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Development of a Model for Flystrike Resistance Management

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Contents

Executive Summary

Flystrike is of major concern to the Australian sheep industry, with the Australian sheep blowfly (Lucilia cuprina) demonstrating the ability to develop resistance to commonly used insecticides. Over time, chemical and non-chemical strategies have been recommended to sheep producers to manage resistance development, mainly the rotation of chemical groups. Literature regarding the effectiveness of chemical rotations is sparse, with the consensus that rotations should be implemented, but without confidence in which type of rotation strategy is best. Similarly, producers are advised that non-chemical strategies such as shearing and/or crutching during the flystrike season and monitoring the flock for signs of flystrike are worthwhile flystrike management strategies with little knowledge of how these strategies influence flystrike resistance development.

The aim of this study was to develop and utilise a computer model to evaluate the effects of rotations, monitoring, and shearing or crutching on resistance development in various resistance genes. The data collected from the model was then used to assess the current advice given to producers regarding flystrike resistance management on the FlyBoss website. The model consisted of various assumptions and settings that were tested for their functionality and importance. Then various rotation, shearing and crutching simulations were run for simulated periods of 20 or in some cases 50 years, with and without a genetic disadvantage for genes for resistance. Two types of monitoring were tested to explore the effect of monitoring on resistance development and reduction in flystrike related costs.

All simulated rotations delayed the onset of resistance development against individual products and were more cost-effective than using any insecticide continuously, but rotations do not prevent resistance from accumulating over time. Shearing in spring, summer or autumn proved more cost-effective than shearing in winter, although shearing in summer increased the rate of resistance development, possibly due to shearing when the use of treatment has resulted in a highly resistant population of flies. Similarly, including a crutching in spring, summer or autumn also proved more cost-effective than not crutching, but with summer crutching increasing the rate of resistance development. Evaluating monitoring was more complex, with the cost of labour being an important factor in determining the cost-effectiveness of implementing a higher frequency or more intense monitoring. More intense monitoring, with the physical or chemical killing of flies on the struck sheep, reduced the rate of resistance development. The advice given in FlyBoss was regarded as partially incomplete, with areas regarding the impact of flystrike management strategies on flystrike resistance development requiring elaboration.

1. Introduction/hypothesis

Historically, the introduction of insecticides against the blowfly has been followed by resistance – with the first reported resistance against organophosphates arising shortly after its introduction (Shanahan and Hart 1966). At the time, pesticide resistance management was not of high priority as new pesticides were continuing to be developed (Sawicki 1981). Recently, resistance to the largely reliable chemicals dicyclanil and cyromazine has been confirmed, posing a major threat to the Australian sheep industry (Sales *et al.* 2020). Insecticide resistance may reduce the protection period of treatments and therefore compromise flystrike control, subsequently impacting production and exacerbating to welfare issues (Sales 2020).
For study of resistance development, data needs to be collated over long periods of time – proving difficult for experimental research and relying on anecdotal evidence. A computer model was used for this research as a model offers a non-invasive solution for studying resistance development for long period of time, e.g., 20 years.
This study aimed to test the sensitivity and functionality of assumptions in the model and therefore identify assumptions that have a strong influence on the results; and test various management strategies on the resistance of blowflies to different chemical treatments, such as: rotation of chemicals, monitoring levels, and shearing or crutching times; while providing information that can be used to advise wool producers on how to limit future blowfly resistance and/or deal with existing resistance to various chemical groups. Currently, FlyBoss (www.flyboss.com.au) offers advice on flystrike resistance, and it is hypothesised that the advice given on the FlyBoss website is the best available advice to producers regarding the management of flystrike resistance.

2. Literature Review

Introduction

Flystrike in Australia costs approximately $173 million annually in treatment, prevention and production losses (Lane *et al.* 2015). Insecticides are a cost-effective means of flystrike control, in which a chemical is applied to the sheep via dipping, jetting or spraying, to prevent flystrike, or a dressing is applied to an already flystruck sheep (Tellam and Bowles 1997; Heath and Levot 2015). However, over the past 60 years, the development of resistance has caused some chemicals used to treat flystrike to become ineffective, resulting in reduced protection periods (Levot 2001) and loss of production through sheep mortality, reduced wool production and quality (Colditz *et al.* 2005) and lamb losses associated with severe flystrike in ewes (Horton *et al.* 2018). Historically, the production and use of new chemicals to treat flystrike have mostly been followed by the rapid development of blowfly resistance to the insecticide (Levot 2001).

The basic mechanism of insecticide resistance development is as follows: A population of blowflies is exposed to a new chemical treatment with high mortality, so individuals in the population that can survive this toxicity continue to breed with a selective advantage, selection pressure on these surviving individuals continues and the proportion of blowflies resistant to the chemical treatment increases with successive generations (if the chemical treatment is continuously used) (Heath and Levot 2015). In this review, resistance is defined as the ability of insects to tolerate concentrations of chemical treatments that would normally be lethal to the majority of members of that species.

Flystrike

Flystrike, or cutaneous myiasis, is a parasitic disease that occurs when the female blowfly *L. cuprina* lays eggs on the skin or in the wool and resulting larvae feed on the sheep (Phillips 2009). Although the immediate mortality due to flystrike is relatively small, morbidity remains quite high. The low mortality rate of 2% seen by Horton *et al.* (2018) is a result of good monitoring that encourages early detection of flystrike - where early detection allows for treatment before flystrike increases in severity.

Therapeutic treatment applied when flystrike is detected early prevents further production losses as well as reducing the risk to animal welfare (Horton *et al.* 2018). The majority of flystrike is recorded in the breech area in an unmulesed flock (Horton *et al.* 2018), as mulesing reduces wool staining, dags and breech wrinkle – which all lead to an increased risk of breech strike due to a favourable moist environment for blowfly larval growth (Phillips 2009).

Losses due to flystrike

Production losses due to flystrike can arise directly due to damage to the sheep itself, through reduced growth and decreased wool quality (Heath 1994). Flystrike causes significant losses in body weight and condition score, effects which were still considerable 3 months after flystrike occurred (Horton *et al.* 2018). Severe flystrike decreased wool production by reducing the amount of clean fleece produced (Horton *et al.* 2018) and decreasing staple length and staple strength (Colditz *et al.* 2005). Horton *et al.* (2018) demonstrated a relationship between the severity of flystrike and the decrease in wool quality, highlighting the importance of a high-level of monitoring to detect flystrike while still at a low-level of severity. There is a large cost associated with preventative and therapeutic chemical treatment, as well as the labour required to apply this treatment (Heath 1994). Other labour costs include time spent monitoring the flock for flystrike, and crutching and shearing with the intention of reducing the risk of flystrike (Heath 1994). The study conducted by Sackett *et al.* (2006) calculated a total cost of $280m due to flystrike, with a loss of production of $83m and a cost of prevention of $197m.

Flystrike Management

A national survey of management strategies for internal and external parasites of sheep was conducted in 2018 with 354 respondents (Colvin *et al.* 2020). Survey results are summarised in Table 2.1, showing a high reliance on the use of preventive chemical treatment. The low proportion of mulesing as a form of flystrike management in 2018 may be due to the incentive for producers to move away from mulesing due to concerns related to animal welfare.

Table 2.1 Proportion of flystrike management strategies used by respondents in 2018**.** Adapted from (Colvin *et al.* 2020).

Management Strategy	Proportion (%)
Timing of crutching	76.4
Preventative chemical treatment	75.9
Timing of shearing	63.1
Mulesing	46.8
Breeding (Genetic selection)	46.4
Flytraps	5.1

Non-pesticide management

General management strategies for flystrike control include shearing, crutching and mulesing, and optimising the timing of these strategies can reduce the risk of flystrike (Tellam and Bowles 1997; Heath and Levot 2015). Short wool after shearing reduces the risk of flystrike as short fleece dries faster than long fleece, and moisture is required for the development of the maggot (Tellam and Bowles 1997; Wardhaugh 2001). Crutching removes dags and urine-stained wool - reducing the likelihood of breech strike (Phillips 2009). Mulesing is an effective way of preventing breech strike through the surgical removal of skin from the breech area, however, there is public pressure to stop this practice due to the perceived ethics of this procedure (Tellam and Bowles 1997; Phillips 2009). Alternative control strategies that do not rely on the use of chemicals (to slow down the rate of resistance development), or mulesing (due to public concern of sheep welfare), should be integrated with current chemical control strategies (Levot 2001; Phillips 2009).

Breeding for resistance to flystrike

Long-term flystrike management strategies include breeding for sheep resistance to flystrike, where producers could potentially purchase sheep with flystrike resistance and breed these genes into their flock, or identify resistant sheep from their flock through resistance testing (Tellam and Bowles 1997). Resistance genes could result in sheep naturally resistant to flystrike due to the introduction of plain-bodied sheep (Greeff and Karlsson 2005). Greeff *et al.* (2013) found that breech strike is a heritable trait, with indicator traits such as dags, urine stain and breech cover. Selecting against these indicator traits could indirectly select for breech strike resistance. The authors also found a correlation between breech strike before weaner shearing and breech strike later in life, suggesting that sheep struck early in life should be removed from the flock and breeding programmes as breech strike is a repeatable trait (Greeff *et al.* 2013). James (2006) reviewed the approach of breeding to replace mulesing and tail docking in the prevention of flystrike.

Vaccination

Vaccinations to protect sheep against flystrike or fleece rot offer another non-pesticide management strategy (Tellam and Bowles 1997; Heath and Levot 2015). A hormone-based approach to vaccine development was used by Bowles and Mancuso (2001). Antibodies were generated against a hormone involved in the moulting stages of the blowfly. Although there was a 27% reduction in the weight of blowfly larvae and a 23% reduction in the number of larvae in vaccinated sheep, these results were not statistically significant due to the variation in the response between sheep in the trial. Another study conducted by Bowles (2001) found 8 potential vaccine candidates that could inhibit larval growth at a statistically significant level. Antibodies were raised to larval antigens native to the blowfly. Similarly to the results of Bowles and Mancuso (2001), a reductions in the weight of blowfly larvae up to 60% was recorded but was not statistically significant due to the variation in the response between sheep in the trial.

CSIRO is currently designing a vaccine against flystrike that initiates the production of antibodies against proteins in the blowfly maggot (Vuocolo 2021). The commercialisation of a flystrike vaccine is not expected in the near future – impeded by the currently expensive methodology in extracting natural protein from the blowfly itself, rather than the cost-effective alternative of artificially synthesising these vaccine candidates (Vuocolo 2021).

