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Fertility control for managing macropods – Current approaches and future prospects

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Summary Macropods play an important ecological role in the Australian environment; however, at high population densities can adversely affect biodiversity and primary production and result in human–wildlife conflicts. While shooting is recognised as the most humane and species-specific method for controlling macropod populations, in peri-urban situations fertility control provides an attractive option to replace or reduce lethal interventions. An appropriate fertility control agent for managing overabundant macropods needs to provide long-lasting infertility following a single treatment, be species-specific in its action or administration method, and be safe, humane, and cost-effective. Several contraceptive methods that induce infertility for multiple years have been tested on macropods. These include surgical techniques; hormonal implants containing deslorelin, a gonadotrophin-releasing hormone (GnRH) agonist, or levonorgestrel, a progestin; and immunocontraceptive vaccines (zona pellucida vaccine and the GnRH-based vaccine, GonaCon). These methods vary in the complexity of delivery and therefore their potential for adverse welfare impacts. Minimal side effects on behaviour and health have been observed. Despite some recent progress with remote dart delivery of deslorelin implants and GonaCon, efficient deployment of all existing methods is currently restricted to either captive or small, wild populations where individuals can be approached closely enough for safe capture and treatment. Of the currently available methods, levonorgestrel and GonaCon are the most suited to population-scale management. To date, studies addressing the effect of fertility control on the growth rate of macropod populations have been limited but are essential to enable full evaluation of the efficacy and cost/benefit analysis of the different approaches. Mathematical modelling to identify the level of infertility required to meet population management goals, as well as comparing integrated management strategies, will support planning of large-scale field trials. Improving dart delivery of existing contraceptive agents and developing new methods, such as an oral contraceptive, would increase the cost-effectiveness of applying fertility control to free-ranging macropods and may make treating larger populations feasible.

Key words: *contraception, kangaroo, peri-urban, wildlife management.*

Implications to Managers

- For overabundant populations, the population should be reduced using lethal methods before fertility control is applied.
- Current fertility control methods are suited to captive or small, discrete wild populations with minimal immigration, where individuals can be captured and treated efficiently.
- Fertility control methods for macropods include hormonal implants, contraceptive vaccines and surgical techniques; levonorgestrel implants and GonaCon vaccine are currently the most appropriate options for free-ranging populations.
- Remote dart delivery of deslorelin implants and GonaCon vaccine is being trialled to increase the efficiency and cost-effectiveness of administration, which could be further increased in future if an oral contraceptive is developed.

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Introduction

Following European settlement across Australia, the three largest macropods, the Red Kangaroo (*Osphranter rufus*), Eastern Grey Kangaroo (*Macropus giganteus*) and Western Grey Kangaroo (*M. fuliginosus*), generally benefited from the expansion of agricultural lands and the increase in the number of watering points (Archer *et al*. 1985; Caughley *et al*. 1987; Coulson 2008). Unlike smaller marsupials (<5 kg), these macropods have been mostly unaffected by the introduction of vertebrate pests, such as the Red Fox (*Vulpes vulpes*) and European Rabbit (*Oryctolagus cuniculus*). However, as kangaroo numbers increased they were viewed as competitors with domestic livestock, such that commercial harvesting has been implemented across the rangeland areas of Australia since the 1980s (Archer *et al*. 1985; Wilson & Edwards 2019). In the more urbanised areas of the eastern seaboard, where harvesting is not undertaken, individual landholders apply for damage mitigation permits to reduce their macropod numbers. In addition to impacts on rural enterprises, overgrazing by kangaroos causes adverse impacts on biodiversity (e.g. Neave & Tanton 1989; Howland *et al*. 2014, 2016; Snape *et al*. 2018). Continual peri-urban development, including spreading suburbs and high-speed roads, further fragments habitats and leads to more wildlife contact with humans (Coulson *et al*. 2014; Descovich *et al*. 2016; Henderson *et al*. 2018). In particular, Eastern Grey Kangaroo is common in peri-urban areas and its impacts in urban reserves often its require management intervention (Gordon *et al*. 2021; Herbert *et al*. 2021).

