by retrospective observational studies. [38] Their consensus recommendations suggested that one should "always treat" symptomatic flap tears prophylactically, and "almost always treat" people with retinal dialysis regardless of symptoms. One should “sometimes treat” asymptomatic flap tears and symptomatic operculated tears, especially if eyes have other risk factors for RRD, such as previous RRD in the fellow eye or myopia. One should also "sometimes treat" people with lattice degeneration in fellow eyes of those experiencing RRD prophylactically, unless the eye has more than 6 dioptres of myopia, or more than 6 clock hours of lattice degeneration. The method of prophylactic treatment was not specified in the review. [38] The choice of cryotherapy or laser photocoagulation is dependent on the experience of the clinician, the availability of the technology, and clinical appropriateness. Cryotherapy can be applied to the retina in an eye with severe media opacity that precludes the use of laser photocoagulation. Cryotherapy is also easier to apply than laser photocoagulation if pupil size is small and the retinal lesion is anterior. [2] [39] Laser photocoagulation is more easily applied to posterior retinal pathology than cryotherapy, which would require conjunctival opening to treat posterior lesions. [2] [39] Laser photocoagulation is also considered effective in people with symptomatic flap tears or retinal dialysis. Clinical experience suggests that complications of prophylactic treatment can be divided into three groups: failure to prevent retinal detachment, new retinal break formation, and later adverse effects such as macular pucker. However, macular-pucker formation occurs as a primary complication after posterior vitreous detachment, and is reported as occurring in 1% to 2% of people after preventive treatment with either cryotherapy or laser photocoagulation — similar to the rates of untreated eyes with predisposing retinal lesions. [12] Other rarer complications include: choroidal detachment, which may cause anterior chamber shallowing; myopia or reduced accommodation; raised intraocular pressure; pupillary dilation with visual glare; and vitreous haemorrhage. Cryotherapy delivered transclerally is associated with transient postoperative conjunctival erythema, chemosis, and irritation.

OPTION LASER PHOTOCOAGULATION

We found no direct information from RCTs about laser photocoagulation for preventing progression from retinal breaks or lattice degeneration to rhegmatogenous retinal detachment. However, laser photocoagulation is widely used, and there is consensus that it is effective, particularly in people with symptomatic flap tears and retinal dialysis.

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For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits: We found one systematic review (search date 2006), which identified no RCTs assessing laser photocoagulation for preventing progression from asymptomatic retinal breaks or lattice degeneration to rhegmatogenous retinal detachment. [37]

Harms: We found no RCTs.

Comment: **Clinical guide:**
See comment on cryotherapy, p 4 .

QUESTION **What are the effects of different surgical interventions in people with rhegmatogenous retinal detachment?**

OPTION **SCLERAL BUCKLING VERSUS PNEUMATIC RETINOPEXY**

Re-attachment rate
Compared with pneumatic retinopexy Scleral buckling and pneumatic retinopexy seem equally effective at increasing re-attachment rates (after one operation and final rate) in people with phakic, pseudophakic, or aphakic rhegmatogenous retinal detachment (RRD) and superior retinal breaks (moderate-quality evidence).

Visual acuity
Compared with pneumatic retinopexy Scleral buckling and pneumatic retinopexy seem equally effective at improving visual acuity in people with phakic, pseudophakic, or aphakic RRD and superior retinal breaks. However, in eyes with preoperative detachment of the macula for up to 14 days, scleral buckling seems less effective at improving visual acuity (moderate-quality evidence).

Adverse effects
Scleral buckling has been associated with higher rates of refractive change (usually a myopic shift in refraction), diplopia with extraocular muscle dysfunction, and subretinal haemorrhage compared with pneumatic retinopexy.

For GRADE evaluation of interventions for retinal detachment, see table , p 21 .

Benefits: We found two RCTs. [40] [41] The first RCT (198 people; 198 eyes with phakic [108 eyes], pseudophakic [70 eyes], or aphakic [20 eyes] rhegmatogenous retinal detachment [RRD], involving retinal breaks within 1 disc diameter of each other located in the superior retina, without severe proliferative vitreoretinopathy [PVR]) found no significant difference between scleral buckling and pneumatic retinopexy at 6 months in re-attachment rates after one operation (78/95 [82%] eyes with scleral buckling *v* 75/103 [73%] eyes with retinopexy) or in final rate of re-attachment (93/95 [98%] eyes with scleral buckling *v* 102/103 [99%] eyes with retinopexy; P values not reported; both differences reported as not significant). [40] Scleral buckling and pneumatic retinopexy resulted in similar visual acuity at 6 months (proportion of eyes with visual acuity of 20/50 or better on the Snellen scale: 64/95 [68%] with scleral buckling *v* 90/103 [87%] with pneumatic retinopexy; P value not reported; proportion of eyes with visual acuity of 20/25: 12/95 [13%] with scleral buckling *v* 25/103 [24%] with pneumatic retinopexy; P = 0.05). Subgroup analysis of eyes that had preoperative detachment of the macula for up to 14 days found that scleral buckling was significantly less effective than pneumatic retinopexy in improving visual acuity (proportion of eyes with visual acuity of 20/50 or better on the Snellen scale: 27/48 [56%] with scleral buckling *v* 49/61 [80%] with pneumatic retinopexy; P = 0.01). There were insufficient data to assess eyes with macula detachment for more than 14 days. The RCT found no significant difference in final visual outcome between eyes with successful RRD repair with initial scleral buckling surgery and eyes that failed with initial pneumatic retinopexy and required further surgery (P > 0.05; absolute data for final vision outcome in each group not reported). [40]

The second RCT (20 people with RRD and single retinal break or small group of breaks in phakic or pseudophakic eyes without severe PVR) found that a similar proportion of people had retinal re-attachment with scleral buckling and pneumatic retinopexy (8/10 [80%] with scleral buckling *v* 7/10 [70%] with retinopexy; significance not assessed). [41]

Harms: The first RCT found that more eyes with phakic RRD receiving scleral buckling than pneumatic retinopexy developed progressive lens opacities over 24 months (21/44 [47%] with scleral buckling *v* 10/53 [19%] with retinopexy; P value not reported). [40] Of phakic eyes, four times more eyes in the scleral buckling group required cataract surgery compared with the pneumatic retinopexy group (8/44 [18%] phakic eyes with scleral buckling *v* 2/53 [4%] with pneumatic retinopexy; P value not reported). Significantly more people receiving scleral buckling developed myopia (proportion of eyes with at least 1 dioptre of myopia: 65/95 [68%] with scleral buckling *v* 3/103 [3%] with pneumatic

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retinopexy; P = 0.0001). More people receiving scleral buckling than retinopexy developed persistent diplopia, PVR, macular pucker requiring surgery, and macular subretinal haemorrhage (persistent diplopia: 3/95 [3%] with scleral buckling *v* 0/103 [0%] with retinopexy; PVR: 5/95 [5%] with scleral buckling *v* 3/103 [3%] with retinopexy; macular pucker requiring surgery: 2/95 [2%] with scleral buckling *v* 0/103 [0%] with retinopexy; macular subretinal haemorrhage: 2/95 [2%] with scleral buckling *v* 0/103 [0%] with retinopexy; significance not assessed). [40]

The second RCT found that PVR with recurrent RRD occurred in 2/10 (20%) people receiving pneumatic retinopexy compared with 0/10 (0%) receiving scleral buckling (significance not assessed). One person in each group had redetachment because of new retinal holes. [41]