Pesticide management

Pesticide treatment is commonly used for the prevention of flystrike when the strike risk is high and prolonged periods of protection are required (Horton and Hogan 2010; Levot 2013). Producers primarily rely on the chemical treatments dicyclanil, cyromazine and ivermectin to provide long periods of flystrike protection (Heath and Levot 2015). Cyromazine only exhibits a relatively low level resistance and therefore is crucial for flystrike control (Levot 2001). Previously used insecticides for flystrike control included dieldrin and organophosphates. However, dieldrin resistance developed within three years and organophosphate resistance developed within 8 years (Levot 2001). Pesticide management can be used in conjunction with optimising shearing times as the insecticide has a higher concentration in shorter wool and is, therefore, more effective (Tellam and Bowles 1997).

How Flystrike Management Causes Resistance

Lice mitigating practices

Chemicals traditionally used for lice control have unintentionally selected for resistance in the blowfly, by reducing the efficacy of similar chemicals used for flystrike control (Levot 2001). If lice are present in the flock and treatment is needed, the chemical used to treat lice should not be from the same chemical group used to treat flystrike in the population during that wool-growing season (Levot and Sales 2004). Alternatively, if no lice are present in the flock, then avoiding chemical treatment will prevent the development of insecticide resistance (James *et al.* 2011). Diflubenzuron is an insect growth regulator commonly used for lice treatment. Resistance to diflubenzuron is also seen in the blowfly, where this chemical is now unable to prevent flystrike in some parts of Australia (Levot and Sales 2004). Levot and Sales (2004) suggests that the use of diflubenzuron lice treatments may have contributed to the development of diflubenzuron resistance in the blowfly. Therefore, regular rotation of louse treatments needs to be considered alongside rotation of flystrike treatments (Levot 2001; James 2010; Heath and Levot 2015).

Flystrike Resistance

If the frequency of resistance is high in a population, it may lead to a reduced length of protection. Nevertheless, chemicals with some resistance can still achieve an economically viable level of control (Jutsum *et al.* 1998). Cyromazine resistance has been detected, but this current level of resistance does not pose a major threat to the long period of protection required by producers (Levot 2013). Cyromazine has been used for flystrike control for the past 40 years and has not developed strong resistance as has been seen in other pesticides developed within a similar time frame (Levot 2001). Cyromazine is not effective for lice control, which alongside its potential for homozygous lethality (Yen *et al.* 1996), may explain its low level of resistance (Levot 2001).

The risk of insecticide resistance development is increased by frequent application of the chemical, or a similar chemical, and a poor application method or underdosing. Factors relating to the blowflies themselves also impact the rate of development of resistance, such as the proportion of the blowfly population subjected to the chemical treatment (Heath and Levot 2015).

Cross resistance

Cross-resistance is where resistance to one insecticide also results in reduced susceptibility to another insecticide through a single resistance mechanism (due to the same gene) (Cloyd 2010). The blowfly does not need to be exposed to the alternative insecticide to have resistance or reduced susceptibility to this insecticide. Multiple resistance is where the blowfly is resistant to different insecticides through different resistance mechanisms (Cloyd 2010). Levot and Sales (2004) found cross resistance between a diflubenzuron-resistant laboratory strain to dicyclanil and, to a smaller extent, cyromazine. Concerningly, diflubenzuron and dicyclanil are unrelated compounds - highlighting the importance of this cross-resistance discovery. With the industry's reliance on dicyclanil, flystrike prevention would be compromised if this cross-resistance were to develop in the field. Similarly, Sales *et al.* (2001) found statistically significant correlation between diflubenzuron resistance and resistance to the organophosphate diazinon in blowfly populations.

Flystrike Resistance Strategies

Chemical management

To manage resistance, susceptibility of the blowfly to chemicals must be maintained, either by dealing with current resistance or preventing the development of future resistance (Denholm and Rowland 1992; Heath and Levot 2015). Chemicals with some levels of resistance can still achieve an economically viable level of control – causing them to be used by producers until the blowflies are completely resistant (Jutsum *et al.* 1998). Overuse of the same chemical or chemicals from the same group can lead to resistance. Rotating chemical treatments by alternating between dissimilar chemicals may reduce the risk of insecticide resistance development – especially when producers need to apply insecticide twice in a flystrike season to achieve the required protection period (Waghorn *et al.* 2013). Using mixtures of unrelated chemicals may reduce the risk of development of resistance to a single insecticide, however there is little evidence to advocate for the effectiveness of mixtures in mitigating resistance (Cloyd 2010). Pesticide mixtures expose the blowfly to different chemicals simultaneously, whereas pesticide rotations use chemicals with different modes of actions and/or active sites alternatively (Heath and Levot 2015). The complexity of resistance suggests producers should not rely on the production of new insecticides to manage flystrike resistance, as it has been predicted that current resistance may confer resistance to future novel insecticides (Denholm and Rowland 1992). The production of new insecticides is only a short-term solution as the consequent development of insecticide resistance cannot be prevented. Principally, developing new insecticides is a complex and expensive task that does not offer a sustainable long term solution in managing flystrike resistance (Denholm and Rowland 1992).

Shearing and crutching

Reducing the exposure of blowflies to insecticides in a season by suitable scheduling of shearing and crutching may reduce the risk of resistance development (Horton *et al.* 2019). The timing of shearing and crutching can be optimised to remove remaining insecticide treatment on the wool when the insecticide is at a sub-lethal concentration, which otherwise would be selecting for resistant blowflies and therefore contributing to resistance development. Using a computer model, Lucas and Horton (2013) found that the timing of shearing was important, since shearing during the flystrike season could increase costs of flystrike management by interrupting the effectiveness of preventative treatment.

Resistance management of other sheep parasites

Resistance to treatment is seen in other sheep parasites and different management strategies used for different parasites may be of use for flystrike resistance management.

Worms

Internal parasites, especially worms such as *Haemonchus contortus*, also pose a major threat to the sheep industry. Resistance to commonly-used anthelmintics is widespread, leaving some anthelmintics ineffective. Resistance to anthelmintics can be a result of over-use/frequent treatment, underdosing and unnecessary treatment - similar causes as seen in pesticide resistance in flystrike (Leathwick *et al.* 2001; Hale 2006). The concept of "refugia" has become crucial in managing anthelmintic resistance, where a proportion of worms are intentionally untreated to ensure susceptibility in the population to the anthelmintic, thus reducing the frequency of resistance genes (Van Wyk 2001; Hale 2006). Methods such as FAMACHA© and smart drenching ensure selective and effective use of anthelmintic treatment, so that only sheep that need treatment are treated. These methods offer a sustainable approach when using chemical management and when used in conjunction with non-chemical management, should reduce the rate of resistance development (Hale 2006). Targeted selective treatments strategies are being developed to reduce the rate of anthelmintic resistance (Berk *et al.* 2016, 2017). Adopting a similar approach in selectively treating sheep that are flystruck, rather than treating the whole flock, may also reduce the rate of insecticide resistance. The use of combination anthelmintics has been predicted to maintain efficacy of chemicals in cases of established drug resistance and slow down the development of future resistance (Leathwick *et al.* 2009; Bartram 2013). This method may also be useful for control of flystrike.

Lice

Resistance to chemicals used to treat lice has been documented, including resistance to the insect growth regulator diflubenzuron (James 2010). Similar to flystrike resistance, poor application and overuse of chemicals probably led to the development of current resistance and will lead to further resistance in the future. Recently, there has been a shift from annual lousicide treatment, regardless of lice infestation, to an integrated and insecticide-conscious approach for lice control as resistance develops (James *et al.* 2011). Similar to flystrike management, rotating chemicals and optimising the timing of shearing can be integrated into lice control. In contrast to the management of the development of resistance to flystrike control chemicals, it is assumed that complete eradication of a resistant genotype of lice is possible by rotating chemicals. This type of eradication is not possible with blowflies or internal parasites due to their off-host life cycle stages (James *et al.* 2011).

Current Advice

FlyBoss

The FlyBoss system includes up-to-date information relevant to flystrike management and offers a flystrike risk simulator that can target strategies to individual sheep producers. FlyBoss supports producers in decision-making and allows for comparison between an existing management strategy and a future management strategy (Horton and Hogan 2010). The FlyBoss system (www.flyboss.com.au) suggests various methods for preventing future development of resistance on a property or to prevent the further development of current resistance on a property. Notably, an integrated management approach is suggested, where a combination of long-term management strategies (such as breeding for resistance) and short-term (such as efficient insecticide usage) is used. Chemical rotation is encouraged, stating that rotating insecticides from different chemical groups will decrease the rate of resistance development – even though there is sparse literature to support whether chemical rotations prevent resistance development in blowflies. The FlyBoss decision-making tool uses a weather-driven flystrike risk model (Wardhaugh *et al.* 2007) to estimate strike risk, adjusting for individual shearing or crutching schedules and chemical treatments. The program can then be used to compare the effects of adjusting shearing and crutching times, mulesing or alternative breech modifications and different chemical treatments (Horton and Hogan 2010). However, the advice provided in the model does not include insecticide resistance management.

Benefits and limitations of models
Models can be run for many simulated years, allowing for comparisons of multiple management choices over a prolonged period without waiting for field data. For example, Lucas *et al.* (2016) was able to run a predictive model for lice infestation over 20 years for 50,000 simulated sheep properties in Australia.

Models depend on assumptions, some of which have little to no literature to provide a reliable value. Therefore, there is the possibility that the assumptions of the model are wrong, decreasing the validity of the results produced. However, models can be used to check ranges of values for assumptions and their effect on the model, therefore indicating the importance of that assumption to the model. These indications can be used to direct future research into determining estimates for assumptions of value to the model.

Conclusion

Continual research through experimental studies and modelling is essential for the discovery of new and improved methods of insecticide resistance management, and moreover, the prediction and monitoring of future resistance. The production of new insecticides is appealing, although expensive, and resistance to any new insecticides may develop rapidly. The development of effective non-pesticide management strategies such as vaccines is desirable for avoiding widespread failure for flystrike control as a result of resistance. An integrated approach that combines many different control strategies is needed to manage flystrike and to prevent the development of resistance of blowflies to insecticides, where non-chemical control methods complement chemical control methods. Tools such as FlyBoss can be used by sheep producers to make informed decisions regarding flystrike management, however FlyBoss is a single-year model and cannot offer advice for dealing with insecticide resistance development over the course of many years. A multi-year flystrike model is needed to inform producers on the best flystrike control strategies while considering the possibility for resistance. This could ensure that management practices used at the time are also sustainable in maintaining insecticide susceptibility in blowflies in the future.

