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 Public Summary Document

Application No. 1559 – Endoscopic Mucosal Resection

**Applicant: Gastroenterological Society of Australia**

**Date of MSAC consideration: MSAC 79th Meeting, 28-29 July 2020**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](http://www.msac.gov.au/)

# Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of endoscopic mucosal resection (EMR) for patients with large (≥ 25 mm) sessile colorectal polyps was received from the Gastroenterological Society of Australia by the Department of Health.

# MSAC’s advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported public funding for endoscopic mucosal resection (EMR) for patients with large (≥25 mm) sessile colorectal polyps. MSAC accepted that EMR was safe, effective and cost-effective compared with surgical resection and noted EMR is the current standard of care. However, MSAC considered that the proposed fee was inappropriate, as it was not aligned with comparable MBS items. MSAC also considered the proposed item should be restricted to credentialed users, which could be addressed through the Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy.

MSAC recommended that utilisation and post-procedure outcomes of EMR and surveillance should be monitored.

| **Consumer summary** |
| --- |
| The Gastroenterological Society of Australia requested public funding through the Medicare Benefits Schedule (MBS) for the use of endoscopic mucosal resection (EMR) to remove large sessile (flat) polyps in the colon.A colon polyp (or lesion) is an abnormal growth of cells that forms on the lining of the colon, which is also known as the large intestine. Most colon polyps are harmless, but some can develop into colon cancer. During an EMR procedure, fluid is injected under the polyp to lift it away from the colon wall, making it easier to snare (catch) and remove using a wire loop. MSAC noted that the procedure is already being used and is safe and effective, but MSAC was concerned about the fee being requested by the applicant. MSAC calculated a new (lower) fee, based on the fee for other similar procedures.**MSAC’s advice to the Commonwealth Minister for Health**MSAC supported the public funding of EMR and has suggested a lower MBS fee than what was in the application so that the fee is in line with similar procedures. |

# Summary of consideration and rationale for MSAC’s advice

MSAC noted that this is a new application requesting Medicare Benefits Schedule (MBS) listing of EMR for patients with large (≥25 mm) sessile colorectal polyps, which is currently being performed as standard of care in public hospitals. MSAC also noted that it is also likely EMR is already being claimed on the MBS, as colonoscopy and polypectomy (MBS items 32222-32226, 32228 and 32229).

MSAC noted that proposed MBS item can be claimed for both EMR performed during diagnostic colonoscopy and following referral after colonoscopy but unlikely that a diagnostic colonoscopy also includes EMR because of preparation/theatre use.

MSAC noted that ESC queried whether the minimum size of the lesion should be 20 mm; however, in its pre-MSAC response, the applicant considered the most appropriate minimum to be 25 mm to avoid leakage. MSAC noted that, in practice, the actual measurement is imprecise, so it is possible that the person doing the procedure will estimate a polyp to be 25mm when it may be a few mm smaller, which means that suitable patients will not miss out on having the procedure yet leakage to lesions less than 20mm will be minimised. MSAC also noted that lesions >40 mm would be referred to expert centres.

MSAC noted that no relevant randomised or non-randomised comparative studies comparing the intervention to the comparator in the population of interest were identified. As such, a naïve comparison between EMR and surgery outcomes was undertaken. MSAC noted that EMR with three different co-interventions was included as a secondary analysis.

MSAC noted that relative to the comparator, the intervention has uncertain safety and effectiveness due to a lack of direct comparative studies. Although MSAC considered the superiority of EMR compared with surgery to be uncertain, the clinical evidence suggests that it is an effective treatment for large benign colorectal polyps.

MSAC noted that the benefits of EMR (e.g. reduced mortality and length of stay) have been accepted in clinical practice as outweighing the comparative disadvantages of EMR relative to surgery (i.e. surgery is considered curative, whereas there is a risk of residual adenoma/recurrence following EMR). Although EMR, unlike the comparator, cannot be considered “curative”, it does allow the majority of patients to avoid surgery, reserving surgical resection as a second-line option for cases where EMR treatment is not feasible, fails or unexpected malignancy is detected.

MSAC noted some minor issues with the economic model including that the costs of ongoing surveillance post-EMR may not be adequately costed. However, MSAC considered given the magnitude of the modelled incremental savings per patient, which increased with the applicant’s revised fee (see Table 7), that EMR was dominant compared with surgical resection.

MSAC noted that this procedure is available in the public sector and that cost-shifting from the state/territories to the Commonwealth will reduce the budget impact to the MBS. MSAC also noted using the applicant’s revised fee for EMR significantly decreased the budget impact to the MBS, and resulted in overall cost saving with the inclusion of public hospital costs (see Table 9).

MSAC noted that the EMR consisted of the equipment (e.g. electrocautery machine, which most units would have) and per patient consumables (e.g. snares, injectors), which are non-implantable, that will not be covered under the MBS item or the current Prostheses List.

MSAC considered that the original fee of $1,750 proposed by the applicant is excessive. MSAC also considered that the revised fee of $1,000 proposed by the applicant also to be inappropriate, as it was not sufficiently justified, nor aligned with comparable MBS items. MSAC proposed a fee of $695, based on the fee for a polypectomy (MBS item 32229).

MSAC noted the potential leakage to cold snare EMR (polyp removal without the electrocautery), given that cold snare is an easier procedure. MSAC noted that there was an upcoming randomised controlled trial comparing cold snare EMR (i.e. snare without electrocautery) *vs.* EMR ([NCT04138030](https://clinicaltrials.gov/ct2/results?cond=&term=NCT04138030&cntry=&state=&city=&dist=)) in 2024.

MSAC suggested the following revised item descriptor:

*Endoscopic mucosal resection using electrocautery of a non-invasive sessile or flat superficial colorectal neoplasm which is at least 25mm in diameter by a specialist gastroenterologist or surgical endoscopist, supported by photographic evidence\* to confirm the size of the polyp in situ, in association with a service to which item 32222, 32223, 32224, 32225, 32226, or 32228 applies. (Anaes.). Limit 1 claim per lesion.*

*Fee: $695.25 Benefit: 75% = $521.45*

*\*requires pre-procedure image of the lesion relative to an open snare of known dimensions placed adjacent to the lesion and post-procedure image of resection bed*

MSAC noted the proposed service would be performed exclusively in-hospital and that the proposed item descriptor does not include an 85% out-of-hospital benefit.