Comment:

Clinical guide:
RRD is repaired using techniques to close retinal breaks and relieve vitreoretinal traction. Although some RRDs could potentially be repaired by all three surgical techniques (scleral buckling, vitrectomy, or pneumatic retinopexy), this is not universally the case, and choice of surgery will depend on various factors, including: the number, location, and size of retinal breaks present; the ability of the patient to posture to position tamponade agents in the correct place; lens status; and surgeon experience, including access to equipment. Vitrectomy techniques require specialist training, and equipment is expensive; access is thus limited in resource-poor areas. In clinical practice in the UK, Europe, and North America, people with phakic eyes and localised RRD with small anterior holes or retinal dialysisare usually treated with scleral buckling, especially if there is no associated posterior vitreous detachment. Eyes in which a scleral buckle cannot be placed (e.g., thin sclera) and people with vitreous opacity obstructing the retinal view, giant retinal breaks, or very posterior retinal breaks are usually treated with vitrectomy. Pneumatic retinopexy is usually reserved for people with a single or localised group of breaks in the superior retina. People with pseudophakic RRD represent about 40% of all RRD that presents in clinical practice in the UK. Retinal breaks in these cases are often small and difficult to see because of the intraocular lens and capsule remnants restricting the fundal view. There is an increasing trend to treat these people with vitrectomy, which allows accurate break localisation with the technique of internal searching. Furthermore, with the eye already being pseudophakic, a common adverse effect of vitrectomy surgery — cataract formation — is avoided.

OPTION SCLERAL BUCKLING VERSUS PRIMARY VITRECTOMY

Re-attachment rate
Compared with primary vitrectomy in people with pseudophakic or aphakic rhegmatogenous retinal detachment (RRD

) Scleral buckling may be less effective at increasing re-attachment rates after one operation at 6 months to 1 year, but equally effective as primary vitrectomy at increasing final re-attachment rates (low-quality evidence).

Compared with primary vitrectomy in people with phakic RRD We don't know whether scleral buckling is more effective at increasing re-attachment rates after one operation at 6 months to 1 year (very low-quality evidence).

Visual acuity
Compared with primary vitrectomy We don't know whether scleral buckling is more effective at improving visual acuity at 6 months to 1 year in people with pseudophakic, aphakic, or phakic RRD (low-quality evidence).

Re-operation rate
Compared with primary vitrectomy in people with pseudophakic or aphakic RRD Scleral buckling and primary vitrectomy seem equally effective at reducing re-operation rate (moderate-quality evidence).

Adverse effects
Scleral buckling has been associated with higher rates of refractive change (usually a myopic shift in refraction), diplopia with extraocular muscle dysfunction, and subretinal haemorrhage compared with vitrectomy. Vitrectomy has been associated with higher rates of cataract formation in phakic eyes compared with scleral buckling.

For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits:

We found six RCTs comparing scleral buckling versus primary vitrectomy in people with phakic, pseudophakic, or aphakic rhegmatogenous retinal detachment (RRD) (see table 2, p 17). [42] [43] [44] [45] [46] [47]

Pseudophakic or aphakic RRD:
We found four RCTs in people with pseudophakic or aphakic RRD. [42] [43] [44] [45] One RCT comparing scleral buckling versus pars plana vitrectomy found that a significantly smaller proportion of people in the scleral buckling group had successful re-attachment after one operation compared

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with the vitrectomy group (length of follow-up not clear; see table 2, p 17). [42] However, the RCT found no significant difference between groups in final rate of re-attachment. One multicentre RCT (45 surgeons; 681 people; 681 eyes with RRD involving multiple large breaks between 1 and 2 clock hours in size and associated superior bullous RRD) compared scleral buckling versus pars plana vitrectomy with short-acting gas in two subgroups of RRD: pseudophakic or aphakic RRD (265 people; 265 eyes; in addition to other inclusion criteria; people with unseen breaks were included in this subgroup) and phakic RRD (416 people; 416 eyes). [45] In pseudophakic and aphakic RRD, the RCT found a significantly lower primary anatomical success rate (defined as retinal re-attachment without a retina-affecting re-operation) at 1 year with scleral buckling compared with vitrectomy. However, the RCT reported that additional scleral buckling was used (carried out at surgeon's discretion) at the time of primary surgery in 88/132 (67%) of the vitrectomy group. The RCT did not carry out separate analysis on the effects of combined surgery versus scleral buckling alone. Results should be interpreted with caution, as the true effects of vitrectomy alone are unclear. Two RCTs found no significant difference between groups in re-attachment rates at 6 months after one operation. [43] [44] The RCTs found similar final rates of re-attachment for the two surgeries.

One RCT found that visual acuity at 6 months was significantly worse post-scleral buckling compared with vitrectomy (see table 2, p 17). [43] One RCT found no significant difference between groups in visual acuity at 6 months for eyes with successful retinal re-attachment after one operation. [44] Another RCT and the subgroup analysis of pseudophakic or aphakic RRD found no significant difference between groups in visual acuity at 1 year. [42] [45]

One RCT found no significant difference between groups in the proportion of people requiring re-operation, although rate of re-operation was higher with scleral buckling. Some people required more than one additional operation (see table 2, p 17). [42]

Phakic RRD:
We found three RCTs in people with phakic RRD. [45] [46] [47] One RCT found no significant difference between surgeries in primary success rate (not defined) at 6 months (see table 2, p 17). [47] One RCT found the same rate of retinal re-attachment after one operation with scleral buckling and vitrectomy at 3 months. [46] The RCT defined an unsuccessful result as recurrence of retinal detachment within 3 months of surgery. The subgroup analysis of phakic RRD (416 people; 416 eyes) found no significant difference between scleral buckling and vitrectomy in primary anatomical success rate at 1 year. [45] The RCT reported that additional scleral buckling was used (carried out at surgeon's discretion) at the time of primary surgery in 105/207 (51%) of the vitrectomy group. The RCT did not carry out separate analysis on the effects of combined surgery versus scleral buckling alone. Results should be interpreted with caution, as the true effects of vitrectomy alone are unclear. The three RCTs found similar final rates of re-attachment for the two surgeries. [45] [46] [47]

One RCT found a significant improvement in visual acuity at 1 week and 1 month post-surgery in the scleral buckling group compared with the vitrectomy group (see table 2, p 17). [47] However, the RCT found no significant difference between groups in visual acuity at 6 months. The subgroup analysis of phakic RRD found a significantly greater improvement in visual acuity at 1 year after scleral buckling compared with vitrectomy. [45] One RCT found that a significantly smaller proportion of people achieved a best corrected visual acuity of 0.8 or more at 6 months post-surgery in the scleral buckling group compared with the vitrectomy group. [46]

Harms:

Pseudophakic or aphakic RRD:
One RCT found that the rate of retinal redetachment at 1 year was higher with scleral buckling compared with vitrectomy (see table 2, p 17). [45] However, one RCT found no significant difference between groups in rates of retinal redetachment over 6 months. [44] The RCT reported that retinal redetachment was caused by new breaks or PVR in a similar proportion of people in both groups (new breaks: 2% with scleral buckling *v* 3% with vitrectomy; PVR: 92% with scleral buckling *v* 95% with vitrectomy; absolute numbers presented graphically). One RCT found a larger proportion of people with new postoperative retinal breaks after scleral buckling compared with vitrectomy (see table 2, p 17). [42]