3. Project Objectives

• Development of a model and testing to confirm that obvious scenarios for a single property at a time can be covered. (The broader examination of a wide range of scenarios, in different regions and with different shearing regimes, is outside the scope of this project).

• Demonstrate the functional ability of the model by reporting the effect on gene frequencies of standard management, such as regular use of the same chemical group, vs switching two groups during the same fly season, or in successive fly seasons. Examine the effect of summer vs winter shearing, since summer shearing will remove intermediate concentrations of pesticide used in spring, possibly reducing selection pressure for resistance.

• By using sensitivity analysis, identify assumptions that have a strong effect on the results, to find areas where additional research or information is needed, from current studies on resistance, from genetic studies, or from surveys of producer management and their experience with decreased protection periods. When available, this information will be used to fine-tune the assumptions in the model.

4. Success in Achieving Objectives

The Flystrike Resistance Decision Support System has been shown to be suitable for standard scenarios, such as the examination of rotation options, with or without a genetic disadvantage for resistance genes. It can be used to examine the benefits or disadvantages of changes in shearing or crutching schedules, and the effects of increasing monitoring and the killing of flies found on struck sheep.

Rotation of products used to prevent flystrike will delay the development of resistance to each product. However, unless there is a disadvantage for the resistance genes the delay will be short-term. For example, the rotation of three products will maintain the functionality of the products for approximately the same total period of time as if each product was used continuously until no longer effective. There is little difference between rotation of products within each year (when two treatments are required each year) compared with rotation in successive years. However, use of only one product each year is always preferable to use of two treatments each year.

The time of shearing and crutching is important and although these can reduce the need for extra chemical treatment, there are situations when the timing of shearing or crutching can increase the rate of development of resistance.

Several assumptions required by the model are not well known and they may affect the rate of development of resistance. The background level of genes for resistance is probably low, but cannot easily be measured until it reaches levels where resistance is obvious. However, the gene frequency may have been increasing for several years before this occurs. The proportion of flies that are able to reproduce without being exposed to any pesticide on the sheep is not known. This proportion strongly affects the rate of increase of resistance. Although this information is not currently available, and these values affect the rate of increase of resistance, they do not necessarily alter the benefits of using any particular management system.

It is not known whether some genes for resistance give a disadvantage to the flies when there is no exposure to the relevant pesticide. If there is a disadvantage, then rotations become much more useful, since the frequency of resistance genes will fall in the period when another pesticide is used. However, if there is no disadvantage, then rotation of products is less useful and other methods must be used to manage flystrike.

5. Methodology

The main feature of this project was modelling flystrike resistance development using an existing computer program. This section provides definitions of terms used in the program and descriptions of the calculations made by the program. There were 11 sections of the settings in the program that had to be determined: chemicals, strike severity, wool loss, death loss, fertility loss, cost of strike, other costs, flies, genes, resistance, and miscellaneous program settings; which will all be described here.

Program function

Flystrike Resistance Decision Support System uses a weather-driven model (Wardhaugh *et al.* 2007) to estimate the risk of flystrike, while considering the effect of shearing, crutching and chemical treatment. The program was developed by Brian Horton, Tasmanian Institute of Agriculture, University of Tasmania. The program was based on the model used by Lucas and Horton (2013) and Percival and Horton (2014) but was modified to allow for resistance.

Weather and Properties

Weather data is used from three locations: Inverell (latitude –29.8, longitude 151.1, 1965–2005), Gunning (latitude –34.8, longitude 149.7, 1978–2005) and Flinders Island (latitude –40.1, longitude 148.9, 1962–

2005). The weather data is used to estimate the flystrike risk using the flystrike model created by Wardhaugh *et al.* (2007).

Each location has different lengths of flystrike season, with Gunning having a flystrike season representative of an average farm and therefore was allocated the default location for testing purposes. The overall flystrike risk in Inverell is similar to Gunning, except that Inverell has no overwintering period. Gunning has a higher proportion of breech strike than Inverell. Flinders Island has the lowest flystrike risk out of the three locations. The program uses sliders to indicate the level of strike risk in untreated sheep and the level of breech strike compared with body strike. The value for these sliders used was an average flystrike risk for the region and 3x breech strike compared to body strike. Other regions could have been used if they had a similar weather pattern to one of the three included regions and if the relative flystrike risk for that region was known.

Sheep

The program included five sheep classes: ewes, rams, wethers, hoggets, and lambs. The program allowed customisation of the sheep variables to make the output unique to each property. The number of each class of sheep, the shearing and crutching dates and breech modification could be chosen. Breech modifications included mulesing, clips, or intradermal injection. The age/sex of the sheep could have been chosen to allow sub-group analysis, as different ages/sexes have different flystrike risk. Only one class of sheep can be tested at a time in the model, so the default sheep class was ewes, and the default mob size was 10,000 sheep to represent an average sheep population (Hall *et al.* 2014).

Shearing and crutching

Crutching and shearing dates were included due to the influence they have on chemical concentration in the wool and flystrike risk. The program allowed for one shearing date and up to four crutching dates to be selected.

Labour

Cost of monitoring

It was assumed that a producer could spend extra time monitoring the flock for signs of flystrike in order to apply treatment. The time spent monitoring did not include time spent treating struck sheep (which is costed separately) or monitoring conducted while undertaking other farm tasks (such as checking water troughs or fences). The $25.51/hour cost of monitoring was taken from the 2020 Pastoral Award Pay Guide (www.fairwork.gov.au) for a farm and livestock hand at level 2, as level 2 was the minimum level that a farm and livestock hand could handle and apply chemicals (D. Emmerton 2021, personal communication, 2 March). The farm and livestock hand carrying out monitoring would need to be able to apply treatment to a flystruck sheep if required. Monitoring was represented by two factors: monitoring level for routine monitoring and monitoring intensity for extra monitoring. Monitoring level is the number of days per week monitoring occurs. Monitoring is assumed to be conducted 1 day a week for a poor level, 3 days a week for an average level, 5 days a week for a good level and every day of the week for an excellent level of monitoring. Extra monitoring is assumed to be conducted when sheep have been treated and monitoring is intended for detecting and killing the maggots before they fall off the sheep and survive on the ground. This extra monitoring is represented by a monitoring intensity factor, which indicates the proportion of maggots that are killed. For an average level of monitoring, with no extra monitoring, the cost of monitoring was $25.51 per 1000 sheep per week.

Cost of labour for preventative treatment

The cost of labour for application of preventative treatment included the hourly pay rate for a farm and livestock hand at level 2 ($25.51/hour) with the time required depending on the method of application. Cost of labour when using a spray-on treatment was lower ($0.12 per sheep) than for jetting ($0.28 per sheep) when treating for both body and breech. Proportions were included to represent the labour associated with only treating to prevent body strike or only treating for breech strike.

Cost of crutching

The cost of crutching a mulesed sheep was set at $1.09 and the cost of crutching an unmulesed sheep was set at $1.29. The cost of crutching was adapted from the 2020 Pastoral Award Pay Guide (www.fairwork.gov.au), with added costs associated with crutching such as shed staff and rounding up the flock. It was decided that the cost of crutching should be at least 20% higher for unmulesed sheep in comparison to mulesed sheep due to the additional time it takes to crutch unmulesed sheep with a larger dag load (Horton and Iles 2007).

Chemicals

The program allowed for the choice of chemical (Table 5.1), the date, site and method of application and any rotations. If no treatment was selected, then the only influence on flystrike risk would have been from shearing and/or crutching. A two-year, three-year, or four-year rotation was available.

Abbreviations

Table 5.1. Chemical abbreviations.

Abbreviation	Chemical
DHi	Dicyclanil extra
Dic	Dicyclanil
DLo	Dicyclanil low dose
Cyr	Cyromazine
CyS	Cyromazine spray-on
CyJ	Cyromazine jet
NN	Neonicotinoid
ML	Macrocyclic lactone
NP	New Product
Spn	Spinosyn

NP is a theoretical chemical that may be produced in the future that does not have any pre-existing resistance towards it. It has the same properties as ML and was used to test rotations with ML. Resistance to this chemical is represented by a different gene with the same resistance factor as ML.

Maximum and lethal concentration, day reduction and withholding interval

The maximum and lethal concentrations were taken from the WoolRes program (Campbell and Horton 2002). A 50kg sheep in 3 months of wool was used. The concentration of the chemical in the wool on the day the treatment was applied was the maximum concentration. The concentration of the treatment when the protection period ends and the lowest concentration of treatment that should kill susceptible flies was the lethal concentration. The concentration of the chemical was then converted from mg/kg in wool to mg of chemical on the sheep. A log linear decay rate was assumed for the chemical concentration and the number of days since the treatment was applied. Fitting a line to this relationship gave the day reduction. This is summarised in Table 5.2.

Table 5.2. Summary of treatment variables.

Treatment	Maximum Concentration (mg/sheep)	Lethal Concentration (mg/sheep)	Day Reduction*	Cost per Sheep ($)
DHi	638	13	2.06	1.92
Dic	573	13	2.06	2.04
DLo	168	13	3.46	1.25
CyS	911	40	3.93	0.65
CyJ	620	40	1.74	0.31
ML	41.8	5.5	1.46	0.29
NN	81.5	10	1.49	1.32
Spn	31.8	10	2.78	0.28
NP	41.8	5.5	1.46	0.29

*Day Reduction is the percentage of the chemical on the sheep that is lost each day.

Calculating cost of pesticide treatment

An average of three retail prices of the same pesticide for the largest quantity available for purchase, was calculated. Then using this average, the cost of chemical per sheep was calculated by dividing the average cost of treatment by the number of 50kg sheep that can be treated for both breech strike and body strike when treated as per the manufacturer's instructions. The price of the largest quantity of product available for purchase was used (i.e., the price of a 20L container rather than the price of a 5L container). Costs for DLo and DHi were calculated using equal volumes for body treatment and breech treatment in accordance with label instructions, while all other chemicals assumed a 2/3 body to 1/3 breech volume ratio.

Each chemical had different lengths of protection periods as recommended by the manufacturer (Table 5.3), which were taken into consideration by the program when calculating flystrike risk. The method of application also had an effect on the cost of pesticide treatment (See Section *Labour*).

Table 5.3. Protection periods for each chemical.

Chemical	Application	Protection (Weeks)
DHi	Spray on	29
Dic	Spray on	18-24
DLo	Spray on	11
Cyr	Spray on	11
Cyr	Jetting	14
ML	Jetting	12
NN	Spray on	14
Spn	Jetting	4-6

Severity

The program included the option to select a level of flock monitoring standard ranging from excellent, good, average to poor. It was assumed that increasing the quality of monitoring would decrease the severity of flystrike as the struck sheep could be identified sooner and treated before the flystrike worsened. Table 5.4 shows the estimated percentage of sheep flystruck at each severity level for a given monitoring standard, which was used to calculate the loss of production based on each severity level (Table 5.5).