MSAC considered that people doing the procedure must be credentialed, which can be managed through the Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy. MSAC noted that this committee is responsible for quality of screening colonoscopy, and thus the performance of the EMR procedure could be assessed through this framework. MSAC considered that recurrence of disease is always a risk of EMR type procedures and that data collection could include findings from follow up colonoscopies, incidence of incomplete excisions and colorectal cancer (if possible). The committee could provide their data to MSAC to monitor actual use, as well as post-procedure outcomes and surveillance.

MSAC noted the complexity of performing pathology on an EMR derived specimen.

MSAC considered that utilisation of EMR will increase relative to surgical resection, given the minimally invasive nature of EMR. MSAC recommended that a post listing review of MBS utilisation be performed.

# Background

This is the first submission (Department-contracted assessment report [DCAR]) for EMR for patients with large (≥ 25 mm) sessile colorectal polyps. MSAC has not previously considered this application.

The [Medicare Benefits Schedule Review Taskforce 2016](https://www1.health.gov.au/internet/main/publishing.nsf/content/8D8DD5BA20AF8C3ACA2580290013AD4D/%24File/MBS%20Gastroenterology%20Report%20FINAL.pdf) recommended an MSAC assessment of EMR.

# Prerequisites to implementation of any funding advice

The DCAR considered it is likely EMR is already being claimed on the MBS (as colonoscopy and polypectomy: MBS items 32222-32226, 32228 and 32229.

# Proposal for public funding

The proposed MBS item descriptor and revised fee is summarised in Table 1. Prior to the MSAC meeting, the applicant advised the Department that it had revised the proposed fee to $1,000 (from $1,750) stating *"GESA feels that the proposed remuneration for the EMR item number is too high. Based on the remuneration of current colonoscopy item numbers (32222, 32223, 32224, 32225, 32226, 32227, 32228, 32229), GESA feels that the remuneration for the EMR item number should be about $1,000."*

**Table 1 Proposed MBS item descriptor (including applicant’s revised MBS fee)**

| Category 3 – Therapeutic procedure | MBS XXXXX |
| --- | --- |
| Endoscopic mucosal resection of a non-invasive sessile or flat superficial colorectal neoplasm which is at least 25mm in diameter by a specialist gastroenterologist or surgical endoscopist, supported by photographic evidence to confirm the size of the polyp *in situ*. (Anaes.)**Fee:** ~~$1,750~~$1,000 **Benefit:** ~~75% = $1,312.50~~ $750 |

Source: Table 1, p17 of DCAR, and updated for applicant’s revised fee on 8 July 2020

The DCAR stated that there is no proposed limit on the number of procedures for this item, or its use with other procedures. The applicant has outlined that up to one EMR per patient per calendar year should be required, although patients may require additional polypectomy or EMR services to treat recurrent or residual polyps [[Application 1559 Ratified PICO Confirmation](http://www.msac.gov.au/internet/msac/publishing.nsf/Content/33926FFFFEB77C2FCA25838500181915/%24File/1559_RATIFIED_PICO_CONFIRMATION.docx)].

The proposed item indicates a specialist gastroenterologist or surgical endoscopist should perform the EMR procedure. It was agreed by the Gastroenterology Clinical Committee of the Medicare Benefits Schedule Review Taskforce that EMR funded through the MBS will not be restricted to tertiary referral, maintaining the flexibility for experienced practitioners to perform EMR during routine colonoscopies [Application 1559 Ratified PICO Confirmation].

In the pre-ESC response, the applicant highlighted concern with the current descriptor:

* “It is important to specify that “cold EMR” are excluded from this item number as there is currently insufficient evidence relating to long-term clinical efficacy” (see Table 15 on p51 of DCAR describing ongoing trials of EMR). Cold EMRs (i.e. snare without electrocautery) are currently performed for ‘flat’ polyps and are less technically challenging (and ought not attract a fee of $1,750).

In addition, the applicant highlighted the importance of ensuring leakage is prevented with:

* the current use of the size criterion of ≥25mm in the proposed MBS item descriptor
* the exclusion of cold EMR. However, the applicant did not provide a revised MBS item descriptor to exclude this procedure.

In the Rejoinder, the DCAR highlighted that:

* cold-snare EMR was not reported on, nor applicable to the proposed EMR service and thus consistent with the approach of the DCAR to restrict the proposed item to exclude cold-snare EMR
* it did not consider the proposed EMR service to be a significant leakage risk, nor consider that issue of practitioners using hot snare vs. cold snare to be an issue of leakage; the DCAR considered this to be more an issue of clinical judgement.

In the pre-MSAC response, the applicant acknowledged the ESC concern regarding 2-stage EMRs, but noted that these should be considered as salvage therapy for large polyps that cannot be resected in a single session for patients in whom other options such as surgery are not preferred or possible. The applicant also considered it may be appropriate to restrict the Item descriptor to diathermy cases only as there is a paucity of long-term data on cold snaring.

# Summary of public consultation feedback/consumer Issues

One response was received from the Royal College of Pathologists of Australasia (RCPA), supporting the listing of the proposed item, noting that EMR can provided adequate treatment of colorectal lesions, avoiding the need for surgical resection. The response highlighted the opinion of the RCPA that the current histopathology complexity level for submucosal resected neoplasia as level 5 (Australian Government Department of Health, 2019) is inadequate should EMR be listed, failing to capture the added complexity of performing pathology on an EMR derived specimen.

# Proposed intervention’s place in clinical management

**Description of Proposed Intervention**

EMR is performed during a colonoscopy by a gastroenterologist or endoscopic surgeon trained in the procedure. When a non-invasive sessile polyp or flat superficial colorectal lesion is identified, a solution is injected into the submucosal space to separate the lesion from the underlying muscularis propria. The lesion is then resected by snare electrosurgery; either *en bloc* (in a single piece) or piecemeal (in several pieces). A mucosal margin of
2-3 mm is employed, and the resected specimen(s) are retrieved for histological assessment.