Managing overabundant wildlife requires achieving a balance between several competing goals: mitigating the impacts of the overabundant species, maintaining the ecological role of that species within the environment, ensuring high animal welfare standards and managing public expectations. If some degree of management is not applied, the consequences for the welfare of individuals can lead to death due to disease or starvation, a potential increase in vehicle collisions and degradation of the environment (Herbert *et al*. 2021; Coulson 2007). Selecting the technique(s) that will successfully reduce abundance and, in turn, mitigate the negative impacts caused by the species to an appropriate level becomes the key challenge. Within peri-urban environments, use of firearms for management of overabundant macropods by culling may raise public safety concerns and is seen as undesirable by some members of the public. Alternative options include capture and translocation, which may have undesirable welfare impacts (Fischer & Lindenmayer 2000), or application of fertility control to prevent reproduction and reduce recruitment over time (Massei & Cowan 2014; Rutberg *et al*. 2017).

Fertility control has been proposed as a method for managing wildlife for several decades (Bomford & O'Brien 1992) and is often favoured as it is deemed to be more humane than lethal methods. As noted by many others (see Kirkpatrick & Turner 1991; Massei & Cowan 2014; Hobbs & Hinds 2018), several highly desirable characteristics have been defined for the development of fertility control agents, which will underpin their likely success for field use. These include the following: (i) specificity of the control agent and/or its delivery to the target species; (ii) high efficacy with a preference for a single treatment, which is fast acting and of long duration (several years); (iii) humane such that there are no or minimal negative effects on social behaviour or animal welfare; (iv) safe to deliver if administered during pregnancy and lactation, or where an individual receives multiple treatments; and (v) cost-effective in terms of the control agent and its delivery mechanism over the necessary time frame for control. Fertility control strategies targeting females only are usually more productive in terms of efficiency, absence of adverse side effects on behaviour or welfare, duration of infertility and overall cost-effectiveness (Bomford 1990). For example, in species in which females mate with multiple males, reproduction is unlikely to be inhibited unless all males are sterilised, because any remaining fertile males can mate successfully with several females.

Although many fertility control approaches have been assessed in laboratory and pen studies, few have reached the stage of being implemented at a population level (Massei & Cowan 2014). The main reason for this is that the transfer to field settings is limited by the absence of cost-effective, efficient and practical field delivery techniques. There are no proven orally deliverable contraceptive formulations available for field animals (Sharma & Hinds 2012); thus, all current agents require capture of individuals for treatment. That said, remote dart delivery of some agents (e.g. some immunocontraceptive vaccines) is possible in the field (e.g. Kirkpatrick *et al*. 1990; Turner *et al*. 1992; Rutberg *et al*. 2017) and may prove the most efficacious approach in the medium to long term for relatively small, discrete populations where immigration is minimal, such as on golf courses and parks and reserves surrounded by urban development. Other issues may arise with remote delivery (e.g. Naugle & Grams 2013), such as how best to remotely mark animals at the time of treatment.

The purpose of this review was to describe the status of various fertility control agents that have been assessed for their effect on reproduction in macropods and provide a perspective on which techniques might be used safely and efficiently for managing kangaroo populations, particularly in peri-urban areas.

Fertility Control Methods for Macropods

Surgical sterilisation

Surgical sterilisation, including vasectomy or castration of males and tubal ligation or ovariectomy of females, provides permanent control and has been used in macropods in captive and semi-captive situations. In the 1990s, the semi-captive Eastern Grey Kangaroo population at Government House, Canberra, was managed by a combination of culling, translocation and vasectomy of remaining males, and this successfully controlled the growth of the population for four years (Coulson 1998, 2001). However, small numbers of fertile males entered the site annually and successfully bred with resident females. Consequently, the population has increased and ongoing vasectomies have been required (Karen Viggers, Veterinarian, *pers. comm.*, 2019). This example effectively demonstrates how a small number of fertile males can contribute significantly to the growth of a population. Vasectomies of a limited number of Eastern Grey Kangaroo males for management were partially successful at Coranderrk Bushland, Victoria (Coulson 1998); similarly, a programme of vasectomising or castrating males and administering hormonal implants to females had short-term effects on Eastern Grey Kangaroo numbers at a semi-enclosed golf course in Queensland (Tribe *et al*. 2014). Colgan and Green (2018) developed a laparoscopic ovariectomy technique for efficiently sterilising Eastern Grey Kangaroo and Red Kangaroo females within an enclosed site in western Sydney, performing 1409 surgeries over an eight-year period. Between 2005 and 2018, the site's population declined from an estimated 4342 animals to approximately 374 animals, but it is not clear whether this was due only to the fertility control programme (Colgan *et al*. 2019).