Table 5.4. Percentage of sheep at each flystrike severity level for a given monitoring standard. Adapted from Horton *et al.* (2018).

	Monitoring Standard			
Severity	Excellent	Good	Average	Poor
1	70	64	53	35
2	24	26	32	40
3	6	10	15	25

Table 5.5. Percentage of loss of production for a given severity level. Adapted from Horton *et al.* (2018).

	Production Losses			
Severity	% Mortality	% Lamb loss	% GFW loss	% Staple strength loss
1	0.3	19	5.2	6
2	10.5	53	12.6	12
3	18.3	76	42.4	18
Combined*	6.3	38.4	13.1	9.7

*Combined is the weighted average percentage for all severity levels calculated using the previous table for average monitoring.

Good and excellent standards of monitoring would be expected to yield a higher proportion of severity 1 strikes and lower proportion of severity 3 strikes. Average monitoring was the default monitoring level, with monitoring conducted every second day instead of every day. Poor monitoring was an infrequent standard of monitoring that would yield more severity 3 strikes and therefore more losses. The resulting severity level influenced the loss of production in relation to the struck sheep, in terms of mortality, lamb loss, greasy fleece weight loss and staple strength loss (Table 5.5).

Cost of Strike

The program summarised all calculations to provide a total cost per flystruck sheep, which was then used to calculate savings due to flystrike management.

Cost associated with wool loss and tender wool

The losses in wool associated with a struck sheep was a function of greasy fleece weight (GFW) lost and the value at auction of wool (c/kg). The wool value was based on the clip composition being 80% fleece, 10% skirtings and 10% crutchings. As flystrike increased in severity the loss of greasy fleece weight and reduction in staple strength increased. Flystrike will often cause tender wool, reducing the value of the wool and therefore becoming a cost to the producer. The values used to calculate the cost associated with wool loss and tender wool are provided in Table 5.6 (S Raine 2021, personal communication, 16 April).

Table 5.6. Values associated with wool loss.

Sheep class	GFW (kg)	Wool c/kg	% Tender reduction*
Ewes	4.5	1400	7
Rams	6		
Wethers	4.5		
Hoggets	4		
Lambs	1.5		

*Tender reduction is the percent reduction in value for rotten wool (14N/ktex) calculated from the AWEX premium and discount report for the 19th of May 2021 (available by subscription at http://www.online.awex.com.au/BOE/AWEXonline).

Cost associated with fertility loss

The cost associated with fertility loss was influenced by severity scores (Tables 5.4 and 5.5). Ewe fertility loss referred to the dollar loss for each lamb not born ($40), due to the fertility loss experienced by the ewe flystruck before the mating period or during gestation.

It was assumed that rams experience a complete loss of fertility if the ram was flystruck before the mating period. The program assumed that the producer uses a backup ram for that year, so that if one ram becomes infertile the percent chance of complete ram fertility loss if struck is 50%. The value of the ram was estimated at $300, a combination of both the initial cost of the ram and the years of use, therefore the fertility loss for rams would be $150. It was assumed that a flystruck ram would not be fertile for that year but would be used for reproduction in future years if the ram recovered.

Cost associated with deaths

The value of the sheep class (Table 5.7) was calculated by averaging the sheep purchase price ($/head) and the sheep value when culled ($/head) (i.e., the average of the cost to restock a sheep in the flock after its death due to flystrike and what that sheep could have been worth in meat if it had survived). The sheep price was estimated from an average over three years using a graph of market prices in Inverell, NSW (www.mla.com.au/prices-markets/market-reports-prices/) for each sheep class. The sheep value was estimated using the National Lamb and Mutton Market Reporting Values (50th percentile) from 2004 to 2020 (www.mecardo.com.au/percentiles-february-2021/). The percentiles were only given for lambs (restocker, light, trade, heavy and merino) and mutton. The value for restocker lambs were used for lambs and the value for mutton was used to represent rams, wethers, hoggets, and ewes.

Table 5.7. Sheep values.

Sheep class	Sheep value ($)
Ewes	130
Rams	600
Wethers	120
Hoggets	140
Lambs	180
Sheep	125

Cost associated with chemical treatment

The expense associated with chemical treatment for a struck sheep referred to the cost of the chemical used to treat an already struck sheep ($0.05/sheep), not as a preventative measure. This is the cost of the chemical and not the cost in labour for applying the treatment.

Cost associated with labour for treatment of a struck sheep

The cost associated with labour for treating a struck sheep was calculated given that a farm and livestock hand was being paid at $25.51 an hour (Section 4. Labour) and could treat a struck sheep in 10 minutes.

Summary

A summary of the losses calculated by the program for each flystruck sheep is provided in Table 5.8.

Table 5.8. Summary of the losses per flystruck sheep ($)

Sheep class	Wool Lost	Tender Wool	Fertility	Deaths	Chemical	Labour	Total
Ewes	11.96	1.24	15.37	8.14	0.05	4.25	41.02
Rams	14.73	1.52	150.00	37.58	0.05	4.25	208.14
Wethers	12.89	1.33	0.00	7.52	0.05	4.25	26.04
Hoggets	8.28	0.66	0.00	8.77	0.05	4.25	22.21
Lambs	3.68	0.38	0.00	11.28	0.05	4.25	19.64

Flies

Fly life cycle

Variables relating to the fly life cycle were determined to calculate the number of flies in the population during the year (Table 5.9).

Table 5.9. Values used for a fly life cycle. Values were based on a summer period. Adapted from Wardhaugh (2001)

Variable	Value
Eggs laid per batch	100
Batches of eggs laid	3
Number of days maggots spend on sheep	5
Prepupa days	3
Pupa days	3
Adult days before mating	5

As these values were determined for a summer period, they may be an overestimate for cooler periods, which may affect the number of generations that occur during a treatment period.

Fly deaths

Variables relating to fly deaths were determined to calculate the number of flies in the population during the year (Table 5.10).

Table 5.10. Values used for fly deaths. Adapted from Abou Zied *et al.* (2003); De Cat *et al.* (2012).

Variable	Value
Deaths between maggots and prepupae	15%
Deaths between prepupae and pupa	42%
Deaths during overwintering	90%
Surviving population adult deaths each day	5%
Maximum fly lifetime as an adult	35 days

The values used for variables associated with fly deaths (Table 5.10) resulted in approximately the same number of flies in the population at the end of the year as the start of the year. Ideally the fly population was stable from year to year, but the population could increase if no treatment or not enough treatment was used.

Unselected flies multiplier

The original unselected flies multiplier of 1.0 was the default for this program and could be increased or decreased. This value was used to adjust the number of flies that were not exposed to treatment and were therefore unselected by resistance. This multiplier affected the rate of resistance development. Flies may not be exposed to treatment if they laid eggs on sheep that were not treated, came from neighbouring properties with no treatment or reproduced on carcasses. The percentage of flies that reproduced off the sheep was calculated for each unselected multiplier and this percentage aided in the selection of a suitable multiplier. An off-sheep reproduction percentage between 1.5% and 3% was judged as a reasonable value (Lang *et al.* 2006), although there is sparse literature to suggest the correct value for this percentage.

The unselected flies multiplier was changed in an updated version of the program to the percent of flies reproducing off-sheep as a percentage of those on-sheep when no treatment was used, rather than a multiplier, to estimate the number of maggots on and off-sheep to a realistic value.

Genes

Seven genes were used in the program, each representing resistance and cross-resistance to common chemicals used for flystrike prevention (Table 5.11).

Table 5.11. The chemicals which each gene was resistant to and their partial dominance.

Gene	Chemical	Partial dominance
1	Cyr (lethal)	100
2	Cyr (non-lethal) with Dic and NN cross resistance	50
3	Dic, DLo, DHi	10
4	NN	20
5	ML	20
6	Spn	20
7	NP	20

Partial dominance

Partial dominance was used to determine the resistance factor for the heterozygotes in relation to the homozygotes (Table 5.11). For example, a partial dominance of 100% meant that the heterozygotes had the same resistance as the homozygotes. A partial dominance of 50% meant that the resistance level of the heterozygotes was half-way between the resistance level of the wild type and the resistance level of the homozygotes, and 0% meant fully recessive. Genes 4 to 7 were given an estimated partial dominance of 20% as the true value of this partial dominance was not known.

Gene frequency
All resistance genes began with a starting gene frequency of 0.001% but this could be set at any value, as the true value is not known. It is expected that a small number of genetic mutations exist naturally in a population of blowflies that allow some blowflies to be resistant to a pesticide. The starting resistance gene frequency only applied to the percent of resistance genes (R), not the percent of the homozygous resistant genotype (RR) in the starting population. The proportion of genes that were susceptible or resistant and the frequency of homozygotes and heterozygotes were calculated by the program from day to day. The proportion of eggs that became maggots after body strike, breech strike or due to off-sheep reproduction was estimated based on any preventative treatment that may have been applied.

Gene 1
Yen *et al.* (1996) discovered that three of the four genes found for Cyr resistance had homozygous lethality, with a resistance level of approximately three times that of wild flies. Gene 1 represented these findings.

Gene 2
Gene 2 represented one of the four genes discovered by Yen *et al.* (1996) that was not homozygous lethal, but did not have a level of Cyr resistance as high in the heterozygotes as in the homozygotes (Table 5.11).

A resistant strain named 'Nimmitabel-selected' was studied by Levot *et al.* (2014) who did not find homozygous lethality in this strain. The authors also found that this strain was resistant to Cyr and Dic. In a recent study conducted by Sales *et al.* (2020) the authors found evidence to suggest that blowflies resistant to Dic have cross resistance towards Cyr and NN. The authors also suggested that Cyr resistance is required before blowflies can obtain Dic resistance.

Gene 3
Sales (2021, in preparation) found that a much higher resistance to Dic is possible, therefore gene 3 represented high resistance to Dic, albeit this high resistance is rare (partial dominance of 10%). Sales *et al.* (2020) found that Dic resistance cannot exist without existing Cyr resistance. A checkbox is used so that the frequency of gene 3 could only increase in the population when gene 2 is present as heterozygous or homozygous resistant, the default was for this option to be used but this setting could be turned off.

Genetic disadvantage (%)
Gene 1 was the only gene that had a disadvantage (100%) as it has been shown that Cyr resistance can experience homozygous lethality (Yen *et al.* 1996). All other genes had a 0% disadvantage as the default setting. A 100% disadvantage meant that all homozygotes for resistance died, with heterozygotes surviving.