Two RCTs found a larger proportion of people in the scleral buckling group had proliferative vitreoretinopathy (PVR) compared with vitrectomy; [43] [45] one RCT found the difference between groups was not significant (see table 2, p 17). [45] One RCT found that vitrectomy was associated with higher rates of postoperative raised intraocular pressure. [43]

Two RCTs found similar rates of macular pucker with scleral buckling and vitrectomy (see table 2, p 17). [42] [44] Two RCTs found that a larger proportion of people developed diplopia in the scleral buckling group compared with the vitrectomy group; [42] [43] one RCT found the difference between groups was not significant. [42] One RCT found that more people receiving scleral buckling had

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choroidal haemorrhage or subretinal haemorrhage related to subretinal fluid drainage. [42] One RCT found that scleral buckling was associated with a significant increase in mean axial length, resulting in a myopic shift in refraction, compared with vitrectomy, [42] and another RCT found mild myopic shift from baseline in both groups. [43]

One RCT found that clinically apparent macular oedema was present in a similar proportion of people in each group. [44] However, extraocular muscle dysfunction was higher with scleral buckling than with vitrectomy. [44] One RCT found similar rates of cellophane maculopathy (macular epiretinal membrane of unspecified severity) in the groups. [43]

Phakic RRD:
Two RCTs found that a significantly larger proportion of people in the vitrectomy group developed cataracts, or their cataracts progressed, post-surgery compared with the scleral buckling group (see table 2, p 17). [45] [47] One RCT also found that a significantly smaller proportion of people in the scleral buckling group had surgery to remove cataracts compared with the vitrectomy group. [45]

Two RCTs found similar rates of postoperative PVR in the scleral buckling group and the vitrectomy group: [45] [46] one RCT found the difference between groups was not significant (see table 2, p 17). [45] One RCT found similar rates of retinal detachment at 1 year in the groups. [45]

Two RCTs found similar rates between scleral buckling and vitrectomy in elevation of intraocular pressure, [46] [47] and one RCT reported that intraocular pressure increase was managed successfully with medication. [47] One RCT found that a larger proportion of people in the scleral buckling group developed macular pucker compared with vitrectomy. [46] One RCT found that a similar proportion of people in each group developed epiretinal membrane. [47]

Comment: **Clinical guide:**
See scleral buckling versus pneumatic retinopexy, p 5 .

QUESTION **What are the effects of interventions to treat proliferative vitreoretinopathy occurring as a complication of retinal detachment or previous treatment for retinal detachment?**

OPTION **DIFFERENT SUBSTANCES FOR TAMPONADE IN PEOPLE RECEIVING VITRECTOMY FOR PROLIFERATIVE VITREORETINOPATHY**

Re-attachment rate
Silicone oil tamponade compared with long-acting gas tamponade Silicone oil tamponade and long-acting gas tamponade seem equally effective at increasing re-attachment rates in people with severe proliferative vitreoretinopathy undergoing vitrectomy for rhegmatogenous retinal detachment (RRD) (moderate-quality evidence).

Silicone oil tamponade compared with short-acting gas tamponade Silicone oil tamponade seems more effective at increasing re-attachment rates at 6 months in people with severe proliferative vitreoretinopathy undergoing vitrectomy for RRD (moderate-quality evidence).

Visual acuity
Silicone oil tamponade compared with long-acting gas tamponade Silicone oil tamponade and long-acting gas tamponade seem equally effective at improving visual acuity in people with severe proliferative vitreoretinopathy undergoing vitrectomy for RRD (moderate-quality evidence).

Silicone oil tamponade compared with short-acting gas tamponade Silicone oil tamponade seems more effective at improving visual acuity at 6 months in people with severe proliferative vitreoretinopathy undergoing vitrectomy for RRD (moderate-quality evidence).

Adverse effects
Silicone oil may cause less hypotony compared with long-acting gas, especially in people with severe anterior proliferative vitreoretinopathy.

For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits: We found two RCTs comparing silicone oil tamponade versus long-acting gas (C_3F_8, perfluoropropane) [48] or short-acting gas (SF_6, sulphur hexafluoride) [49] in people with severe proliferative vitreoretinopathy (PVR) receiving vitrectomy. Both RCTs were conducted simultaneously by the same group.

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Silicone oil tamponade versus long-acting gas tamponade:
We found one RCT (265 eyes undergoing vitrectomy for RRD with severe PVR) comparing silicone oil versus long-acting gas (C_3F_8) in two groups (131 eyes undergoing initial vitrectomy; 134 eyes undergoing a second vitrectomy after previous failed vitrectomy surgery). [48] The authors performed an intention-to-treat analysis over 36 months using data from the last available examination; data were available for 100% of eyes at 3 months, 91% to 95% of eyes at 12 months, and 50% of eyes at 36 months. In eyes undergoing initial vitrectomy (131 eyes), there was no significant difference between silicone oil and C_3F_8 in rates of retinal re-attachment and visual acuity at the last examination (re-attachment: 38/59 [64%] with silicone oil *v* 45/62 [73%] with C_3F_8; P = 0.33; proportion who achieved a visual acuity of 5/200 or better: 29/64 [45%] with silicone oil *v* 29/67 [43%] with C_3F_8; P = 0.82). In eyes undergoing a second vitrectomy (134 eyes), there was also no significant difference between silicone oil and C_3F_8 in visual acuity at the last examination (proportion who achieved a visual acuity of 5/200 or better: 21/63 [33%] with silicone oil *v* 27/71 [38%] with C_3F_8; P = 0.57). However, rates of retinal re-attachment were lower with silicone oil (37/61 [61%] with silicone oil *v* 50/68 [74%] with C_3F_8; significance not assessed). [48]

Silicone oil tamponade versus short-acting gas tamponade:
We found one RCT (101 eyes undergoing initial vitrectomy for RRD with severe PVR), which found that silicone oil significantly increased re-attachment rates and significantly improved visual acuity at 6 months postoperatively compared with SF_6 (re-attachment: 31/51 [61%] with silicone oil *v* 23/46 [50%] with SF_6; P < 0.05; proportion of eyes with 5/200 or better on the Snellen scale: 31/51 [61%] with silicone oil *v* 15/46 [33%] with SF_6; P < 0.05). [49] The RCT also found that silicone oil significantly increased the proportion of eyes with subtotal retinal attachment but successful macular attachment at 6 months postoperatively compared with SF_6 (10/51 [20%] with silicone oil *v* 5/46 [11%] with SF_6; P < 0.05).

Harms:

Silicone oil tamponade versus long-acting gas tamponade:
The RCT found no significant difference between silicone oil and C_3F_8 in rates of keratopathy (30% with silicone oil *v* 33% with C_3F_8; P = 0.70; absolute numbers not reported). [48] Data from the RCT were also reported in additional studies. [50] [51] One analysis combining data in people receiving initial or second vitrectomy found that silicone oil significantly increased the proportion of eyes with chronically elevated intraocular pressure (raised intraocular pressure to >25 mmHg on 2 or more consecutive visits over 6 months) compared with C_3F_8 (9/120 [8%] with silicone oil *v* 2/121 [2%] with C_3F_8; P < 0.05). [50] The analysis also found that chronic hypotony (intraocular pressure <5 mmHg on 2 or more consecutive or 3 visits over 6 months) was significantly more common in people receiving C_3F_8 than in those receiving silicone oil (21/120 [18%] of eyes with silicone oil *v* 37/121 [31%] of eyes with C_3F_8; P < 0.05). Another analysis of data from the RCT found no significant difference between silicone oil and C_3F_8 in rates of macular pucker (12% with silicone oil *v* 19% with C_3F_8; P = 0.15; absolute numbers not reported). [51]

Silicone oil tamponade versus short-acting gas tamponade:
The RCT found no significant difference between silicone oil and SF_6 in rates of hypotony at 24 months, although the proportion of people with hypotony was larger with SF_6 (5/47 [11%] with silicone oil *v* 7/40 [18%] with SF_6; P = 0.35). [49] The RCT also found that a significantly larger proportion of people in the SF_6 group had keratopathy compared with the silicone oil group (19/40 [48%] with SF_6 *v* 10/47 [21%] with silicone oil; P = 0.01). Rates of both hypotony and keratopathy were higher in eyes that had not achieved macular detachment, although differences between groups were not significant (reported as not significant; P value not reported).