Contraceptive implants

Deslorelin

The GnRH agonist, deslorelin, is a slow-release hormonal implant (Suprelorin®, Virbac Australia, Macquarie Park, NSW), which was originally developed for the domestic pet market (Trigg *et al*. 2001). In females, deslorelin acts by desensitising and downregulating pituitary gonadotrophs, thereby inhibiting the production of luteinising hormone (LH) and follicle-stimulating hormone (FSH), and in turn suppressing follicular development and ovulation (Herbert & Trigg 2005). These small implants are administered via subcutaneous injection following animal capture, although intramuscular placement is also effective, and remote dart delivery trials have been conducted (Herbert & Silva unpublished).

The efficacy of deslorelin implants in macropods has been the subject of numerous trials. Treatment of captive Tammar Wallaby (*Notomacropus eugenii*) individuals demonstrated that a single 5-mg implant rendered females infertile for one or two breeding seasons (Herbert *et al*. 2004, 2005). Pen trials in captive Eastern Grey Kangaroo individuals established the efficacy of a 9.4-mg implant, which inhibited reproduction in 94% of females for 1-2 breeding seasons (Herbert *et al*. 2006, 2010).

Deslorelin has also been administered to the Eastern Grey Kangaroo in field trials. Treatment of Eastern Grey Kangaroo females with a single 9.4-mg implant at three sites in Victoria resulted in high efficacy in year 1 (100% infertility at two sites), but contraceptive reversal commenced in year 2, and contraception was ineffective by year 3 (Wilson *et al*. 2013). Current field trials have focussed on trialling dart delivery of a lower dosage (4.7 mg) deslorelin implant to Eastern Grey Kangaroo females at four sites on the NSW east coast. Preliminary results suggest a contraceptive duration of approximately one year following dart delivery of this lower dose (Herbert, Cope & Silva unpublished).

Levonorgestrel

Levonorgestrel is a synthetic progestin that mimics the hormone progesterone. Subcutaneous implants of levonorgestrel have been used extensively as long-term contraceptives in women (Diaz *et al*. 1982; Meirik *et al*. 2001) and in wildlife, such as Chimpanzees (*Pan troglodytes*) (Bettinger *et al*. 1997), White-faced Sakis (*Pithecia pithecia*) (Savage *et al*. 2002) and Koalas (*Phascolarctos cinereus*) (Middleton *et al*. 2003; Hynes *et al*. 2010). Levonorgestrel inhibits ovulation by suppressing the pre-ovulatory surge of LH (Segal *et al*. 1991; Hynes *et al*. 2007). Treatment with levonorgestrel is a minor surgical procedure performed in the field. It involves capture, chemical restraint, local anaesthesia, a 1-cm incision, insertion of implants and closure with degradable sutures.

Many trials have assessed the efficacy of levonorgestrel implants for fertility control of macropods. Captive female Tammar Wallabies treated with a 70-mg implant of levonorgestrel ($n = 8$) did not mate or give birth for three years after treatment, while all control females ($n = 11$) continued to breed (Nave *et al*. 2000). At two field locations in Victoria, free-ranging Eastern Grey Kangaroo individuals that were treated with two 70-mg implants showed 80–86% infertility in the first 3 years after treatment (Nave *et al*. 2002; Coulson *et al*. 2008) with efficacy declining thereafter. At a third location, when three 70-mg implants were used in Eastern Grey Kangaroo (Wilson & Coulson 2016), efficacy was high, with over 90% infertility during the first five years, and over 57% infertility eight years after treatment. Of interest is that two treated females are still alive 12 years after treatment and have never bred (Wilson & Coulson unpublished).