Resistance factors
The lethal dose of a treatment is the concentration of the pesticide just before the treatment is no longer effective. Wild flies that are susceptible are killed by any pesticide concentration greater than 1.0 times the lethal dose but survive at pesticide concentrations less than 1.0 times the lethal dose. Therefore, wild flies are given a resistance factor of 1.0. The resistance factor is a measure of the concentration of insecticide a resistant fly can survive as a multiple of the lethal dose. For example, a resistance factor of 2.0 meant that a resistant fly could survive up to twice the lethal dose of pesticide, but no higher than 2.0 times the lethal dose.

Yen *et al.* (1996) found Cyr resistance with a factor of approximately 3, which was used for Cyr resistance in genes 1 and 2 (Table 5.12), this was consistent with Cyr resistance found by Levot *et al.* (2014). Sales (2020) found that a homozygous dominant strain resistant to Cyr only had a resistance factor of 3.6 to Dic. The authors also found a strain with a higher level of resistance towards Dic with a high resistance factor of 48.7 (Sales 2021, in preparation). Therefore, Dic resistance was covered over two genes, one with resistance factor of approximately 3.6 and another with a resistance factor of approximately 14 so when combined there was a resistance factor close to 48 (Table 5.12). The authors found cross resistance between Dic resistance and NN resistance with a resistance ratio of approximately 3.4 for NN (Sales 2021, in preparation). A resistance factor of 8.0 was chosen for the treatments ML, NN, Spn and NP as this resistance factor is reasonable during the early stages of resistance but may increase when other genes act in combination with genes for resistance (Levot *et al.* 2014). After initial testing, the resistance factors for ML and NP were decreased from 8 to 6. The resistance factors used by the program are summarised in Table 5.12.

Table 5.12. Resistance factors for each gene and treatment combination. Cells shaded grey denote a resistance factor of 1.

Treatment	Gene 1	Gene 2	Gene 3	Gene 4	Gene 5	Gene 6	Gene 7
DHi		3.6	14				
Dic		3.6	14				
DLo		3.6	14				
CyS	3	3					
CyJ	3	3					
ML					6		
NN		3.4		8			
Spn						8	
NP							6

Graphs and Reports

Graphs

The program produced outputs in the form of a graph and a report. The graph allowed a visual summary of the difference in flystrike risk between treating and not treating the flock (Figure 5.1).

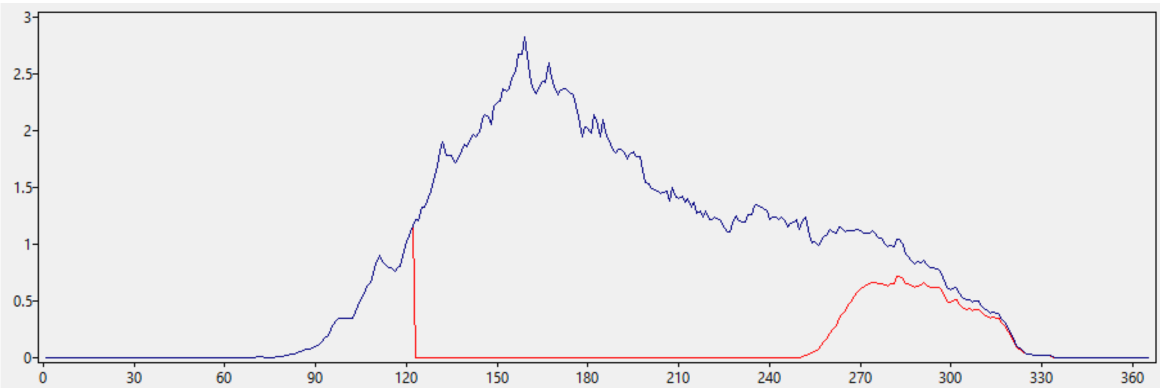

Figure 5.1. Example of a graph produced by the program. The blue line represents no treatment, and the red line represents treatment. The treatment used was a one-time application of Dic on the 31st of October. The Y-axis is the flystrike risk, and the X-axis is days from the 1st of July. The gradual increase between days 240 and 270 is a result of a fuzzy response value of 0.3.

Reports

The report section showed an overview of the costs for treated and untreated sheep.

Savings

This part of the program also calculated the savings due to the use of pesticide treatment, which was the difference between the total costs of the chosen management strategy (including costs of all treatment and costs of flystrike with the treatment applied) and no pesticide (costs of flystrike with no treatment used).

Net Present Values (NPVs)

The savings data produced in the report was used to calculate Net Present Values (NPVs), which was used to compare similar management strategies for a flock of 10,000 sheep. NPVs were calculated on the reduction in flystrike and related costs for using a management strategy compared to the default strategy, which was no treatment, no crutching and winter shearing. Savings were adjusted for time and future savings were discounted at a rate of 5%.

6. Results

Strike Treatment Optimiser

Optimum method and date for each chemical

The Strike Treatment Optimiser was used to calculate the optimum method of application and date of application for each chemical. These are shown in Tables 6.1 (two treatments a year) and 6.2 (one treatment a year). For the chemicals not available in the Strike Treatment Optimiser (DHi, NN and NP), manual optimisation using the Flystrike Resistance Decision Support System was used. The Strike Treatment Optimiser has an option to disallow jetting as an application method, because many wool producers consider jetting too laborious and time consuming compared with spray-on application. But jetting is less expensive, so was always chosen if it was a permitted option.

Table 6.1 Optimum method and date of application for each chemical when two treatments are applied each year. 1 and 2 signifies the first and second treatment each year.

Chemical	Optimum method 1	Optimum date 1	Optimum method 2	Optimum date 2
DHi	Body and Breech	19-Sep	Body and Breech	29-Jan
Dic	Breech only	14-Sep	Breech only	16-Dec
DLo	Body and Breech	30-Oct	Breech only	18-Jan
CyS	Body and Breech	27-Oct	Body and Breech	21-Jan
CyJ	Body and Breech	4-Oct	Body and Breech	19-Jan
ML	Body and Breech	4-Oct	Body and Breech	19-Jan
NN	Body and Breech	18-Oct	Body and Breech	24-Jan
Spn	Body and Breech	4-Nov	Body and Breech	17-Dec
NP	Body and Breech	4-Oct	Body and Breech	19-Jan

Table 6.2 Optimum method and date of application for each chemical when one treatment is applied each year.

Chemical	Optimum method	Optimum date
Dic	Body and Breech	26-Oct
DLo	Body and Breech	4-Nov
CyS	Body and Breech	3-Nov
CyJ	Body and Breech	29-Oct
ML	Body and Breech	29-Oct
NN	Body and Breech	6-Nov
Spn	Body and Breech	17-Nov
NP	Body and Breech	29-Oct

For the remainder of this report, the method of application for each chemical was breech and body unless otherwise stated as breech only or body only.

Chemical costs

The chemicals had to reach unrealistically high prices for no treatment to be more cost effective than treating the flock. The costs used are shown in Table 6.3

Table 6.3 Default chemical prices in the Strike Treatment Optimiser and Flystrike Resistance Decision Support System.

Chemical	Cost per sheep ($)
DHi	1.92
Dic	2.04
DLo	1.25
CyS	0.65
CyJ	0.31
ML	0.29
NN	1.32
Spn	0.28
NP	0.29

Wool prices and ewe values

The optimum method and date of application did not change with changes in wool prices. The optimum method and date of application only changed once the ewe value exceeded $2177 per ewe. Wool and lamb prices affected the total costs due to flystrike, by changing the loss due to each struck sheep. However, large changes in these prices did not alter the recommended treatment, nor the rate of development of resistance.

Testing assumptions in Flystrike Resistance Decision Support System

Starting resistance level

The starting resistance level was the gene frequency of resistance genes in the starting population. Decreasing the starting resistance level for each gene delayed high resistance development in that gene. The effect of the starting resistance level on resistance development was tested with CyS treatment (Figure 6.1) or Dic (Figure 6.2).

The starting gene frequency of resistance genes affects the number of years until resistance develops. However, the curves are approximately parallel during the period from low to high resistance, so any arbitrary starting gene frequency can be used in the model.

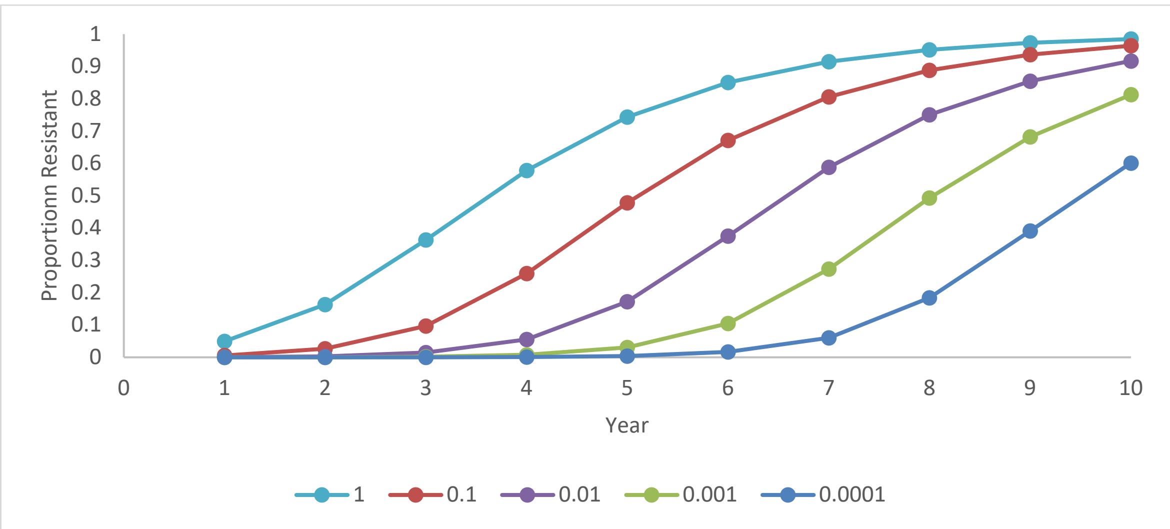

Figure 6.1. Resistance development in gene 2 over 10 years as the starting resistance level (%) varies. Treatment was one application of CyS each year.