**Description of Medical Condition(s)**

A colon polyp (or lesion) is an abnormal growth of cells that forms on the lining of the colon; most are harmless, but some, over time, have the potential to develop into colon cancer. Ninety-five per cent of colorectal cancers arise from pre-neoplastic lesions; known as adenomas. Therefore, early detection and removal of colorectal polyps and lesions, before the “adenoma-carcinoma sequence” can take place is key in preventing colorectal cancer.

**Place in clinical management**

The current and proposed clinical management algorithms are presented in Figure 3 and Figure 4, respectively.



**Figure 1 Clinical management algorithm for selection of suitable resection technique for colorectal lesions**

Source: Figure 3, p40 of DCAR



**Figure 2 Proposed clinical management algorithm for patients using EMR**

Source: Figure 3, p40 of DCAR

Expert advice is that the decision to perform EMR at the initial *vs.* at a repeat colonoscopy depends on the type of patient consent received prior to the initial colonoscopy, as well as the theatre time required for the EMR procedure. In practice, whether or not patients are consented for EMR prior to the initial colonoscopy varies between practitioners. (Expert Colorectal Surgeon, 2019, Applicant Expert Gastroenterologist, 2019).

The DCAR stated that the main difference between the two treatment pathways (current *vs*. proposed algorithms) is the size of lesion amenable to EMR. The proposed pathway suggests only lesions greater than or equal to 25 mm be treated with EMR (with no upper limit on lesion size). This contrasts with the recommended use of EMR in lesions greater than or equal to 20 mm (but not larger than 40 mm) based on clinical practice guidelines.

# Comparator

Surgical removal of colorectal lesions (laparoscopically, or open surgery) is the comparator for EMR in this assessment. There are currently several MBS items listed for the comparator (MBS items 32000, 32003-32006), including right and left hemicolectomy, and subtotal colectomy.

It should be noted that EMR is the established standard of care for the removal of non-invasive colorectal lesions ≥ 20 mm. As mentioned in the PICO confirmation, surgery is considered the historical comparator for EMR which, for the purposes of this assessment, will be used to determine the comparative safety, effectiveness and cost-effectiveness of EMR.

In clinical practice, it is likely EMR is taking place either at the expense of local jurisdictions or it is being claimed for through the MBS (as colonoscopy and polypectomy). As such, any changes in number of MBS claims should the proposed item be listed are expected to be to colonoscopy and polypectomy MBS items (MBS items 32222-32226, 32228 and 32229) and not surgical resection MBS items.

# Comparative safety

In total, eight publications describing five studies (Australia [k=1; n=2,675]; Europe [k=4; n=2,055]) were included in the primary safety and effectiveness analysis of EMR. Four publications reporting on a single prospective study enrolling patients from eight tertiary centres – the Australian Multicentre Colonic Endoscopic Mucosal Resection (ACE/EMR) Study – were included; one as the primary data source (Sidhu et al., 2018[[1]](#footnote-1)) and three as supplementary sources of information only (Bahin et al., 2016[[2]](#footnote-2), Moss et al., 2015[[3]](#footnote-3), Tate et al., 2017[[4]](#footnote-4)).

The DCAR stated all five studies were well conducted case series and scored highly on the Institute of Health Economics (IHE) quality assessment tool; however, were classified at high risk of bias. Populations of the included studies were very well matched with the population specified in the PICO Confirmation.

A recently published (October 2019) systematic review informed the safety and effectiveness analysis of the comparator (de Neree Tot Babberich et al., 2019[[5]](#footnote-5)). The DCAR stated that the studies included in the review provided only case series data thus; the findings are limited by the high risk of bias of the included studies. The population and surgical procedures included in the systematic review were relatively well matched with the population and comparator specified in the PICO Confirmation, therefore the extracted data allowed an indirect analysis to be conducted.

An additional five studies, all randomised controlled trials (RCTs), were included to inform secondary analyses, including an extended assessment of the effect of three different cointerventions on key outcome measures.

The DCAR stated key complications associated with EMR included post-polypectomy bleeds (weighted rate: 5.2%, range: 0 to 9.9%), intraprocedural bleeds (IPBs) (range: 5.3 to 19.9%), deep mural injury (1.9%) and perforation (range: 0% to 1.6%) [see Table 2].For the Australian cohort, post-polypectomy bleeds occurred at a rate of 5.5%, IPBs at a rate of 19.9%, deep mural injury at a rate of 1.9% and delayed perforations at a rate of 0.4%. Results for the Australian cohort generally aligned with the remaining four studies with the exception of IPBs, which were considerably more prevalent in the Australian cohort. It is possible that this difference is due to a varying outcome definitions although this is unclear as not all studies provided a definition. Generally, complications could be treated endoscopically or with conservative management, while surgical intervention was only required in rare instances to treat post-polypectomy bleeds or a perforation.

The DCAR stated complications associated with surgical resection included anastomotic leakage (range: 0.3 to 8.7%), bleeding (range: 0.6 to 11.4%), ileus (range: 0.6 to 28.2%), infections (range: 1.1 to 22.2%) and wound dehiscence/hernia (range: 0.5 to 9.7%). Surgical re-intervention was required to treat a complication in a weighted rate of 3.6% of patients (range: 0 to 8.9%) [see Table 3]. The most commonly reported complications requiring surgical treatment included anastomotic leakages and bleeding.

No mortality associated with EMR was reported in any study. In comparison, the pooled,
1-month mortality rate for surgery was 0.7% (95% CI: 0.6 to 0.8%).

EMR was associated with a significantly lower intraprocedural event rate than TEM (10.1 *vs.* 4.5%, p = 0.03) however, the number of patients having a postprocedural complication after EMR or TEM did not differ significantly.

The DCAR stated that the use of clipping to achieve complete closure of the mucosal defect following EMR may reduce the risk of post-polypectomy bleeding. However prophylactic coagulation of all visible vessels does not appear to reduce the risk. Expert advice is that in Australia, prophylactically clipping of the EMR defect after EMR may or may not be performed (i.e. no standard practice).