Comment:

Clinical guide:
In people with RRD and advanced PVR, the PVR-associated membranes can sometimes prevent closure of retinal breaks when using either scleral buckling surgery or pneumatic retinopexy. In this situation, vitrectomy surgery may be indicated to allow the surgical removal of these membranes, and hence allow retinal re-attachment. Tamponade of retinal breaks postoperatively can be achieved with long-acting gas or silicone oil. The advantages of silicone oil include its transparency, which allows some vision when walking immediately after surgery. Silicone oil also facilitates postoperative laser photocoagulation, which is more difficult through a gas bubble. Being non-dissolvable, silicone oil also provides long-term tamponade over a large area of the retina in contrast to gas. Disadvantages include the need to remove the oil at a second operation to avoid complications. Oil can be left *in situ* to provide continuous retinal tamponade and avoid retinal detachment, but this carries the risk of long-term complications. Leaving oil *in situ* may be necessary in conditions such as: CMV-associated retinal detachment with multiple atrophic breaks in areas previously affected by retinitis; cases with persistent unrelieved retinal traction; or cases at high risk of hypotony after oil removal.

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OPTION CORTICOSTEROIDS DURING VITRECTOMY SURGERY FOR PROLIFERATIVE VITREORETINOPATHY

New

Re-attachment rate
Compared with no corticosteroid Adding intravitreal triamcinolone acetonide to the vitreous cavity (direct injection into silicone oil) at the completion of vitrectomy surgery seems no more effective at improving retinal re-attachment rates (after 1 operation and final rate) at 6 months in people with rhegmatogenous retinal detachment and grade C proliferative vitreoretinopathy (moderate-quality evidence).

Visual acuity
Compared with no corticosteroid Adding intravitreal triamcinolone acetonide to the vitreous cavity (direct injection into silicone oil) at the completion of vitrectomy surgery seems no more effective at improving visual acuity at 6 months in people with grade C proliferative vitreoretinopathy (moderate-quality evidence).

For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits:

Corticosteroids versus no corticosteroid/placebo/standard care:
We found one RCT (75 people; 75 eyes with rhegmatogenous retinal detachment [RRD] and grade C proliferative vitreoretinopathy [PVR]) comparing adjunctive triamcinolone acetonide 4 mg after vitrectomy with silicone oil tamponade versus no adjunctive treatment. [52] Triamcinolone acetonide was injected into the silicone-filled vitreous cavity on completion of surgery. The RCT found no significant difference at 6 months between adjunctive triamcinolone acetonide and no adjunctive treatment in retinal re-attachment rate after one operation (32/38 [84%] with triamcinolone acetonide *v* 29/37 [78%] with no triamcinolone acetonide; P = 0.5), final re-attachment rate (with or without re-operation) at 6 months (35/38 [92.1%] with triamcinolone acetonide *v* 34/37 [91.9%] with no triamcinolone acetonide; P = 0.97), or visual acuity (mean best corrected visual acuity [logMAR units]: 1.2 with triamcinolone acetonide *v* 1.4 with no triamcinolone acetonide; P = 0.21).

Harms:

Corticosteroids versus no corticosteroid/placebo/standard care:
The RCT found no significant difference at 6 months between adjunctive triamcinolone acetonide 4 mg and no adjunctive treatment in intraocular pressure (14.7 mmHg with triamcinolone acetonide *v* 16.4 mmHg with no triamcinolone acetonide; P = 0.25), recurrence of PVR (11/38 [29%] with triamcinolone acetonide *v* 11/37 [30%] with no triamcinolone acetonide; P = 0.94), or macular pucker (8/38 [21%] with triamcinolone acetonide *v* 13/37 [35%] with no triamcinolone acetonide; P = 0.2). [52]

Comment:

Clinical guide:
The antiproliferative and anti-inflammatory properties of corticosteroids are thought to promote repair in RRD. Topical corticosteroids are routinely given by most surgeons post-surgery to correct RRD, and some surgeons give periocular and systemic corticosteroids in cases of RRD with PVR. Triamcinolone acetate is a slow-release corticosteroid preparation, and injection into the vitreous cavity provides a locally higher corticosteroid concentration than can be achieved by systemic or topical administration. Although the small RCT reported here found no benefit associated with using corticosteroids in eyes with RRD and established PVR, [52] corticosteroids may still have a role in other conditions, such as in eyes with inflammation, or after trauma or previous surgery.

OPTION DAUNORUBICIN DURING VITRECTOMY SURGERY FOR PROLIFERATIVE VITREORETINOPATHY

New

Re-attachment rate
Compared with no daunorubicin Infusing daunorubicin intravitreally for 10 minutes during vitrectomy surgery seems no more effective at improving retinal re-attachment rate (after 1 operation) at 3 to 6 months in patients with rhegmatogenous retinal detachment (RRD) and grade C and D proliferative vitreoretinopathy (moderate-quality evidence).

Visual acuity
Compared with no daunorubicin Infusing daunorubicin intravitreally for 10 minutes during vitrectomy surgery seems no more effective at improving visual acuity at 3 to 6 months in people with RRD and grade C and D proliferative vitreoretinopathy (moderate-quality evidence).

Re-operation rate
Compared with no daunorubicin Infusing daunorubicin intravitreally for 10 minutes during vitrectomy surgery is more effective at reducing the requirement for further vitreoretinal surgery at 1 year in people with RRD and grade C2 proliferative vitreoretinopathy (high-quality evidence).

For GRADE evaluation of interventions for retinal detachment, see table , p 21 .