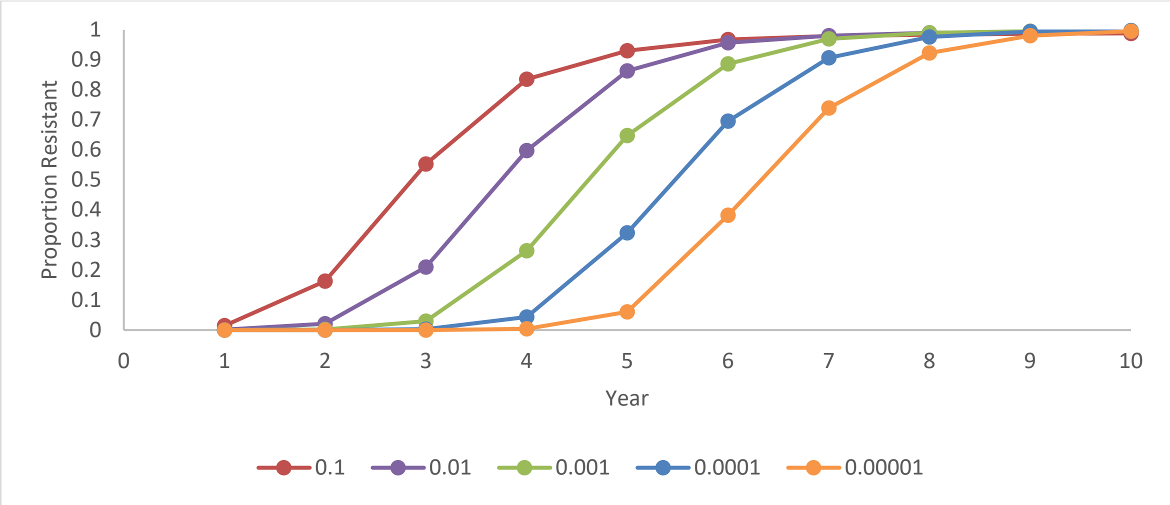

Figure 6.2. Resistance development in gene 2 over 10 years as the starting resistance level (%) varies. Treatment was one application of Dic each year.

Fly variables

Unselected flies multiplier

The unselected flies multiplier controlled the number of flies reproducing off sheep, therefore not being exposed to chemical treatment and subsequent resistance development. Increasing the unselected flies multiplier had a minor increase on the number of body and breech strikes. This would have been due to the increase in the total simulated fly population on the property. Increasing the unselected flies multiplier decreased the development of resistance when CyS was used (Figure 4.3.1). The model is very sensitive to the proportion of flies that can reproduce without exposure to pesticide (i.e. reproduction not on live sheep). This value is not known, but may range from zero to 5% of the flies on the property.

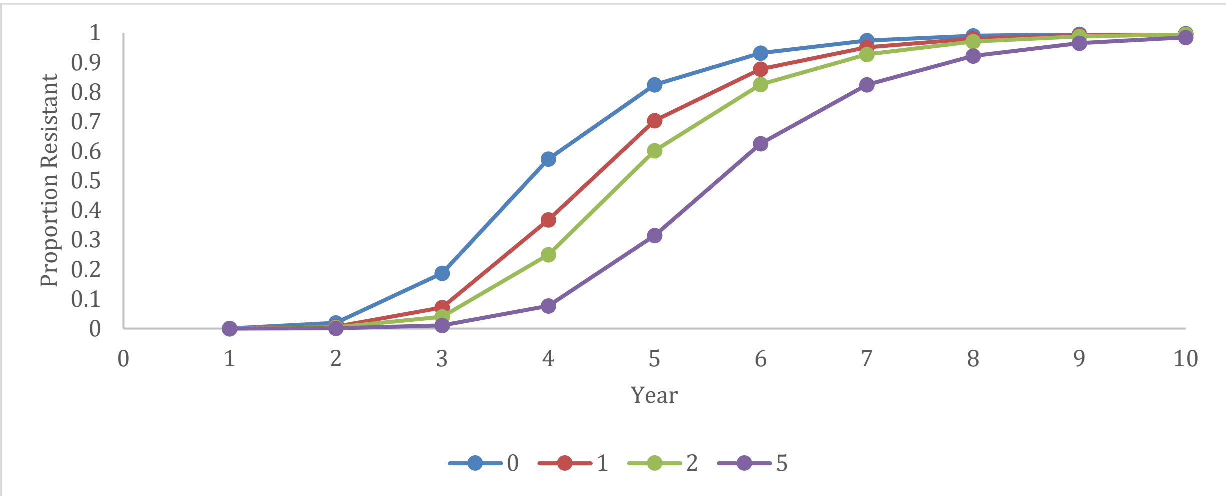

Figure 6.3. Resistance development in gene 2 over 10 years as the unselected flies multiplier varies. Treatment was two applications of CyS each year.

Continuous use of same treatment

Dic breech and body treatment versus breech only treatment

Dic was the only chemical where the breech only method was recommended by the Strike Treatment Optimiser. Testing was conducted to determine the effect breech only application had on the resistance development. When both body and breech are protected every year, resistance increased rapidly from year 3 to year 6. But when Dic was applied only to the breech, resistance development was delayed (Figure 6.4).

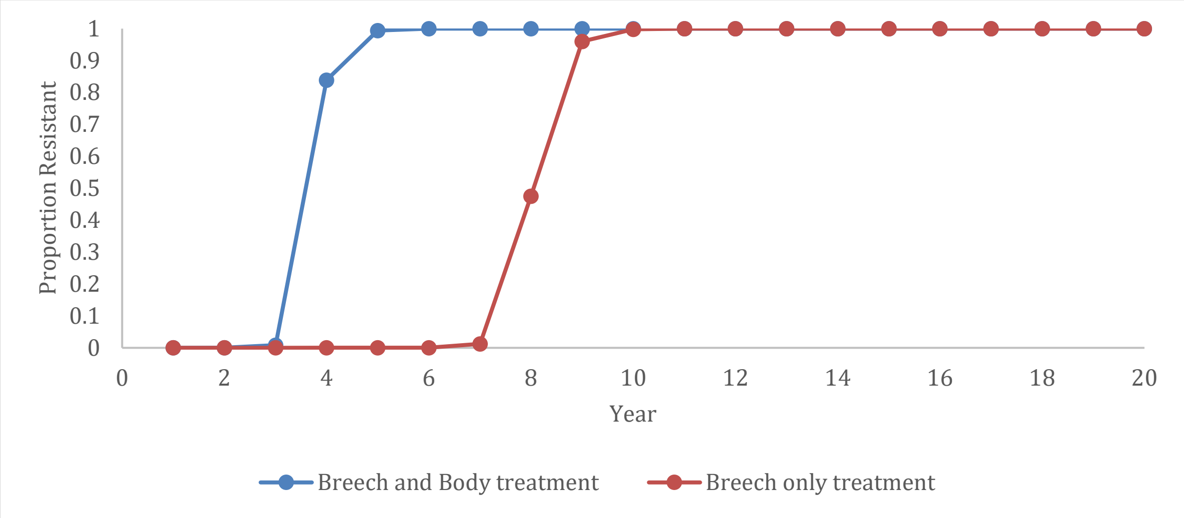

Figure 6.4 Resistance development in gene 3 over 20 years for different application methods. Treatment was two applications of Dic each year to either breech only or to body and breech.

Figure 6.5 shows the actual number of sheep struck under each scenario, with about 45 sheep struck each year (in a flock of 1000) when only the breech was protected. These would be almost all body strikes. When Dic was applied to both body and breech, the number of sheep struck was low, until resistance developed at year 6, after which the number of strikes increased rapidly to almost 40% of the flock, if Dic continued to be used as the sole protection.

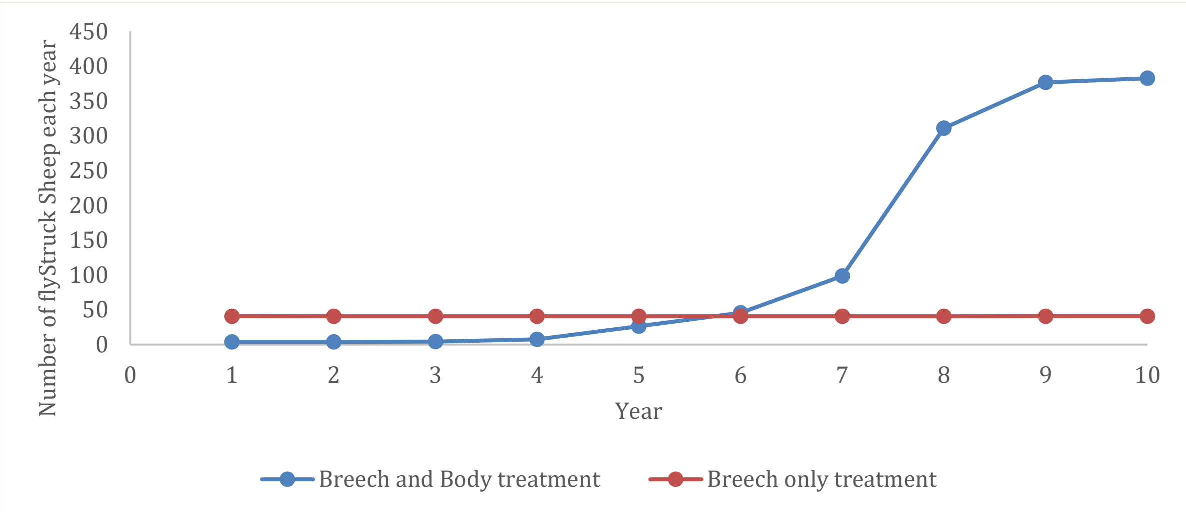

Figure 6.5. Number of flystruck sheep treated with two applications of Dic, either breech only or body and breech, each year over 10 years.

One application of CyS each year (Figure 6.6) produced less resistance development than two applications of CyS (Figure 6.7). Gene 1 never reached high levels of resistance due to the lethality.