# Comparative effectiveness

The DCAR stated that the technical success of EMR was high; complete endoscopic resection rates of 95% were achieved in two studies (Sidhu et al., 2018, Knabe et al., 2014[[6]](#footnote-6)). Recurrences can be expected at both first (range: 16.3 to 32%) and second (range: 6.7 to 16.4%) surveillance colonoscopies although generally, these can be treated endoscopically.

The DCAR stated patients may be referred to surgery after an EMR procedure because malignancy is detected in the resected specimen (range: 3.6 to 5.9% of cases), the EMR procedure is unsuccessful (4.0% of patients, as reported in a single study), or a complication requires surgical intervention (rare). Patients may also require surgery during the surveillance period for the treatment of residual or recurrent tissue which couldn’t be resected endoscopically, or for another reason (e.g. for a complication). Overall, studies reported that surgery post-EMR was required in 3.9% to 10.4% of cases.

Surgical resection for the population of interest is considered curative in clinical practice. Therefore, EMR is inevitably inferior in comparison to surgery with respect to success and recurrence outcomes.

The DCAR stated that the key effectiveness outcome reported for surgery was length of stay (mean 5.1 days, 95% confidence interval [CI]: 4.4 to 5.9 days). Although no EMR case series reported this as an outcome, expert opinion confirms that EMR is, in Australian clinical practice, generally performed as a day-case procedure, with only a small portion (approx. 5%) requiring an overnight admission (Expert Gastroenterologist, 2019a, Expert Colorectal Surgeon, 2019, Expert Gastroenterologist, 2019b).

**Table 2 Balance of clinical benefits and harms of EMR, as measured by the critical patient-relevant outcomes in the key studies**

| **Outcomes** | **Patients (n), (lesions)****Studies (k)** | **Quality of evidence (GRADE)†** | **Absolute effect weight rate (range)** |
| --- | --- | --- | --- |
| Mortality rate (%) | n = 2055k = 4 | ⨁⨁⨀⨀ | 0% |
| Post-polypectomy bleeds rate (%) | n = 4730, (4876 lesions)k = 5 | ⨁⨁⨀⨀ | 5.2%(range: 0 to 9.9%) |
| Perforation ± deep mural injury rate (%) | n = 4730, (4876 lesions)k = 5 | ⨁⨁⨀⨀ | Range: 0 to 2.3% |
| Rate of technical success (%) | n = 2918; (2927 lesions)k = 2 | ⨁⨁⨀⨀ | Range: 95.0 to 95.4% |
| Rate of short-term recurrence (i.e. at SC1) (%) | n = 3261; (3339 lesions)k = 3 | ⨁⨁⨀⨀ | 17.8%(range: 16.3 to 32%) |
| Rate of long-term recurrence (i.e. at SC2) (%) | n = 2918; (2927 lesions)k = 2 | ⨁⨁⨀⨀ | 8.2%(range: 6.7 to 16.4%) |
| Rate of referral to surgery following EMR ǂ (%) | n = 3516; (3621 lesions)k = 4 | ⨁⨁⨀⨀ | 3.9 to 9.3% |

Source: Table 2, p22 of DCAR

**Abbreviations:** EMR = endoscopic mucosal resection; SC1 = first surveillance colonoscopy; SC2 = second surveillance colonoscopy

**Notes:** All included studies were cases series, which are at an inherent risk of bias. All provided direct information on the intervention (EMR) and population (large, nonpedunculated, benign colorectal polyps) of interest. For all outcomes more than 2000 patients were considered – by far, the largest contributing trial to population numbers was the ACE Study (Australian). Generally, reasons for any variability in results could be identified.

† =GRADE Working Group grades of evidence (Guyatt et al., 2013); ǂ = surgery following initial EMR only, not including surgeries at time of surveillance colonoscopies

⨁⨁⨀⨀ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

⨁⨀⨀⨀ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Table 3 Balance of clinical benefits and harms of surgery, as measured by the critical patient-relevant outcomes in the key studies**

| **Outcomes** | **Patients (n) Studies (k)** | **Quality of evidence (GRADE)†** | **Absolute effect** **Mean (95% CI), or range** |
| --- | --- | --- | --- |
| 1-month mortality rate (%) | n = 13198k = 5 | ⨁⨁⨀⨀ | 0.7% (95% CI: 0.6 to 0.8%) |
| 1-month surgical complication rate (%) | n = 13191k = 6 | ⨁⨀⨀⨀ | 17% (95% CI: 10 to 29%) |
| Length of stay (pooled) (days) | n = 13462k = 8 | ⨁⨀⨀⨀ | 5.1 days (95% CI: 4.4 to 5.9 days) |
| Surgical re-intervention rate (%) | n = 14804k = 11 | ⨁⨀⨀⨀ | Range: 0 to 8.9% |

Source: Table 3, p22 of DCAR

**Notes:** All included studies were cases series, which are at an inherent risk of bias. For all outcomes more than 13000 patients were considered. Compared to the intervention arm, which was directly targeted and considered only cases series of the highest methodological rigour, we have relatively lower confidence in the outcomes presented for the surgical arm.

† =GRADE Working Group grades of evidence (Guyatt et al., 2013)

⨁⨁⨀⨀ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

⨁⨀⨀⨀ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Clinical claim**

On the basis of the benefits and harms reported in the evidence base (summarised above), the DCAR suggested that, relative to the comparator, the intervention has uncertain safety and effectiveness due to a lack of direct comparative studies. While the superiority of EMR over surgery is uncertain, the clinical evidence suggests that it is an effective treatment of large benign colorectal polyps.

The DCAR stated that the benefits of EMR (e.g. reduced mortality risk, reduced length of stay) have been accepted in clinical practice as outweighing the comparative shortcomings of EMR relative to surgery (i.e. surgery is considered curative, whilst there is a risk of residual adenoma/recurrence following EMR). Whilst EMR, unlike the comparator, cannot be considered ‘curative’, it does allow the majority of patients to avoid surgery, reserving surgical resection as second line option for cases were EMR treatment is not feasible, fails, or unexpected malignancy is detected.