Immunocontraceptive vaccines

Immunocontraceptive vaccines trigger the immune system to produce antibodies against proteins or hormones that are required for reproduction. Two types of contraceptive vaccines have been trialled on macropods, ZP (zona pellucida) vaccines and the GnRH-based vaccine, GonaCon.

ZP vaccines

ZP vaccines target the protein coating of the oocyte (the zona pellucida), inhibiting conception by blocking sperm from binding to the egg. Multiple doses of Porcine ZP vaccine successfully caused infertility in Tammar Wallaby females (Kitchener *et al*. 2002) and induced a similar immune response in Eastern Grey Kangaroo females (Kitchener *et al*. 2009). The Eastern Grey Kangaroo females were treated with an initial injection of Brushtail Possum ZP3 vaccine ($n = 7$), followed by two booster doses at 12 and 28 weeks, became infertile for the 13-month duration of the trial (Kitchener *et al*. 2009). In comparison, four of the six control-treated kangaroos successfully produced young. The duration of infertility caused by ZP vaccines has not been determined in macropods; however, it appears that a long-lasting effect would be achieved only through administration of multiple booster doses.

GonaCon

GonaCon immunocontraceptive vaccine causes infertility by inducing the production of GnRH-specific antibodies that bind to circulating GnRH and prevent the release of FSH and LH from the pituitary gland, thereby inhibiting the normal function of the ovaries and testes. The vaccine contains GnRH peptide chemically conjugated to an immunogenic, large blue mollusc protein, emulsified with the adjuvant, AdjuVac (mineral oil and heat-killed *Mycobacterium avium*) (Miller *et al.* 2008, 2013). A single injection of GonaCon causes infertility for multiple years in various eutherian species, including White-tailed Deer (*Odocoileus virginianus*), American Bison (*Bison bison*) and wild Boar (*Sus scrofa*) (Miller *et al.* 2004, 2008; Fagerstone *et al.* 2008; Massei *et al.* 2008, 2012; Miller *et al.* 2013), and has been tested in Tammar Wallaby and Eastern Grey Kangaroo. Trials in these macropod species indicate that the contraceptive effect of GonaCon lasts longer in female macropodids than in eutherians. Following injection by hand with a single dose of GonaCon, adult female Tammar Wallabies were rendered infertile for at least 6 years (Snape 2012; Hinds unpublished). Eastern Grey Kangaroo females-treated as subadults with a single injection of GonaCon following capture ($n = 16$) displayed 100% infertility for three years, and over 80% of individuals remained infertile for 8 years (ACT Government 2017).

Current trials are evaluating a remote dart delivery method for administering GonaCon to Eastern Grey Kangaroo females using a dart that simultaneously injects GonaCon and sprays a marking paint on the fur of the animal to allow identification of treated individuals. Results to date indicate that the efficacy of dart-delivered GonaCon is comparable to injection by hand, with both methods inducing over 90% infertility in the third year after treatment (Wimpenny & Hinds unpublished). Administering GonaCon via a dart has also been evaluated in a small trial on White-tailed Deer; however, only low levels of infertility were achieved by both dart delivery and injection by hand in this instance (Evans *et al.* 2015). Remote delivery of GonaCon is currently being evaluated in wild Horses (*Equus caballus*) in Theodore Roosevelt National Park, North Dakota, USA, and is delivering promising results (Dr Doug Eckery, NWRC, USDA, *pers. comm.,* 2020).

Effects of Fertility Control on the Welfare, Behaviour and Health of Macropods

The potential for side effects must be considered when assessing the suitability of fertility control methods for macropods. Short-term welfare impacts related to administration may occur, as well as longer-term effects on welfare, behaviour and health.