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Benefits:

Daunorubicin versus no daunorubicin/placebo/standard care:
We found two RCTs comparing the use of daunorubicin intraoperatively during vitrectomy surgery for rhegmatogenous retinal detachment (RRD) and proliferative vitreoretinopathy (PVR) versus no adjunctive treatment. [53] [54] In the first RCT (286 people; 286 eyes with RRD and PVR of grade C2 or more; multicentre RCT; 24 surgeons), if the surgeon determined that the retina could be successfully re-attached, the vitreous cavity was perfused with daunorubicin (7.5 micrograms/mL in balanced saline solution) for 10 minutes. [53] Before silicone oil exchange, daunorubicin was exchanged with balanced saline, perfluorocarbon liquid, or air. The RCT found that a significantly smaller proportion of people in the daunorubicin group required further vitreoretinal surgery within 1 year of initial surgery compared with the group not receiving daunorubicin (50/145 [34%] with daunorubicin *v* 65/141 [46%] with no daunorubicin; P = 0.005). However, the RCT found no significant difference between groups in retinal re-attachment rate (after 1 operation) at 6 months, although the proportion of eyes with retinal re-attachment was larger with daunorubicin (89/142 [63%] with daunorubicin *v* 73/135 [54%] with no daunorubicin; OR 1.43, 95% CI 0.88 to 2.30; P = 0.07), or in overall re-attachment rate (with or without re-operation) at 1 year (105/131 [80%] with daunorubicin *v* 103/126 [82%] with no daunorubicin: reported as not significant; P value not reported). There was also no significant difference between groups at 6 months in the proportion of people with visual acuity rated as either improved, unchanged, or deteriorated (improved: 113/136 [83%] with daunorubicin *v* 98/128 [77%] with no daunorubicin: unchanged: 17/136 [13%] with daunorubicin *v* 25/128 [20%] with no daunorubicin; deteriorated: 6/136 [4.4%] with daunorubicin *v* 5/128 [3.9%] with no daunorubicin; P = 0.17 for between-group comparison). Improvement in visual acuity was defined as a positive difference between preoperative logMAR score and score at 6 months; unchanged as no difference between scores; and deterioration as a negative difference between the two scores.

In the second RCT (30 people; 30 eyes with RRD and grade D1 PVR or more), daunorubicin (5 micrograms in 0.1 mL balanced saline solution) was injected into the vitreous cavity and left for 10 minutes, after which time it was flushed out of the vitreous cavity and silicone oil exchange was carried out. [54] The RCT found no significant difference between daunorubicin and no daunorubicin in rate of retinal re-attachment at 3 months (13/15 [87%] with daunorubicin *v* 10/15 [67%] with no daunorubicin; reported as not significant; P value not reported), or in the proportion of people with an improvement in visual acuity (14/15 [93%] with daunorubicin *v* 12/15 [80%] with no daunorubicin; reported as not significant; P value not reported).

Harms:

Daunorubicin versus no daunorubicin/placebo/standard care:
The RCTs gave no information on adverse effects associated with daunorubicin. [53] [54] The authors of both RCTs reported no treatment-related adverse effects with daunorubicin, and no data on other possible adverse effects associated with its use were given.

Comment:

Clinical guide:
Daunorubicin acts by inhibiting both cell proliferation and cell migration. It can be infused into the vitreous cavity for short periods during vitrectomy surgery without apparent adverse effects. However, it is unclear whether use of daunorubicin as an adjunctive treatment confers benefits in eyes with RRD and established PVR.

OPTION FLUOROURACIL PLUS HEPARIN DURING VITRECTOMY SURGERY FOR PROLIFERATIVE VITREORETINOPATHY

Re-attachment rate
Compared with placebo Adding fluorouracil plus low-molecular-weight heparin to the intraocular infusion may be no more effective at increasing surgery success rates (re-attaching with removal of silicone oil without further operations and final re-attachment rate) in people with grade C anterior or posterior proliferative vitreoretinopathy (low-quality evidence).

Visual acuity
Compared with placebo Adding fluorouracil plus low-molecular-weight heparin to the intraocular infusion seems no more effective at improving visual acuity in people with grade C anterior or posterior proliferative vitreoretinopathy (moderate-quality evidence).

For GRADE evaluation of interventions for retinal detachment, see table, p 21 .

Benefits:

We found one RCT (157 people with grade C anterior or posterior proliferative vitreoretinopathy [PVR]) comparing adding perioperative fluorouracil plus low-molecular-weight heparin to the intraocular infusion versus adding placebo to the intraocular infusion in people having vitrectomy with silicone oil tamponade. [55] Successful surgery was defined as re-attachment with removal of silicone oil without further operations. At 6 months, the RCT found no significant difference between fluorouracil plus heparin and placebo in the proportion of people with successful surgery (39/70 [56%]

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with fluorouracil plus heparin *v* 40/78 [51%] with placebo; P = 0.589), or in the overall complete retinal re-attachment rate with or without re-operation (56/67 [84%] with fluorouracil plus heparin *v* 65/77 [84%] with placebo; reported as not significant; P value not reported). The RCT also found no significant difference in mean visual acuity between fluorouracil plus heparin and placebo (logMAR visual acuity scale: 1.8 with fluorouracil plus heparin *v* 1.4 with placebo; P = 0.126).

Harms: Data on complications apparent at 12 months' follow-up were reported on 98/157 (62%) participants. [55] There was no significant difference in the proportion of people with glaucoma, hypotony, or keratopathy (glaucoma: 0 with fluorouracil plus heparin *v* 3 with placebo; hypotony: 9 with fluorouracil plus heparin *v* 7 with placebo; keratopathy: 5 with fluorouracil plus heparin *v* 2 with placebo) or in the proportion who required cataract extraction (21 with fluorouracil plus heparin *v* 29 with placebo; unclear whether figures represent percentages or absolute number of people with adverse effect in each group; difference between groups reported as not significant; P values not reported). The RCT found that fewer people receiving fluorouracil plus heparin had macular pucker at 6 months, although the difference between groups was not significant (4/66 [6%] with fluorouracil plus heparin *v* 13/77 [17%] with placebo; P = 0.068).

Comment: **Clinical guide:**
Despite evidence suggesting that 5-fluorouracil plus heparin can prevent PVR in people with high-risk features for PVR undergoing vitrectomy surgery for rhegmatogenous retinal detachment, [56] it is unclear whether fluorouracil plus heparin is effective at improving retinal re-attachment rates in people with established PVR. The prevention of PVR will be addressed in full in future updates of this review.

GLOSSARY

Classification of PVR Grade A PVR denotes vitreous haze and pigment clumping (of RPE cells) in the vitreous cavity (although this grade is rarely used). Grade B PVR shows areas of surface retinal wrinkling with rolled edges to retinal tears. Grade C PVR consists of fixed full thickness retinal folds involving 1-3 quadrants: Grade C1–C3. Grade D was classified as a total RRD with either a wide (D1), narrow (D2), or closed (D3) funnel configuration because of fixed retinal folds. [34] Grade D was removed from the 1991 classification update, [35] and Grade C was divided into anterior and posterior PVR, which is then subdivided based on the number of hours involved (CA1–12 and CP1–12), and on type of fibrosis and contracture present (focal, diffuse, or subretinal, and anteriorly, circumferential, and/or anterior displacement [anterior loop traction]).
Aphakic An aphakic eye has neither a natural crystalline lens nor an artificial lens.
Macular pucker refers to the distorted anatomical appearance of the macular retina caused by localised epiretinal fibrotic membrane formation. It can result in distorted and reduced central vision.
Pars plana is the inner surface of the eye between the ciliary processes and the ora serrata; the anterior termination of the retina inserts into the pars plana at the ora serrata.
Phakic A phakic eye has an intact natural crystalline lens.
Pneumatic retinopexy A small volume of gas, primarily expansile gas, is injected into the vitreous cavity and used to close the retinal break(s). No attempt is made to relieve vitreoretinal traction. Once closure of retinal breaks is achieved, the physiological retinal pigment epithelium pump removes subretinal fluid resulting in retinal reattachment. Before or after gas injection, laser or cryotherapy is usually applied to the retinal breaks (retinopexy) to create a permanent choroidoretinal adhesion.
Proliferative vitreoretinopathy (PVR) after a retinal detachment may occur either spontaneously before surgery or after treatment. PVR refers to the growth of avascular fibrocellular membranes within the vitreous cavity and on the front and back surfaces of the retina. These membranes, which are essentially scar tissues, occur in the mildest form as fine fibrous membranes on the retinal surface without visible retinal distortion or merely rolling of the edges of retinal breaks. In more severe forms, the membranes cause fixed retinal folds, preventing closure of retinal breaks and exerting traction on the retina. Retinal folds may also result in recurrence of retinal detachment, even after an initially successful retinal detachment procedure, because of spontaneous reopening of otherwise successfully treated retinal breaks, or because of the development of new retinal breaks. Epiretinal membranes on the surface of the macula causing macular pucker and ocular hypotony secondary to PVR involving the ciliary body may also occur. PVR may result in disappointing visual results. [58]
Pseudophakic A pseudophakic eye has had the natural lens removed and replaced with an artificial intraocular lens implant.
Retinal dialysis is a separation of the retina where it inserts into the pars plana at the ora serrata.
Retinal operculum This is a separated flap of retina avulsed from the retinal surface by vitreoretinal separation, leaving a retinal hole.
Retinal-flap tear This is a tear in the retina associated with local vitreoretinal traction, separation, or both; the flap of the tear remains attached to the vitreous and connected by its base to the anterior edge of the retinal tear.
Scleral buckling surgery A buckling element or explant, usually made of either solid silicone or silicone sponge, is sutured to the sclera externally to indent the sclera and underlying retinal pigment epithelium towards the detached retina at the site of the retinal break(s), to close the break and relieve vitreoretinal traction. Buckles can be either segmental or encircling. Once closure of retinal breaks is achieved, the physiological retinal pigment epithelium pump removes subretinal fluid resulting in retinal reattachment. This process can be assisted by subretinal fluid drainage