# Economic evaluation

A cost-utility analysis, using a Markov model, was undertaken by the DCAR to determine the value of EMR compared with surgery (Table 4).

**Table 4 Summary of the economic evaluation**

| **Perspective** | Health system |
| --- | --- |
| **Intervention** | Endoscopic mucosal resection |
| **Comparator** | Surgical resection *(i.e. laparoscopic resection)* |
| **Type of economic evaluation** | Cost-utility analysis |
| **Sources of evidence** | Observational studies in Australia |
| **Time horizon** | 40 months |
| **Outcomes** | QALYs |
| **Methods used to generate results** | Cohort expected value analysis |
| **Health states** | Polyp + EMR, No polyp + surveillance, Polyp + surveillance, Polyp + Laparoscopic resection, Polyp + EMR/LR & Adverse event requiring surgical management, Polyp + EMR/LR & Adverse event requiring observation that with no surgery, Death |
| **Cycle length** | 1 month (30 days) |
| **Discount rate** | 5% used for base, 3.5% and 7% sensitivity analyses |
| **Software packages used** | Microsoft Excel 2010 |

Source: Table 4, pp23-24 of DCAR

**Abbreviations**: EMR= endoscopic mucosal resection, LR = laparoscopic resection; QALY, quality adjusted life year

Key structural assumptions of the DCAR’s model are:

* all patients in the EMR arm of the model are assumed to have an EMR attempted when they enter the model;
* patients entering the laparoscopic resection (LR) arm are only able to avail LR and no recurrence is assumed to be associated with this procedure;
* mortality is only possible for patients experiencing LR adverse events which require surgery.
* the base time horizon assumed for the analysis is 40 months as this reflects the maximum follow-up of the ACE study. Studies such as Law et al. (2016[[7]](#footnote-7)) extrapolated health outcomes over a longer time horizon using a systematic review of the literature to derive recurrence assumptions. However, given the uncertainty surrounding the duration of clinical benefits, and limited impact longer term recurrence is likely to have on economic modelling results, the timeframe of the economic model is limited to maximum follow-up of the observational studies in Australia.

The DCAR presented incremental cost-effectiveness ratio (ICER) results using 1 year and
40-month analyses (Table 5). The ICER was dominant with the results being largely driven by the assumed saving in procedural costs. The difference in quality-adjusted life years (QALYs) is largely a result of the longer time for LR hospitalisation of around 6 days compared to EMR and inclusion of mortality for LR-related adverse events. EMR has a shorter length of hospital stay of 1 day, which does not increase substantially as recurrence is less than 20% over the first year.

**Table 5 Incremental Cost Effectiveness Ratio**

|   | Discounted cost | Incremental cost | Effectiveness (QALYs) | Incremental effectiveness | ICER |
| --- | --- | --- | --- | --- | --- |
| **1 year** |  |  |  |  |  |
| Endoscopic Mucosal Resection (EMR) | 8,145 | -11,983 | 0.90 | 0.01 | Dominant |
| Surgical Resection | 20,128 |   | 0.88 |   |   |
| **40 months (Base case)** |   |   |   |   |   |
| Endoscopic Mucosal Resection (EMR) | 11,335 | -11,756 | 2.68 | 0.02 | Dominant |
| Surgical Resection | 23,091 |   | 2.65 |   |   |

Source: Table 5, pp24-25 of the DCAR

**Abbreviations**: EMR = endoscopic mucosal resection; ICER = Incremental Cost Effectiveness Ratio; QALYs = quality-adjusted life-years.

The DCARs model results are robust to changes in key assumptions presented in a sensitivity analysis (i.e. EMR is dominant over LR for all included scenarios for both 1 year and 40 months base case analysis) [see tornado diagram for base case in Figure 3].

**Figure 3: Univariate sensitivity analysis EMR verse LR for 40-month projection**

Source: Figure 12, p148 of DCAR

**Abbreviations:** AE= adverse event; EMR= endoscopic mucosal resection; LR = Laparoscopic resection; QALYs= quality adjusted life years

The assumption about the days which accrue a reduced utility (0.5 compared to 0.85) and LR costs have the largest impact on model results (Table 6).

**Table 6 Drivers of the economic model**

| Description | Method/Value | Impact |
| --- | --- | --- |
| Hospital days for intervention and comparator | The average days for overnight inpatient stay was taken from Law et al. (2016) and is similar the AR-DRG for G02C Major Small and Large Bowel Procedures, Minor Complexity.  | Reductions in the assumed number of hospital days and mortality for LR have the largest impact on the estimated ICER. Changes to hospital stay included in the sensitivity analyses of only 2 days does not change model results as EMR has a stay of 1 day.  |
| Cost of the proposed EMR Item Number | PASC noted that the applicant has proposed a fee of $1,750 for EMR; however, it was not clear how that figure was derived.  | A reduction in the EMR fee favours the *intervention*. It is the largest single cost item in the EMR budget and equal to all costs in Jayanna et al. (2016)[[8]](#footnote-8). The reduction does not change results. |
| Recurrence rate for EMR | Sidhu et al. (2018) found 16.1% recurrence at 4-6 months for EMR. This is converted to a monthly rate for the model and compared to zero recurrence for LR. Higher recurrence results in higher follow-on costs, as further procedures are required to that for the index EMR. | Despite the higher recurrence rate for EMR, changes in this assumption are not enough to change model results. The cost difference between EMR and LR is large. |

Source: Table 75, p148 of DCAR

**Abbreviations**: EMR = endoscopic mucosal resection; AR-DRG =Australian refined diagnosis related groups; G02C = Major small and large bowel procedures, minor complexity (AR-DRG v.9 code); LR = laparoscopic resection; ICER = Incremental Cost Effectiveness Ratio’ PASC = PICO Confirmation Advisory Sub-Committee.