Short-term effects on welfare

Currently, most contraceptive methods for macropods require individuals to be captured by trapping and injecting anaesthetics (Nave *et al.* 2002; Wilson *et al.* 2013) or administering anaesthetics via free-range darting (Coulson *et al.* 2008; Wimpenny & Hinds 2018), pole syringe (Wilson & Coulson 2016) or yarding and darting (Colgan *et al.* 2019). All these techniques have the potential to induce short-term physiological stress including a risk of injury or death. Reported mortality rates resulting from darting and anaesthesia range from 1.4% to 10.5% (Tribe *et al.* 2014; Wimpenny & Hinds 2018; Colgan *et al.* 2019). Remote delivery via dart, as has been trialled for deslorelin and GonaCon, reduces a proportion of this risk by eliminating the need for capture and use of anaesthetics. Administration techniques are also a source of potential welfare impacts. Surgical procedures are invasive and complex, whereas other methods require a small skin incision (levonorgestrel), subcutaneous injection of an implant (deslorelin) or intramuscular injection of vaccine. The dart designed for remote delivery of deslorelin allows for simultaneous treatment with a non-steroidal anti-inflammatory agent, which will minimise any pain that may be associated with darting (Herbert & Silva unpublished).

None of the currently available contraceptive implants or vaccines for macropods interfere with active pregnancy, lactation or development of pouch young, so all are safe for use in females supporting young (Nave *et al.* 2002; Herbert *et al.* 2010; Snape 2012; Wilson *et al.* 2013; Wimpenny & Hinds 2018).

Longer-term impacts on the welfare, behaviour and health of female macropods

Minimal impact on health and behaviour has been documented for macropods treated with fertility control. Many changes observed can be attributed to treated females being freed from the costs of reproduction. For example, Eastern Grey Kangaroo females treated with levonorgestrel spent less time in foraging areas (Poiani *et al.* 2002) and had increased survival (Wilson & Coulson unpublished), while deslorelin-treated females spent less time feeding and had a lower forage intake (Cripps *et al.* 2011; Gélin *et al.* 2013) in the field, but not in captive conditions (Woodward *et al.* 2006). Females treated with either implants grew faster and gained more body mass than untreated females (Gélin *et al.* 2016). Similar responses in terms of body parameters are observed in Eastern Grey Kangaroo females treated with GonaCon, and longevity is potentially enhanced (Wimpenny & Hinds unpublished).

Wilson (2012) found no effect of levonorgestrel or deslorelin treatment on the frequency, intensity and duration of sexual interactions, or on social structure. However, Eastern Grey Kangaroo males have been shown to associate less with females treated with levonorgestrel (Poiani *et al.* 2002). Behavioural effects from GonaCon have not been investigated in detail in female macropods, though once infertile, they elicit minimal male sexual interest (Hinds & Wimpenny unpublished). Increased home range and exploratory movements have been detected in females treated with deslorelin (Wilson 2012).

Kangaroos and wallabies treated with GonaCon develop sterile granulomas at the injection sites (Snape 2012; Wimpenny & Hinds 2018); however, these have no apparent impact on welfare or mobility and no infection or open abscesses have been detected. Similar reactions have been recorded in White-tailed Deer (Gionfriddo *et al.* 2011) and are thought to contribute to the longevity of the contraceptive effect (Miller *et al.* 2013). No infection has been detected at the implantation site in over 200 Eastern Grey Kangaroo females treated with levonorgestrel (Wilson & Coulson unpublished) or in over 100 Eastern Grey Kangaroo females treated with deslorelin subcutaneously (Herbert, Cope & Silva unpublished).

Fertility control is often promoted as a more humane option to lethal methods such as shooting. Conversely, it is argued that fertility control is less desirable from a welfare perspective, due to the implications of depriving animals of positive welfare states associated with reproducing and the behavioural impacts of methods that disrupt hormone production (Hampton *et al.* 2015, 2018). That said, current methods are generally applied to females that have already experienced at least one breeding cycle (pregnancy and lactation).