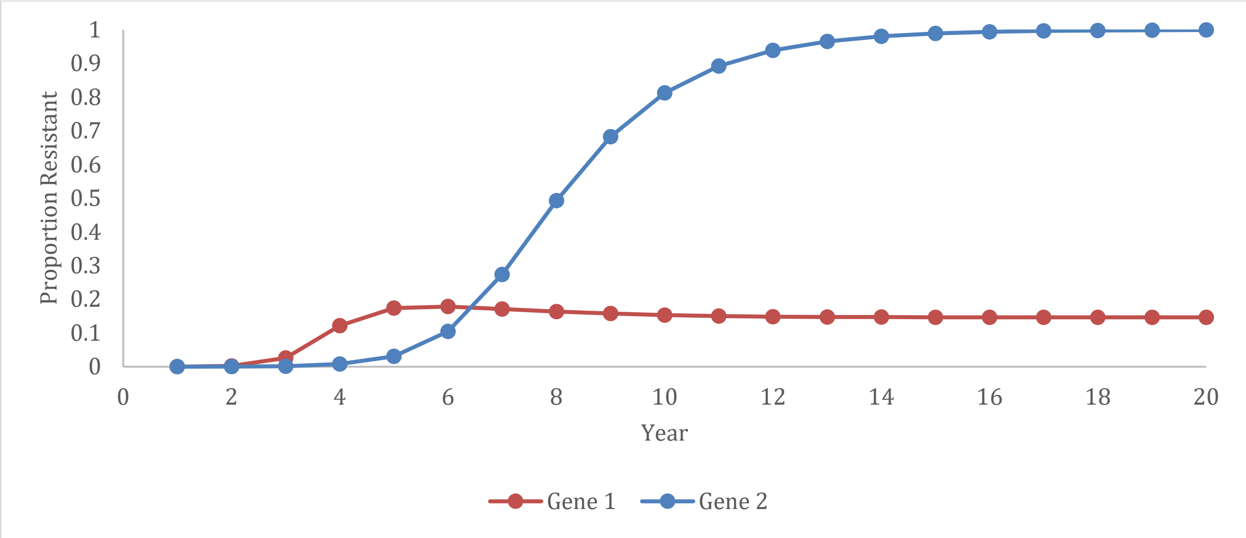

Figure 6.6. Resistance development in genes 1 and 2 over 20 years when one application of CyS was applied each year.

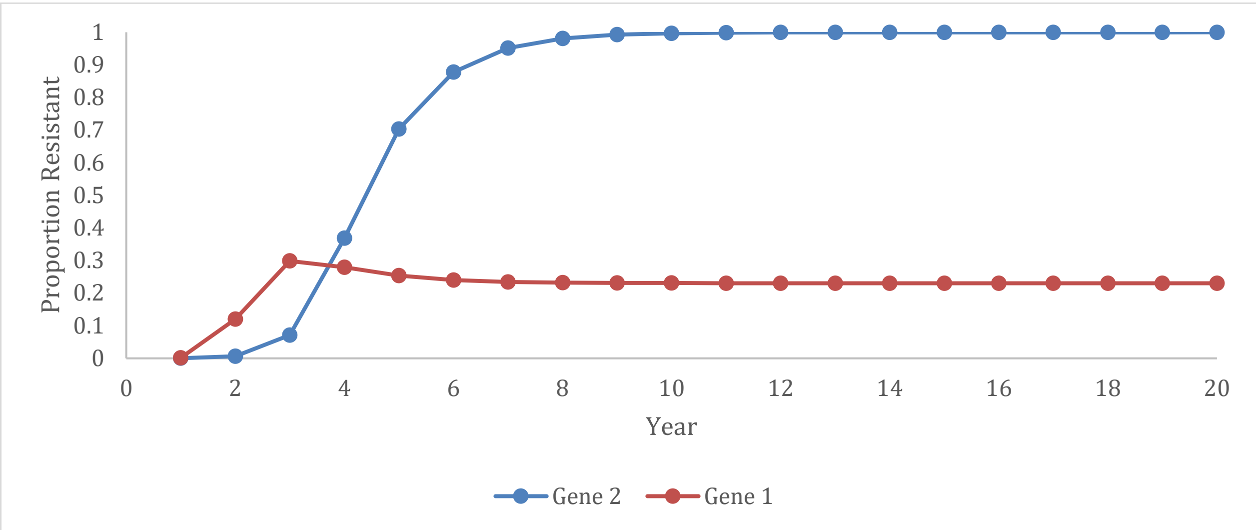

Figure 6.7 Resistance development in genes 1 and 2 over 20 years when two applications of CyS were applied each year.

The resistance development was slower when treating with one application of CyS compared to one application of CyJ (Figure 6.8).

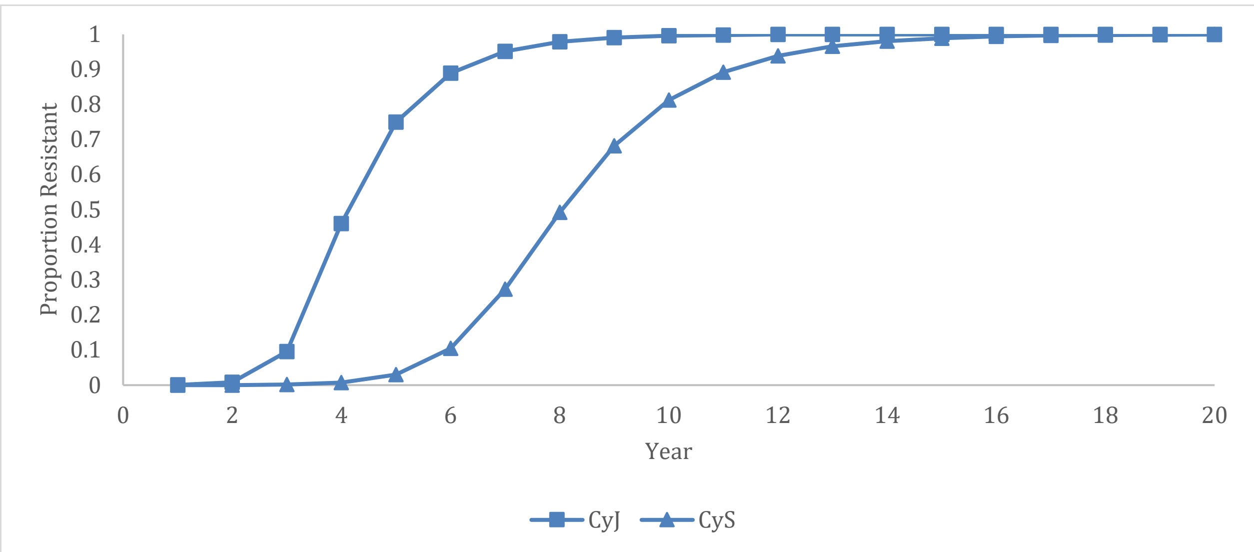

Figure 6.8 CyJ vs CyS: Resistance development in gene 2 over 20 years for one application of CyJ or one application of CyS.

Continuous treatment compared with rotations

Figure 6.9 shows the number of sheep struck each year when alternating ML and NP versus using ML continuously. Use of ML continuously gave no protection after five years, whereas alternating ML and NP resulted in less struck sheep each year until year 10, when neither product provided protection. The rotation has resulted in the loss of two products in 10 years, compared with continuous use losing one product in five years, but over that period less sheep have been struck.

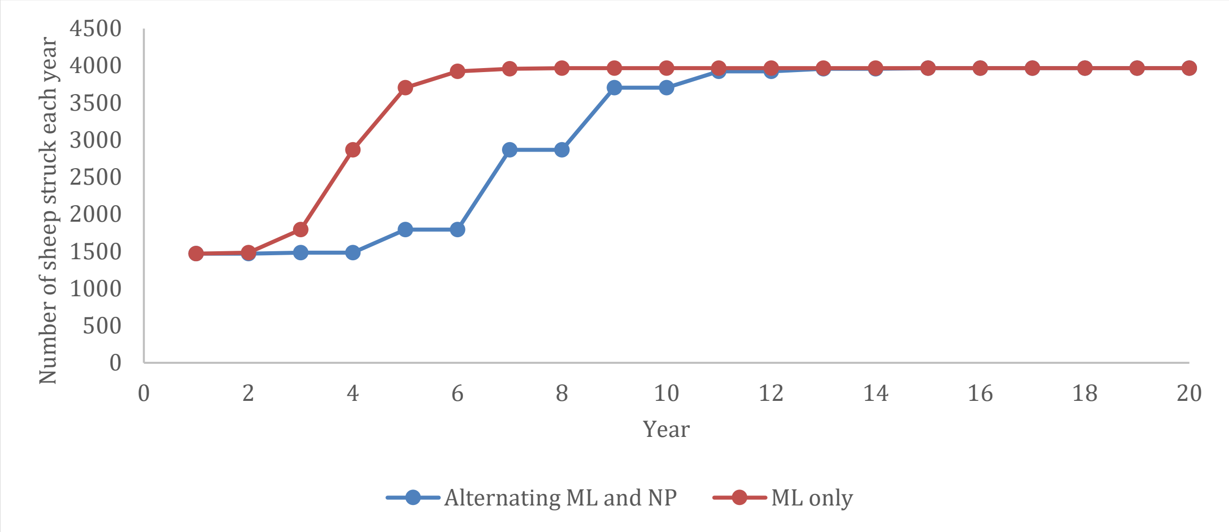

Figure 6.9 Number of sheep struck each year over 20 years when alternating ML and NP and when using ML continuously.

If there was a 40% genetic disadvantage for the homozygotes for resistance, the frequency of resistant genes did not exceed 81% when alternating two treatments each year of NP and ML (Figure 6.10). The use of a third chemical in the rotation would result in even lower levels of resistance over long periods at this degree of disadvantage.

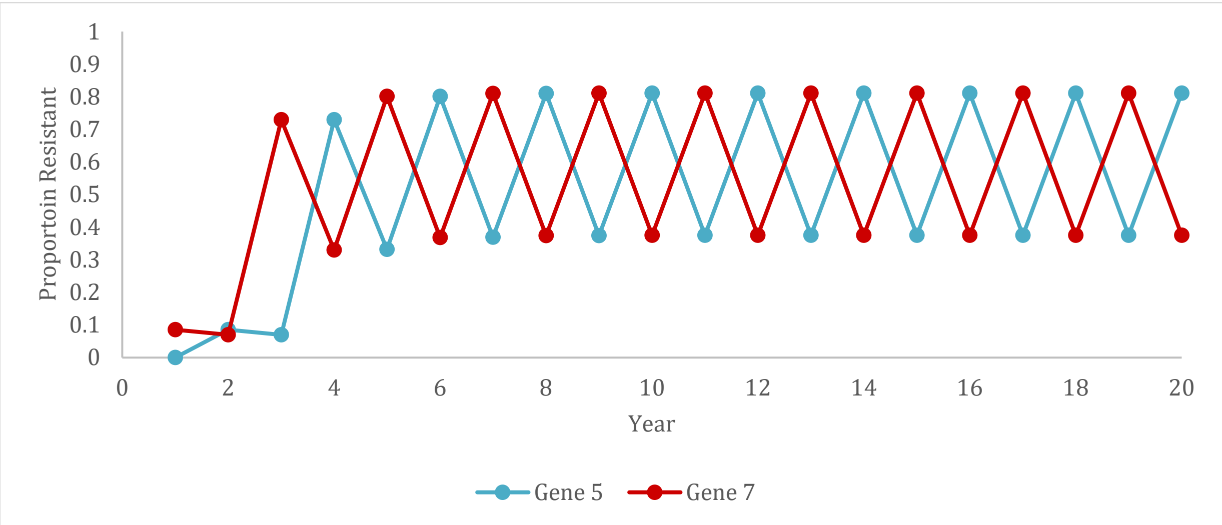

Figure 6.10 Resistance development in genes 5 and 7 over 20 years when two applications of ML were applied one year, and two applications of NP were applied the next year with a 40% genetic disadvantage for each gene.