*Italics represents corrected by Department*

## Post ESC revised MBS fee

The base case economic model was updated by the Department to reflect the applicant’s revised fee for EMR of $1,000 (from $1,750). Expectantly, the ICER remained dominant (Table 7), with higher savings of $12,854 per patient (from $11,983) in the one year model; and $12,647 in the base case model (from $11,756).

**Table 7 Incremental Cost Effectiveness Ratio: applicant’s revised fee of $1,000 (from $1,750)**

|   | Discounted cost | Incremental cost | Effectiveness (QALYs) | Incremental effectiveness | ICER |
| --- | --- | --- | --- | --- | --- |
| **1 year** |  |  |  |  |  |
| Endoscopic Mucosal Resection (EMR) | *7,274* | *-12,854* | 0.90 | 0.01 | Dominant |
| Surgical Resection | 20,128 |   | 0.88 |   |   |
| **40 months (Base case)** |   |   |   |   |   |
| Endoscopic Mucosal Resection (EMR) | *10,444* | *-12,647* | 2.68 | 0.02 | Dominant |
| Surgical Resection | 23,091 |   | 2.65 |   |   |

Source: Table 5, pp24-25 of the DCAR

**Abbreviations**: EMR = endoscopic mucosal resection; ICER = Incremental Cost Effectiveness Ratio; QALYs = quality-adjusted life-years.

*Italicised represents changed values as performed by Department, as result of applicants revised fee*

# Financial/budgetary impacts

The DCAR used an epidemiologic approach to estimate the financial impact of the new EMR item’s introduction. The new item for EMR could also result in patients currently availing EMR in state hospitals switching to private delivery using MBS financing: public delivery of EMR is assumed to decrease from 70% of the patients to 50% with the introduction of the new item. This would reduce state level costs and increase MBS support.

The financial implications to the MBS resulting from the proposed listing is summarised in Table 8. The DCAR stated that a key uncertainty is the number of polyps that would qualify for EMR under the item description (based on an assumed proportion of colonoscopies with polyp removal [MBS Item 32093]) and proportions of public and private patients.

**Table 8 Total costs to the MBS associated with EMR**

|  | **2020** | **2021** | **2022** | **2023** | **2024** |
| --- | --- | --- | --- | --- | --- |
| **Patient numbers** |  |  |  |  |  |
| EMR with listingPrivate patients (50%), MBS supported Public patients (50%),  | 9,8394,9194,919 | 10,3225,1615,161 | 10,8055,4035,403 | 11,2895,6445,644 | 11,7725,8865,886 |
| EMR without listingPrivate patients (30%), MBS supported Public patients (70%)  | 9,8392,9526,887 | 10,3223,0977,225 | 10,8053,2427,564 | 11,2893,3877,902 | 11,7723,5328,241 |
| SubtotalPrivate patients, MBS supported Public patients | 0-1,9681,968 | 0-2,0642,064 | 0-2,1612,161 | 0-2,2582,258 | 0-2,3542,354 |
| **MBS Costs *(private patients)*** |  |  |  |  |  |
| EMR with listing*a* | 8,736,783  | 9,166,090  | 9,595,398  | 10,024,706  | 10,454,013  |
| EMR without listing*b* | 2,423,410  | 2,542,491  | 2,661,573  | 2,780,654  | 2,899,736  |
| **Subtotal** | **6,313,373**  | **6,623,599**  | **6,933,825**  | **7,244,052**  | **7,554,278**  |
| **State Hospital Costs *(public patients)*** |  |  |  |  |  |
| EMR with listing*c* | 9,695,853  | 10,172,288  | 10,648,722  | 11,125,156  | 11,601,591  |
| EMR without listing*c* | 13,574,194  | 14,241,203  | 14,908,211  | 15,575,219  | 16,242,227  |
| **Subtotal** | **-3,878,341**  | **-4,068,915**  | **-4,259,489**  | **-4,450,063**  | **-4,640,636**  |
| **Total MBS and state** | **2,435,032**  | **2,554,684**  | **2,674,337**  | **2,793,989**  | **2,913,642**  |

Source: *Compiled from* Table 7, p26; Table 82, p157; and Table 83, pp157-158 of the DCAR

**Abbreviations**: EMR = endoscopic mucosal resection, MBS = Medicare Benefits Schedule

*a Using 75% rebate, the EMR cost per patient = $1,776.04 (New proposed item component = $1,312.50 ; other components include specialist consultation, pre-anaeathsia consultation, referred consultation, administration of anaesthesia, blood pressure monitroing and colonscopies proposed for EMR = $473.54)*

*b Using 75% rebate, EMR cost per patient = $821.06 (Current MBS items 32224+32229 component = $357.53; other components include specialist consultation, pre-anaeathsia consultation, referred consultation, administration of anaesthesia, blood pressure monitroing and colonscopies proposed for EMR = $473.54)*

*c EMR cost per patient = $1,970.84, inclusive of MBS costs using 75% hospital rebate and hospital services costs (nurse and surgery accomodation)*

## Post ESC revised MBS fee

The base case financial model was updated by the Department to reflect the applicant’s revised fee and benefit for EMR of $1,000 and $750 respectively (from $1,750 and $1,312.50, respectively). The revised financial analysis has decreased MBS costs by 56% over the first five years to $19,474,033 (from $34,669,127), and is also now cost saving to the MBS and state (Table 9).