Applying Fertility Control Efficiently and Effectively to Macropod Populations

Recommended approaches

The advantages and disadvantages of the currently available fertility control approaches for macropods are compared in Table 1. Two contraceptive methods, levonorgestrel and GonaCon, provide safe, multi-year infertility following a single administration and are best suited to population-scale management. Deslorelin does not provide a long-lasting contraceptive effect so is a less desirable option for free-ranging populations; however, under some circumstances, annual application of deslorelin may be efficacious. Use of deslorelin may be appropriate for captive populations where only temporary contraception is desired. Surgical sterilisation has the benefit of permanency; however, it is an invasive and resource-intensive technique, requiring veterinary expertise and a field-based surgical setup (Table 1). While surgical sterilisation may be acceptable and possible for small, captive populations, effective application to free-ranging populations would be more costly and difficult. A long-lasting effect from ZP vaccines is achieved only through administration of multiple doses, making them an unsuitable option for managing free-ranging populations (Table 1). Administering booster doses may be feasible in small, captive populations, particularly if it can be done remotely as has been trialled in other species such as Horses (Kirkpatrick *et al.* 1990; Naugle & Grams 2013) and White-tailed Deer (Turner *et al.* 1992).

The need to capture individuals for treatment is the major limiting factor determining the scale at which fertility control can be cost effectively applied (Table 1). Administering GonaCon using a dart has increased the efficiency of treatment in small peri-urban sites where kangaroos are habituated to humans and can be approached closely. However, due to the additional weight the marking paint adds to the dart, further refinement of the method is required to allow safe and efficient darting at longer distances (Wimpenny & Hinds unpublished).

A contraceptive that could be delivered in an oral bait would provide a more efficient delivery system for wild populations. However, no fertility control products have reached the stage where they can be applied orally to wildlife species (Sharma & Hinds 2012). A recent study showed some progress: after several consecutive oral doses of a multimer of GnRH formulated with *Mycobacterium avium* fragments, rats successfully produced antibodies and those with higher titres produced fewer litters (Massei *et al.* 2020). Orally delivered agents have the potential to expand the scale at which fertility control could be applied, provided issues related to appropriate individual dosing and eliminating non-target uptake of the contraceptive can be addressed.

The timing of administration is crucial for maximising efficacy of agents that have no effect on active pregnancy or reactivation of dormant blastocysts. Lower rates of infertility, likely attributed to fertilisation prior to (or immediately after) treatment rather than contraceptive failure, have been seen in Eastern Grey Kangaroo females in the year following treatment with GonaCon, levonorgestrel and deslorelin (Nave *et al.* 2002; Wilson *et al.* 2013; Wimpenny & Hinds 2018). The optimum timing of administration of each contraceptive method to Eastern Grey Kangaroo is provided in Table 1. The key factors considered in these recommendations include, where practical, avoiding treating females that may be undergoing pregnancy (no pouch young present); avoiding treating females that have dormant blastocysts that will reactivate once existing pouch young exit the pouch or are removed; maximising the duration of effect by administering treatment close to the next breeding attempt; and, in the case of contraceptive vaccines, ensuring sufficient time for an adequate antibody response to develop before the next breeding attempt. Existing pouch young can be retained with all agents; however, removal of young may be desirable in some cases from a population management perspective. The prevalence of dormant blastocysts in Eastern Grey Kangaroo is unknown but has been observed in females with young aged 112 days and over (Poole 1982) and is predicted to be more common when environmental conditions are favourable (Poole 1973). The ideal timing of administration to other macropod species may differ from the recommendations for Eastern Grey Kangaroo because of differences in the occurrence of dormant blastocysts. For example, blastocysts have never been recorded in the Western Grey Kangaroo (Poole & Catling 1974), while species such as the Red Kangaroo, Common Wallaroo (*Osphranter robustus*) and Proserpine Rock-wallaby (*Petrogale persephone*) undergo post-partum oestrus and are likely to have a dormant blastocyst regardless of the age of their existing pouch young. It is also essential to consider the impacts on the welfare of females and their pouch young

Table 1. Do currently used methods meet the desirable criteria for an ideal fertility control agent for macropods?