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at the time of surgery, which also allows break closure if subretinal fluid is deep. During surgery, laser or cryotherapy is usually applied to the retinal breaks (retinopexy) to create a permanent choroidoretinal adhesion. [59]

Silicone oil tamponade is used in vitrectomy as an alternative to gas. Silicone oil is also now available in a heavier-than-water preparation, allowing inferior retinal tamponade without head-down posturing.

Stickler syndrome (hereditary arthro-ophthalmopathy) is a hereditary disease of type 2 collagen resulting in abnormal vitreous, myopia, and a variable degree of orofacial abnormalities, deafness, and arthropathies.

Cryotherapy (cryopexy) is the transcleral application of cryotherapy to retinal breaks or predisposing rhegmatogenous retinal detachment lesions using a cryotherapy probe. The head of the probe is positioned on the area of sclera overlying the retinal area to be treated using visual control by means of indirect ophthalmoscopy and indentation of the sclera. Overlapping areas are frozen until the whole lesion is treated creating an area of full-thickness chorioretinal adhesion within 7 to 10 days of treatment application. Cryotherapy can be carried out under local anaesthetic. If the retinal lesions to be treated are located on the posterior retinal surface, the conjunctiva is opened to allow probe placement on the corresponding posterior area of sclera.

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Laser photocoagulation refers to the transpupillary application of laser (usually argon laser), to retinal breaks or predisposing rhegmatogenous retinal detachment lesions. It can be delivered either by a slit lamp-mounted laser system or by using a laser connected to an indirect ophthalmoscope. Contiguous laser burns are placed around the lesion in 2 to 3 rows leading to areas of full-thickness chorioretinal adhesion within 2 to 3 days of treatment. Laser photocoagulation can be carried out under local anaesthetic. Because it is delivered through the pupil, posterior retinal lesions can be treated without the need to open the conjunctiva.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Posterior vitreous detachment (PVD) is the separation of the vitreous gel from its posterior attachment to the retina. PVD is associated with aging of the vitreous characterised by liquefaction of the vitreous gel itself. Liquefaction occurs at an earlier age in myopic eyes than in emmetropic and hypermetropic eyes, and can be accelerated by inflammation caused by surgery, trauma, or uveitis. Vitreous liquefaction leads to vitreous gel instability, which triggers PVD. PVD is present in autopsy studies in less than 10% of people aged under 50 years, in at least one eye in 27% of people aged 60 to 65 years, and in 63% of people aged over 70 years. It usually occurs as an acute event with rapid evolution of vitreoretinal separation from the posterior to anterior retina. [57]

Very low-quality evidence Any estimate of effect is very uncertain.

Vitrectomy The vitreous is removed internally using a cutting aspirating instrument relieving vitreoretinal traction directly. A tamponade agent, usually gas or silicone oil, is used to close the break(s). Closure is assisted by postoperative positioning to place the tamponade bubble against the break(s) in an optimum way. Gases can be short- (SF_6), medium- (C_2F_6), or long-acting (C_3F_8), and last a variable period of time depending on concentration and gas fill before being absorbed. Once closure of retinal breaks is achieved, the physiological retinal pigment epithelium pump removes subretinal fluid resulting in retinal reattachment. This process can be assisted by subretinal fluid drainage at the time of surgery. During surgery, laser or cryotherapy is usually applied to the retinal breaks (retinopexy) to create a permanent choroidoretinal adhesion. [60]

SUBSTANTIVE CHANGES

Corticosteroid injection during vitrectomy surgery New option added for which we identified one RCT. [52] The RCT found no significant difference between adjunctive triamcinolone acetonide and no adjunctive treatment in retinal re-attachment rate or visual acuity at 6 months. Categorised as Unknown effectiveness.

Daunorubicin infusion during vitrectomy surgery New option added for which we found two RCTs. [53] [54] Both RCTs found no significant difference between adding daunorubicin and not adding daunorubicin in rate of retinal re-attachment and in visual acuity. [53] [54] One RCT found that a smaller proportion of people in the daunorubicin group required further vitreoretinal surgery within 1 year after initial surgery compared with the group not receiving daunorubicin. [53] Categorised as Unknown effectiveness.

Scleral buckling versus primary vitrectomy Condition restructured and three RCTs added. [45] [46] [47] One large RCT analysed results separately for pseudophakic plus aphakic rhegmatogenous retinal detachment (RRD) and for phakic RRD. [45] In pseudophakic and aphakic RRD, the RCT found a lower primary anatomical success rate at 1 year with scleral buckling compared with vitrectomy, but found no significant difference between groups in visual acuity. However, the RCT reported that additional scleral buckling was used (carried out at surgeon's discretion) at the time of primary surgery in over half of the vitrectomy group. In people with phakic RRD, the subgroup analysis [45] and two other RCTs found similar rates of retinal re-attachment for scleral buckling and vitrectomy. [46] [47] Conflicting results were reported for improvement in visual acuity in people with phakic RRD. [45] [46] [47] Although there is consensus that both techniques are effective in the treatment of RRD, there is insufficient evidence to assess the effects of scleral buckling versus those of primary vitrectomy. Categorisation changed from Likely to be beneficial to Unknown effectiveness.

Scleral buckling versus pneumatic retinopexy Condition restructured. Although there is consensus that both techniques are effective in the treatment of rhegmatogenous retinal detachment, there is insufficient evidence to assess the effects of scleral buckling against those of pneumatic retinopexy. Categorisation changed from Likely to be beneficial to Unknown effectiveness.