**Table 9 Total costs to the MBS associated with EMR: using applicant’s revised benefit of $750 (from $1,313)**

|  | **2020** | **2021** | **2022** | **2023** | **2024** |
| --- | --- | --- | --- | --- | --- |
| **Patient numbers** |  |  |  |  |  |
| EMR with listingPrivate patients (50%), MBS supported Public patients (50%),  | 9,8394,9194,919 | 10,3225,1615,161 | 10,8055,4035,403 | 11,2895,6445,644 | 11,7725,8865,886 |
| EMR without listingPrivate patients (30%), MBS supported Public patients (70%)  | 9,8392,9526,887 | 10,3223,0977,225 | 10,8053,2427,564 | 11,2893,3877,902 | 11,7723,5328,241 |
| SubtotalPrivate patients, MBS supported Public patients | 0-1,9681,968 | 0-2,0642,064 | 0-2,1612,161 | 0-2,2582,258 | 0-2,3542,354 |
| **MBS Costs *(private patients)*** |  |  |  |  |  |
| EMR with listing*a* | *5,969,701* | *6,263,040* | *6,556,379* | *6,849,718* | *7,143,057* |
| EMR without listing*b* | 2,423,410  | 2,542,491  | 2,661,573  | 2,780,654  | 2,899,736  |
| **Subtotal** | *3,546,291*  | *3,720,549*  | *3,894,807*  | *4,069,064*  | *4,243,322*  |
| **State Hospital Costs *(public patients)*** |  |  |  |  |  |
| EMR with listing*c* | 9,695,853  | 10,172,288  | 10,648,722  | 11,125,156  | 11,601,591  |
| EMR without listing*c* | 13,574,194  | 14,241,203  | 14,908,211  | 15,575,219  | 16,242,227  |
| **Subtotal** | **-3,878,341**  | **-4,068,915**  | **-4,259,489**  | **-4,450,063**  | **-4,640,636**  |
| **Total MBS and state** | *-332,050*  | *-348,366*  | *-364,682*  | *-380,999*  | *-397,315*  |

Source: *Compiled from* Table 7, p26; Table 82, p157; and Table 83, pp157-158 of the DCAR

**Abbreviations**: EMR = endoscopic mucosal resection, MBS = Medicare Benefits Schedule

*a Using 75% rebate, the EMR cost per patient = $1,776.04 (New proposed item component = $1,312.50 ; other components include specialist consultation, pre-anaeathsia consultation, referred consultation, administration of anaesthesia, blood pressure monitroing and colonscopies proposed for EMR = $473.54)*

*b Using 75% rebate, EMR cost per patient = $821.06 (Current MBS items 32224+32229 component = $357.53; other components include specialist consultation, pre-anaeathsia consultation, referred consultation, administration of anaesthesia, blood pressure monitroing and colonscopies proposed for EMR = $473.54)*

*c EMR cost per patient = $1,970.84, inclusive of MBS costs using 75% hospital rebate and hospital services costs (nurse and surgery accomodation)*

*Italicised represents changed values as performed by Department, as result of applicant’s revised fee*

# Key issues from ESC for MSAC

| ESC key issue | ESC advice to MSAC |
| --- | --- |
| Safety | ESC considered EMR to be a minimally invasive procedure compared with surgery. Complications reported from 8.6% to 27.7%; most treated endoscopically or with conservative management. |
| Effectiveness  | ESC noted that surgical resection is considered curative, which means that EMR is considered to be inferior, even though the technical success of EMR is considered to be high. In a few (up to 5.5%), EMR may just delay surgery (0-5.5%)ESC noted that if malignancy is detected in the resected specimen (range: 3.6 to 5.9% of cases), patients may be referred to surgery after an EMR procedure.Overall, ESC noted that the benefits of EMR has been accepted in clinical practice as outweighing the comparative shortcomings of EMR relative to surgery (i.e. surgery is considered curative, whilst there is a risk of residual adenoma/recurrence following EMR). |
| Item descriptor issues | Lesion size: ESC also noted that the proposed MBS population is for patients with lesions ≥ 25 mm, even though in clinical practice it is done on lesions that are > 20 mm. ESC queried if a threshold consistent with clinical practice would be more appropriate. However, if there is an expectation that EMR cannot be performed on lesions < 25 mm, then ESC considered there was concern that this may lead to other, potentially higher risk and or less effective procedures for such lesionsESC queried if Service may be claimable if attempted but not technically feasible (e.g. lesions not elevated with submucosal injection)ESC noted that 2-stage EMR can be performed (28.6% of cases in Australian study by Tate et al. 2017) and queried if this was adequately captured in the Item and frequency restrictionsESC noted the potential leakage risk to cold snare EMR, and queried Item descriptor restriction to avoid. |
| EMR setting | Expert opinion indicated a preference for EMR to be performed in tertiary centres. ESC also raised concern about the quality of performing the procedure and patient outcomes in settings with low patient volumes; however, ESC considered restricting EMR to tertiary centres would impact equity of access. |
| Proposed fee of $1,750 is not justified | ESC advises, with the support of the Department, cost calculation anticipating the technical complexity of the procedure and potentially the complexity of the assessment as per RCPA’s recommendation.  |
| Financial implications | ESC noted that uncertainties in the estimates are related to the number of patients eligible for EMR over time and assumptions made about substitution (that is, replacement of other colonoscopy MBS items).  |
| Shift from state-funded hospital budgets to MBS budgets | If listed, it is assumed the delivery of EMR will shift from the public to the private system (from 70% to 50% of procedures in public system), because EMR would become available for private patients at no additional out-of-pocket costs. However, Experts estimate a significant number of EMRs will still be performed in public hospitals. Overall, ESC considered the degree of cost shifting was uncertain and could benefit from further clarification. |
| Economic evaluation is dominant in favour of EMR | The economic evaluation was based on historical controls (i.e. laparoscopic surgery). However, the standard of care in Australia is EMR, making the results of the economic evaluation less relevant. Thus, ESC advises MSAC to consider the economic evaluation results to be supportive but not definitive in making a recommendation.  |

**ESC discussion**

ESC noted that this application is for a new item for endoscopic mucosal resection (EMR) for the removal of non-invasive colorectal lesions ≥ 25 mm, which is currently being performed as standard of care in public hospitals. In addition, ESC noted that it is also likely EMR is already being claimed on the MBS, as colonoscopy and polypectomy (MBS items 32222-32226, 32228 and 32229).

ESC also noted that the proposed MBS population is for patients with lesions ≥ 25 mm, even though in clinical practice it is done on lesions that are > 20 mm. In its pre-ESC response, the applicant highlighted this was decided upon at PASC to reduce risk of leakage; however, the applicant confirmed that expert advice suggested this will not change the generalisability of the results. ESC considered that it is unclear what will happen to patients with lesions between 20-24 mm in both the private and public sectors, but considered EMR to be the most likely treatment option. Thus, ESC queried if a threshold consistent with clinical practice would be more appropriate. However, if there is an expectation that EMR cannot be performed on lesions < 25 mm, then ESC considered there was concern that this may lead to other, potentially higher risk and or less effective procedures for such lesions.