Criteria	Surgery	Implants		Vaccines	
		Deslorelin	Levonorgestrel	Zona pellucida	GonaCon (GnRH)
Mode of action	Vasectomy, tubal ligation or gonadectomy	Inhibits LH and FSH, follicular development and ovulation	Inhibits LH release and ovulation	Antibodies against egg coat proteins disrupt fertilisation and oocyte development	GnRH antibodies prevent binding of GnRH to pituitary, disrupt downstream activity of the gonads
Sex targeted	Males and females	Females only; males resistant to treatment (Tammar Wallaby)	Females only	Females only	Females only; effects in males more variable and shorter duration than females (Tammar Wallaby)
Specificity	High	High	High	High	High
Efficacy/longevity of single treatment	Permanent	1.5 – 2 years; dose-dependent	>7 years in 98% of females administered 5 x 55-mg implants	<2 years; requires several boosters	>5 years in 80% animals after hand injection; >3 years in 90% after dart delivery
Humaneness	Medium due to invasiveness of procedure	High	High	High after hand injection; dart delivery untested	High after hand injection and dart delivery
Safety	Medium due to post-surgery recovery	High; does not affect active pregnancy, lactation or development of young; male interest unaffected	High; does not affect pregnancy, lactation or development of young; male interest unaffected	Medium; multiple captures for boosters required, which increases risk of injury; effect on male interest unknown	High; does not affect active pregnancy, lactation or development of young; minimal male sexual interest thereafter
Ease of delivery	Capture of animals required	Capture of animals required for implantation via SC injection; dart delivery possible	Capture of animals required for implantation via a small skin incision	Capture of animals required for primary and booster injections; dart delivery not tested in macropods	Capture of animals required for IM injection; dart delivery possible
Cost-effectiveness (relative)	Low; not practical for use with large populations	Medium; suitable for small populations for short-term responses	Medium	Low; boosters required	Medium for hand injection; high for dart delivery if animals approachable or maximum darting distance can be improved
Environmentally benign	Yes	Yes	Yes	Yes	Yes
Timing of administration for EGKs	Possible all year	Depending on likelihood of blastocysts, treat adult females when small PY present to ensure they are not pregnant or carrying blastocyst, or when medium to large PY present to maximise duration of effect	Treat adult females when small PY present to ensure they are not pregnant or carrying blastocyst; PY can be retained, but removal recommended for population management purposes	Treat adult females when small to medium PY present to allow sufficient time to administer booster doses before next breeding attempt; retain PY	Treat adult females when medium PY present so breeding females easily identified and to allow sufficient time to mount antibody response before next breeding attempt; retain PY

Table 1. (Continued)

Criteria	Surgery	Implants		Vaccines	
		Deslorelin	Levonorgestrel	Zona pellucida	GonaCon (GnRH)
Advantages	Permanent	Reversible, short-term responses may be useful in some situations; dart delivery possible	Single-treatment, long-term efficacy	Can be reversible if insufficient boosters given or antibody titres not sustained	Single-treatment, long-term efficacy; dart delivery possible and efficacious
Disadvantages	Highly invasive; treating only males not practical for semi-captive populations	Short-term response; male interest and mating can occur soon after implant placement but no young result	Minor surgical procedure for implantation; unable to deliver remotely	Multiple boosters required; long-term efficacy not tested in macropods	Dart delivery needs further refinement, currently animals must be within 25 m; product available under restricted use APVMA permit, application for registration submitted to APVMA
Recommendations	For specific circumstances; small captive populations	Useful if reversibility of response required; product is approved and readily available	Practical and feasible with trained personnel; product is approved and readily available	Not practical at present; no reagents available	Practical and feasible with trained personel, particularly with further improvements to dart delivery

APVMA = Australian Pesticides and Veterinary Medicines Authority; EGK = Eastern Grey Kangaroo; FSH = follicle-stimulating hormone; GnRH = gonadotrophin-releasing hormone; IM = intramuscular; LH = luteinising hormone; PY = pouch young; SC = subcutaneous.

in the timing of administration. Capture and anaesthesia should not be undertaken when ambient temperatures are high, especially during the recovery period. Adults with large fully furred young that may escape during capture should not be targeted.

Population-level studies

Studies on fertility control for macropods have focussed on individual efficacy, with few published studies assessing the long-term effects on populations. However, some long-term studies are currently underway.