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TABLE 1 **Visual acuity scales used in RCTs.**

LogMAR	Snellen (metres)	Snellen (feet)	Snellen (decimal)	
0	6/6	20/20	1	
0.1	6/7.5	20/25	0.8	
0.3	6/12	20/40	0.5	
0.4	6/15	20/50	0.4	
0.6	6/24	20/80	0.25	
1	6/60	20/200	0.1	
1.2	6/96	20/320	0.06	
1.3	6/120	20/400	0.05	
1.6	6/240 (often recorded as 1.5/60)	20/800 (often recorded as 5/200)	0.03	
2	6/600	20/2000	0.01	About equivalent to count fingers vision at 2 feet
3	6/6000	20/20,000	0.001	About equivalent to hand movements vision at 2 feet

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TABLE 2 **Scleral buckling versus primary vitrectomy in people with rhegmatogenous retinal detachment.** [42] [43] [44] [45] [46] [47]

Population	Outcome	Result	Statistical assessment
Pseudophakic or aphakic RRD			
150 people, 150 eyes, with pseudophakic RRD [42] (pars plana vitrectomy with infusion of short-acting gas)	Re-attachment rate after 1 operation (length of follow-up not clear)	62/75 (83%) with scleral buckling *v* 71/75 (94%) with vitrectomy	P = 0.037
	Final re-attachment rate (includes those who required more than 1 operation)	71/75 (94%) with scleral buckling *v* 74/75 (99%) with vitrectomy	P = 0.37
	Re-operation rate	13/75 (17%) with scleral buckling *v* 4/75 (5%) with vitrectomy	P = 0.38
	Visual acuity at 1 year	**Mean visual acuity on the logMAR scale:** 0.40 with scleral buckling *v* 0.33 with vitrectomy	P = 0.26
		Proportion of people with vision of 20/40 or better on Snellen scale: 49/75 (65%) with scleral buckling *v* 54/75 (72%) with vitrectomy	Significance not assessed
	Adverse effects	**Postoperative retinal breaks:** 5/75 (7%) with scleral buckling *v* 1/75 (1%) with vitrectomy	Significance not assessed
		Macular pucker: 3/75 (4%) with scleral buckling *v* 2/75 (3%) with vitrectomy	P = 0.99
		Diplopia: 3/75 (4%) with scleral buckling *v* 0/75 (0%) with vitrectomy	P = 0.25
		Choroidal haemorrhage or subretinal haemorrhage related to subretinal fluid drainage: 8/75 (11%) with scleral buckling *v* 0/75 (0%) with vitrectomy	Significance not assessed
		Mean axial length: 0.95 mm with scleral buckling *v* 0.1 mm with vitrectomy	P = 0.0001
50 people, 50 eyes, with pseudophakic RRD [43] (pars plana vitrectomy with infusion of long-acting gas)	Re-attachment rate at 6 months (after 1 operation)	19/25 (76%) with scleral buckling *v* 21/25 (84%) with vitrectomy	P = 0.48
	Final re-attachment rate (includes those who required more than 1 operation)	25/25 (100%) with scleral buckling *v* 25/25 (100%) with vitrectomy	Significance not assessed
	Visual acuity at 6 months	**Mean best corrected Snellen visual acuity (BCVA) expressed as a decimal:** 0.19 with scleral buckling *v* 0.28 with vitrectomy	P = 0.034
	Adverse effects	**Proliferative vitreoretinopathy:** 5/25 (20%) with scleral buckle *v* 1/25 (4%) with vitrectomy	Significance not assessed
		Raised intraocular pressure: 1/25 (4%) with scleral buckling *v* 8/25 (32%) with vitrectomy	Significance not assessed
		Diplopia: 1/25 (4%) with scleral buckling *v* 0/25 (0%) with vitrectomy	Significance not assessed
		Cellophane maculopathy: 4/25 (16%) with scleral buckling *v* 3/25 (12%) with vitrectomy	Significance not assessed

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Population	Outcome	Result	Statistical assessment
		Myopic shift (mean change in refractive error): –1.38 dioptres of myopia with scleral buckling *v* –0.85 dioptres of myopia with vitrectomy	Significance not assessed
225 people, 225 eyes, with pseudophakic or aphakic RRD [44] (pars plana vitrectomy with infusion of short-acting gas)	Re-attachment rate at 6 months (after 1 operation)	86/126 (68%) with scleral buckling *v* 62/99 (63%) with vitrectomy	OR 1.28, 95% CI 0.73 to 2.24
	Final re-attachment rate (includes those who required more than 1 operation)	85% with scleral buckling *v* 92% with vitrectomy (absolute numbers not reported)	Significance not assessed
	Visual acuity at 6 months (eyes with successful retinal re-attachment)	**Proportion of eyes with a visual acuity of 20/40 or better on the Snellen scale:** 11/86 (13%) with scleral buckling *v* 7/62 (11%) with vitrectomy	P = 0.78
	Adverse effects	**Retinal redetachment:** 40/126 (32%) with scleral buckling *v* 37/99 (37%) with vitrectomy	Reported as not significant P value not reported
		Macular pucker: 22% with scleral buckling *v* 22% with vitrectomy (absolute numbers not reported)	Significance not assessed
		Macular oedema: 6% with scleral buckling *v* 10% with vitrectomy (absolute numbers not reported)	Significance not assessed
		Extraocular muscle dysfunction: 4% with scleral buckling group *v* 0% with vitrectomy (absolute numbers not reported)	Significance not assessed
265 people, 265 eyes with pseudophakic or aphakic RRD (in addition to other inclusion criteria, people with unseen breaks were included in this subgroup) [45] (pars plana vitrectomy with infusion of short-acting gas)	Primary anatomical success rate (defined as retinal re-attachment without a retina-affecting re-operation) at 1 year	71/133 (53%) with scleral buckling *v* 95/132 (72%) with vitrectomy	OR 0.44, 95% CI 0.26 to 0.75 P = 0.002
	Final anatomical success rate (retinal re-attachment at final follow-up visit; any type of re-operation allowed)	124/133 (93%) with scleral buckling *v* 126/132 (96%) with vitrectomy	OR 0.62, 95% CI 0.21 to 1.86 P = 0.9686
	Visual acuity at 1 year	**Mean BCVA (logMAR units):** 0.46 with scleral buckling *v* 0.38 with vitrectomy	Treatment difference +0.09, 95% CI –0.02 to +0.2 P = 0.1033
	Adverse effects	**Proliferative vitreoretinopathy:** 30/133 (23%) with scleral buckling *v* 20/132 (15%) with vitrectomy	P = 0.1073
		Retinal redetachment at 1 year: 53/133 (40%) with scleral buckling *v* 27/132 (20%) with vitrectomy	Significance not assessed
Phakic RRD			
416 people, 416 eyes with phakic RRD [45] (pars plana vitrectomy with infusion of short-acting gas)	Primary anatomical success rate at 1 year	133/209 (63.6%) with scleral buckling *v* 132/207 (63.8%) with vitrectomy	OR 1.01, 95% CI 0.68 to 1.49 P = 0.97