ESC noted that the proposed item descriptor does not include an 85% out-of-hospital benefit, and there was discussion about whether this service would be performed exclusively in-hospital. It was noted that this is increasingly becoming a day-only procedure. However, ESC queried the safety of this procedure performed as day surgery, given the nature of the invasive surgery. In addition, ESC noted the applicant’s concern with some aspects of the descriptor, including that cold EMR (i.e. snare without electrocautery) should be excluded from the item number because it was not reported on, nor applicable to the proposed EMR service. ESC also noted in the applicant’s pre-ESC response that there was an Australian study underway in cold EMR (*vs*. EMR) in patients with 15-40 mm lesions.

ESC noted that there are no randomised controlled trials (RCTs) or comparative studies comparing EMR directly with surgery; the primary analysis of comparative safety and effectiveness was informed by a naïve comparison of:

* EMR, from five studies, including a single prospective study that enrolled patients from eight tertiary centres – the Australian Multicentre Colonic Endoscopic Mucosal Resection (ACE/EMR) Study (n=2,675; primary data source: Sidhu et al. 2018)
* surgery, from a recently published (October 2019) systematic review (de Neree Tot Babberich et al., 2019).

Overall, ESC agreed with the DCAR which considered that the populations (and surgical procedures included for the comparator in the systematic review) were relatively well matched with the population specified in the PICO Confirmation. ESC also noted the DCAR included five RCTs that assessed the effect of EMR with three different cointerventions, included as secondary analysis.

In terms of comparative safety, ESC considered EMR to be a minimally invasive procedure compared with surgery. The five included studies were of high quality but also had a high risk of bias. Generally, complications could be treated endoscopically or with conservative management, while surgical intervention was only required in rare instances to treat post-polypectomy bleeds or a perforation. No mortality was associated with EMR.

In terms of comparative effectiveness, ESC noted that surgical resection is considered curative, which means that EMR is considered to be inferior, even though the technical success of EMR is considered to be high. Neither technical success nor recurrence outcomes differed between EMR and trans-anal endoscopic microsurgery. However, ESC noted that if malignancy is detected in the resected specimen (range: 3.6 to 5.9% of cases), patients may be referred to surgery after an EMR procedure. ESC also noted in Australian clinical practice, that EMR, as estimated by expert opinion, is generally performed as a day-case procedure, with only a small portion (approx. 5%) requiring an overnight admission, compared with an average of 5.1 days for surgery (95% confidence interval [CI]: 4.4, 5.9). Overall, ESC noted that the benefits of EMR (reduced mortality risk [see Table 3], reduced length of stay) has been accepted in clinical practice as outweighing the comparative shortcomings of EMR relative to surgery (i.e. surgery is considered curative, whilst there is a risk of residual adenoma/recurrence following EMR).

ESC noted that expert opinion indicated a preference for EMR to be performed in tertiary centres, due to the expertise of the assisting staff is more advanced (relative to outside tertiary centres). ESC raised concern about the quality of performing the procedure and patient outcomes in settings with low patient volumes, but considered restricting EMR to tertiary centres would impact equity of access.

ESC noted that a cost-utility analysis was used, based on superiority in short-term and non-inferiority in long-term, and based on historical controls (i.e. laparoscopic surgery). However, ESC noted that the standard of care in Australia is EMR, which makes the results of the economic evaluation less relevant for MSAC decision-making. ESC noted the DCARs modelled economic evaluation was largely informed by evidence from Australian cohort studies, and quality-adjusted life years were informed by Australian population norms and applying disutilities from published evidence. ESC accepted that EMR is dominant over laparoscopic resection at 40 months, and noted the DCARs result was consistent with the published evidence, including an Australian cost-effectiveness study (Jayanna et al. 2016). ESC also noted that the incremental cost-effectiveness ratio (ICER) was robust under one-way sensitivity analysis, including when the cost of laparoscopic surgery was the same as the cost of EMR. Overall, ESC considered that results of the economic evaluation to be supportive but not leading in making a recommendation.

ESC considered that the proposed fee (based on Jayanna et al. 2016) was not adequately justified. MSAC may want to work with the Department to calculate cost based on complexity of the procedure, as per the Royal College of Pathologists of Australasia’s recommendation.

ESC noted that the financial implication is an additional $3 million for the MBS, and states and territories in 2024. The additional costs for MBS of $7.6 million in 2024 is compensated by savings of $4.6 million at the state- and territory-level for hospital procedures. However, ESC considered there was considerable uncertainty with these estimates, mainly related to the number of patients eligible for EMR over time (based on an assumed proportion of colonoscopies with polyp removal [MBS Item 32093]) and proportions of public and private patients availing EMR estimated from assumption and applicant observation of EMRs done in public practice. ESC also noted a key driver of the financial impact was the estimated proportion of patients with lesions >25 mm, which can drive cost to the MBS up by 67%.

ESC also noted that it was assumed that listing of EMR will lead to a shift in the delivery of EMR in the public system from 70% of the patients to 50% because EMR now becomes available for private patients at no additional out-of-pocket costs. ESC noted there is an estimated increase in number of EMR procedures even though EMR is currently the standard of care. This is explained by expected expanded access in the private sector, but it is unclear why that is the expectation. ESC noted that experts estimate a significant number of EMRs will still be performed in public hospitals. Overall, ESC considered the degree of cost shifting was uncertain and could benefit from further clarification.

ESC considered that if EMR is mainly done as day surgery it would be reasonable for it to be subject to a cap on Extended Medicare Safety Net (EMSN) benefits.

# Other significant factors

Nil.

# Applicant comments on MSAC’s Public Summary Document

We thank you for the opportunity to review the Public Summary Document (PSD) for Application 1559. We find the document to be accurate according to the current published evidence. We support the current proposed wording of the item descriptor in relation to EMR.

# Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website:
[visit the MSAC website](http://www.msac.gov.au/)

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