Population-level fertility control programmes have been implemented at two sites in Victoria where Eastern Grey Kangaroo was overabundant (Wilson & Coulson unpublished). A fertility control programme was initiated in 2012 at Serendip Sanctuary, a 250-ha nature reserve located 50 km south-west of the Melbourne. A total of 75 adult females were captured, tagged and treated with five 55-mg levonorgestrel implants. Following a culling operation to remove many unmarked kangaroos, the proportion of adult females that had been treated was 73%. This proportion declined over time, so another 45 adult females were implanted in 2017, restoring the proportion of treated females to 74%. Efficacy has been extremely high from the outset of the programme, with 98-100% infertility each year, and has delayed the need for further culls.

The second site, Gresswell Nature Conservation Reserve is a 52-ha nature reserve 15 km north-east of the Melbourne CBD. Culling at this site was vigorously opposed by animal activists, so Parks Victoria initiated an intensive fertility control programme in 2015. A total of 61 adult females, representing 97% of the female population, were progressively treated with five 55-mg levonorgestrel implants over three years (2015, 2016 and 2018). Four females that were treated in 2015 bred in subsequent years. Three of these females were treated again in 2018 and have not bred again. The implants were fully effective (zero breeding) in 2019, and population density was stable.

Population-level efficacy of GonaCon is currently being assessed in Eastern Grey

Kangaroo populations in Canberra (Wimpenny & Hinds 2018). Following treatment of over 90% of females in three small populations, fecundity has decreased to between 0 and 22%, while fecundity of over 53% has been observed in untreated populations (n = 7) (Wimpenny & Hinds unpublished).

Successful and efficient population-level fertility control is achieved by ensuring that the appropriate proportion of females in the population is rendered infertile to have the desired effect on population growth. This proportion needs to be high enough to overcome any compensatory processes that result from the use of fertility control, such as increased survival and breeding of fertile animals, and offset the effects of immigration (Barlow *et al*. 1997; Chambers *et al*. 1999; Hone 2004; Williams *et al*. 2007; Ransom *et al*. 2014). Mathematical models have been developed for various wildlife species to predict the proportion of infertile animals that must be maintained in the population and to evaluate fertility control against or alongside other management tools (e.g. Hobbs *et al*. 2000; Bradford & Hobbs 2008; McLeod & Saunders 2014; Pepin *et al*. 2017; Hynes *et al*. 2019; Croft *et al*. 2020). Current population-level field trials in Eastern Grey Kangaroo have implemented the approach of treating a high proportion of females in the population, but this approach could be refined if population models for macropods were developed.

Fertility control methods aim to reduce recruitment and therefore slow population growth. They are less effective at rapidly reducing population size compared with lethal methods, particularly for long-lived animals, because they rely on natural mortality and emigration over time to reduce the population (Bomford & O'Brien 1992; Hone 1992). While this lag in effect may be acceptable in populations that are yet to reach carrying capacity, a more rapid response is often required in overabundant populations to reduce damage or conflict. In these situations, an integrated management programme that incorporates lethal intervention to initially reduce the population size followed by fertility control applied to females to slow the subsequent growth of the population is likely to be the most effective approach (Hone 1992; Barlow *et al*. 1997; Pepin *et al*. 2017).

Recommendations and Future Research Directions

GonaCon and levonorgestrel are currently the most appropriate fertility control methods for use in free-ranging macropod populations. However, these tools are only suited to relatively small, discrete populations with minimal immigration, where kangaroos can be approached closely for safe and efficient capture and treatment. For overabundant populations, fertility control would be best applied in combination with lethal control to provide an initial reduction in population size. In future years if fertility control is applied to only breeding females, this will likely allow a low level of breeding to occur, which will offset mortality and maintain the desired population size, potentially reducing or eliminating the need for future lethal interventions.

Long-term field trials are necessary to fully evaluate the efficacy of fertility control for managing macropod populations, including consideration of behavioural, health and welfare impacts. In addition, the development of population models for macropods would be beneficial for estimating the proportion of females that must be rendered infertile and would permit evaluation of different tools and scenarios that could be used to achieve the desired management goal.

The development of contraceptive options that can be administered remotely to macropods would increase the scale at which fertility control can be efficiently applied. This could be achieved in the first instance by improving dart delivery for existing agents, while the development of new, orally deliverable products continues to be the longer-term goal.

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