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Population	Outcome	Result	Statistical assessment
	Final anatomical success rate (retinal re-attachment at final follow-up visit; any type of re-operation allowed)	202/209 (96.7%) with scleral buckling *v* 200/207 (96.6%) with vitrectomy	OR 1.07, 95% CI 0.35 to 3.25 P = 0.90
	Visual acuity at 1 year	**Mean BCVA (logMAR units):** 0.33 with scleral buckling *v* 0.48 with vitrectomy	Treatment difference 0.15, 95% CI 0.00 to 0.29 P = 0.0005
	Adverse effects	**Development or progression of cataracts (defined an increase of 1 point or more on the LOCS III scale):** 96/209 (46%) with scleral buckling *v* 160/207 (77%) with vitrectomy	Treatment difference 31.4%, 95% CI 22.5% to 40.2% P < 0.0001
		Surgery to remove cataracts: 43/209 (21%) with scleral buckling *v* 120/207 (58%) with vitrectomy	Treatment difference 37.4%, 95% CI 28.7% to 46.1%
		Proliferative vitreoretinopathy: 26/209 (12%) with scleral buckling *v* 34/207 (16%) with vitrectomy	P = 0.2812
		Retinal redetachment at 1 year: 55/209 (26%) with scleral buckling *v* 52/207 (25%) with vitrectomy	Significance not assessed
46 people aged 50 years and over, 46 eyes with phakic RRD involving the macula with recent posterior vitreous detachment and equatorial tears [46] (pars plana vitrectomy with infusion short-acting gas combined with phacoemulsification surgery)	Re-attachment at 6 months (after 1 operation)	21/23 (91%) with scleral buckling *v* 21/23 (91%) with vitrectomy	Significance not assessed
	Final re-attachment rate	23/23 (100%) with scleral buckling *v* 23/23 (100%) with vitrectomy	Significance not assessed
	Visual acuity at 6 months	**BCVA of 0.8 or more:** 1/23 (4%) with scleral buckling *v* 12/23 (52%) with vitrectomy	P = 0.001
		Mean BCVA (logMAR): Greater improvement in BCVA with vitrectomy than with scleral buckling (absolute numbers not reported: data presented graphically)	P = 0.005
	Adverse effects	**Elevation of intraocular pressure (>30 mmHg):** 3/23 (13%) with scleral buckling *v* 4/23 (17%) with vitrectomy	Significance not assessed
		Macular pucker: 4/23 (17%) with scleral buckling *v* 0/23 (0%) with vitrectomy	Significance not assessed
		Proliferative vitreoretinopathy: 1/23 (4%) with scleral buckling *v* 2/23 (9%) with vitrectomy	Significance not assessed
61 people, 61 eyes, with phakic RRD without PVR of grade C or above [47] (pars plana vitrectomy with infusion of long-acting gas plus 360 laser to peripheral retina)	Primary success rate at 6 months	25/31 (81%) with scleral buckling *v* 24/30 (80%) with vitrectomy	P = 0.213
	Final anatomical success rate at 6 months	31/31 (100%) with scleral buckling *v* 30/30 (100%) with vitrectomy	Significance not assessed
	Visual acuity at 1 week	**Mean BCVA (logMAR units):** 0.84 with scleral buckling *v* 2.0 with vitrectomy	P = 0*

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Population	Outcome	Result	Statistical assessment
	Visual acuity at 1 month	**Mean BCVA (logMAR units):** 0.699 with scleral buckling *v* 1.14 with vitrectomy	P = 0.006
	Visual acuity at 3 months	**Mean BCVA (logMAR units):** 0.676 with scleral buckling *v* 0.773 with vitrectomy	P = 0.395
	Visual acuity at 6 months	**Mean BCVA (logMAR units):** 0.608 with scleral buckling *v* 0.689 with vitrectomy	P = 0.376
	Adverse effects	**Development of cataract:** 0/31 (0%) with scleral buckling *v* 5/30 (17%) with vitrectomy	P = 0.018
		Elevated intraocular pressure: 2/31 (6.5%) with scleral buckling *v* 2/30 (6.7%) with vitrectomy	Significance not assessed
		Epiretinal membrane: 1/31 (3.2%) with scleral buckling *v* 1/30 (3.3%) with vitrectomy	Significance not assessed

* P value as reported in RCT.

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TABLE **GRADE evaluation of interventions for retinal detachment**

Important outcomes			Retinal re-attachment rate, visual acuity, re-operation rate, adverse effects						
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**
What are the effects of interventions to prevent progression from retinal breaks or lattice degeneration to retinal detachment?									
Cryotherapy									
We found no studies									
Laser photocoagulation									
We found no studies									
What are the effects of different surgical interventions in people with rhegmatogenous retinal detachment?									
2 (218) [40] [41]	Re-attachment rate	Scleral buckling *v* pneumatic retinopexy	4	–1	0	0	0	Moderate	Quality point deducted for incomplete re-porting
2 (218) [40] [41]	Visual acuity	Scleral buckling *v* pneumatic retinopexy	4	–1	0	0	0	Moderate	Quality point deducted for incomplete re-porting
4 (690) [42] [43] [44] [45]	Re-attachment rate	Scleral buckling *v* primary vitrecto-my in people with pseudophakic or aphakic RRD	4	0	–1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for inclu-sion of co-intervention (scleral buckling in primary vitrectomy arm)
4 (690) [42] [43] [44] [45]	Visual acuity	Scleral buckling *v* primary vitrecto-my in people with pseudophakic or aphakic RRD	4	0	–1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for inclu-sion of co-intervention (scleral buckling in primary vitrectomy arm)
1 (150) [42]	Re-operation rate	Scleral buckling *v* primary vitrecto-my in people with pseudophakic or aphakic RRD	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (523) [45] [46] [47]	Re-attachment rate	Scleral buckling *v* primary vitrecto-my in people with phakic RRD	4	–1	0	–2	0	Very low	Quality point deducted for incomplete re-porting. Directness points deducted for unclear outcome in 1 RCT and inclusion of co-intervention in 1 RCT (scleral buck-ling in primary vitrectomy arm)
3 (513) [44] [45] [46] [47]	Visual acuity	Scleral buckling *v* primary vitrecto-my in people with phakic RRD	4	0	–1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for inclu-sion of co-intervention (scleral buckling in primary vitrectomy arm)
What are the effects of interventions to treat proliferative vitreoretinopathy occurring as a complication of retinal detachment or previous treatment for retinal detachment?									
1 (265 eyes) [48]	Re-attachment rate	Silicone oil tamponade *v* long-acting gas tamponade	4	–1	0	0	0	Moderate	Quality point deducted for methodological issues (incomplete reporting and poor fol-low-up at 36 months)
1 (265 eyes) [48]	Visual acuity	Silicone oil tamponade *v* long-acting gas tamponade	4	–1	0	0	0	Moderate	Quality point deducted for incomplete re-porting
1 (97 eyes) [49]	Re-attachment rate	Silicone oil tamponade *v* short-act-ing gas tamponade	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

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Important outcomes		Retinal re-attachment rate, visual acuity, re-operation rate, adverse effects							
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consis-tency	Direct-ness	Effect size	GRADE	Comment
1 (97 eyes) [49]	Visual acuity	Silicone oil tamponade *v* short-acting gas tamponade	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (148) [55]	Re-attachment rate	Fluorouracil plus heparin *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and for incomplete reporting
1 (148) [55]	Visual acuity	Fluorouracil plus heparin *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (75) [52]	Re-attachment rate	Corticosteroid *v* no corticosteroid	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (75) [52]	Visual acuity	Corticosteroid *v* no corticosteroid	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (307) [53] [54]	Re-attachment rate	Daunorubicin *v* no daunorubicin	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting
2 (294) [53] [54]	Visual acuity	Daunorubicin *v* no daunorubicin	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting
1 (286) [53]	Re-operation rate	Daunorubicin *v* no daunorubicin	4	0	0	0	0	High	

Type of evidence: 4 = RCT; 2 = Observational.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.

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