Combination/Mixtures (Applying different chemicals on the same day each year)

NP, CyJ and ML had the same optimum date of application and no interactions between resistance genes. There was a considerable reduction in resistance development in genes 5 and 7 compared to two and three chemical rotations (Figure 6.11).

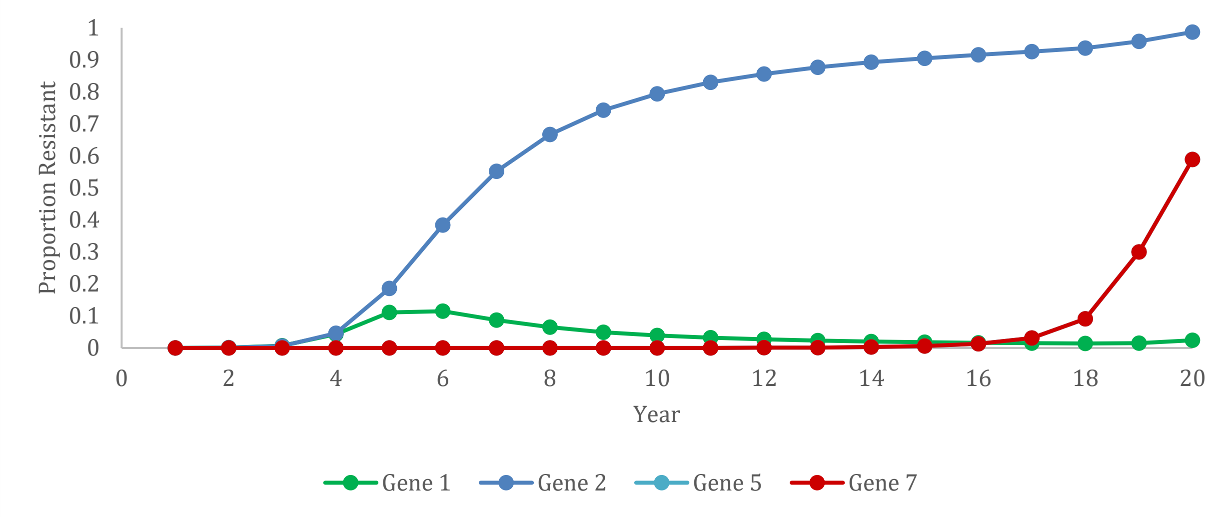

Figure 6.11. NP + CyJ + ML: Resistance development in genes 1, 2, 5 and 7 over 20 years when one application of NP, CyJ and ML was applied on the 29th of October each year. Gene 7 and gene 5 overlap.

When the combination Dic + NN + ML was tested, resistance form gene 2 rose rapidly, although the other genes maintained low levels for about 14 years (Figure 6.12). The protection period for Dic extends at least 2 months beyond the protection periods for NN and ML, so these would have provided no protection against increasing resistance to Dic. This suggests that only products with similar length of protection should be used in combination.

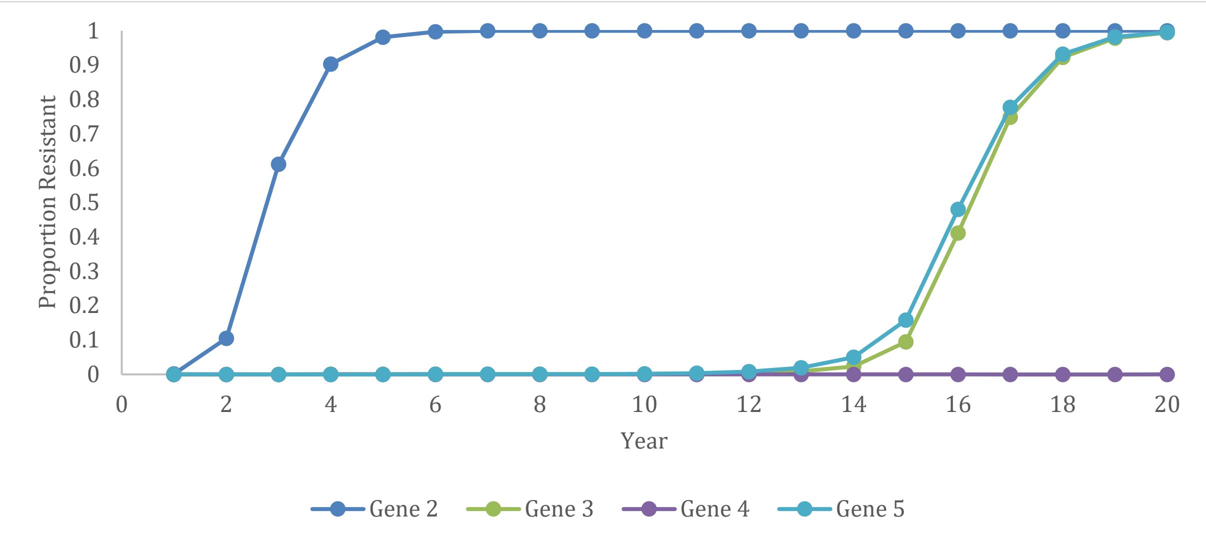

Figure 6.12. Dic + NN + ML: Resistance development in genes 2, 3, 4 and 5 over 20 years when one application of Dic, NN and ML was applied on the 26th of October each year. There was a small development of resistance in gene 4 that is not apparent.

Comparing NPVs – Continuous use of one treatment

NPVs were calculated on the reduction in flystrike related costs for using a management strategy compared to the default strategy, which was winter shearing, no treatment, and no crutching. This is the profit from using the chosen management rather than doing nothing except shear the sheep.

If the same chemical is used continuously for 12 years, then the best option is Dic (breech-only), used once a year (Table 6.4). The breech only treatment has a slow development of resistance, but this is at the expense of some flystrike due to body strike. If full coverage of the sheep is required, then the choice giving highest profit over 12 years is CyJ once a year.

The most cost-effective chemical to use continuously twice a year was Dic (breech only) (Table 6.4) and for body plus breech protection CyS.

The starting resistance level for each gene was set to 0 to calculate the NPVs when there was no resistance development. When there was no resistance present, CyJ was the most cost-effective chemical for twice a year continuous treatment (Table 6.4). There was a $781,509 difference in cost between when resistance was present and when resistance was not present when CyJ treatment was used – the potential cost of CyJ resistance to the Australian Sheep Industry over a span of 12 years. This is equivalent to a cost of $6.51 per sheep per year due to resistance.

Table 6.4. NPVs for all chemicals when used once or twice a year each year over 12 years.

Chemical	Once per year	Twice per year	Twice a year with no resistance
DHi	$497,120	$76,893	$1,181,939
Dic (breech only)	$957,767	$869,030	$ 877,036
Dic	$450,326	$184,738	$1,144,076
DLo	$528,306	$453,069	$902,340
CyS	$604,476	$706,396	$1,087,928
CyJ	$733,448	$638,883	$1,420,392
ML	$342,941	$252,102	$1,306,948
NN	$223,778	-$33,775	$1,237,818
Spn	$301,886	$244,710	$ 607,966
NP	$342,941	$252,102	$1,306,948

Comparing NPVs – Rotations

Two chemical rotations

Rotations were tested using twice-yearly ML or NP continuously for half the period, then changing to the other, compared with rotation of ML and NP each successive year, or treating with one dose of ML and one dose of NP in each year. This applied whether the NPV was calculated over 12 years or 6 years.

Treating with two applications of ML one year and two applications of NP the next year was the most cost-effective ML and NP rotation (Table 6.5), slightly better than using both products within each year.

Table 6.5 NPVs for ML and NP rotations.

Rotation	NPV over 12 years	NPV over 6 years
Two applications of ML each year for half the period, then two applications of NP each year for 6 years	$423,943	$433,100
Two applications of ML one year and two applications of NP the next year	$461,288	$444,512
One application of ML and one application of NP each year	$449,107	$444,028

Comparing NPVs – Mixtures

A combination of ML and NP was the most-cost effective mixture for a single treatment each year (Table 6.6). The ML and NP mixture was more cost-effective than continuous use of the same treatment or rotation counterparts. For all other pairs of chemicals, mixtures were more cost-effective than treating with two different chemicals each year (on different days) but due to the extra cost of the treatment this was not as cost-effective as a single treatment each year.

Table 6.6 NPVs for mixtures.

Rotation	NPV over 12 years
One application of Dic and one application of CyS applied as a mixture on the same day each year	$588,393
One application of Dic (breech only) and one application of CyS applied as a mixture on the same day each year	$872,459
One application of Dic, one application of NN and one application of ML applied as a mixture on the same day each year	$714,319
One application of Dic, one application of NP and one application of ML applied as a mixture on the same day each year	$819,965
One application of ML, one application of NP and one application of CyJ applied as a mixture on the same day each year	$960,245
One application of ML and one application of NP applied as a mixture on the same day each year	$937,308

Mixtures with Dic were generally not as cost-effective as pairs of chemicals with the same length of protection, since the additional chemical used with Dic could not prevent Dic resistance from increasing.

Monitoring levels

Extra monitoring

The monitoring intensity represents the extra time spent ensuring that all maggots found on struck sheep are killed, so that few pesticide-resistant maggots survive. The number of maggots that were killed increased proportionally as the monitoring intensity increased (Table 6.7). Whether or not treatment was applied, extra monitoring reduced the local fly population, and this reduced the number of struck sheep and therefore reduced the total cost of flystrike. As the monitoring intensity increased, the cost of monitoring increased. The value of the reduction in flystrike was larger than the cost of extra monitoring, therefore increasing savings (Table 6.7).

Table 6.7. Percent of maggots that are killed as the monitoring intensity increases, costs of monitoring (labour costs), and savings due to extra monitoring after one year, for a range of monitoring intensities when no treatment was applied.

Monitoring intensity	Maggot death (%)	Cost of Monitoring	Savings due to extra monitoring
No extra monitoring	0	$2,806	$0
1	50	$4,434	$10,577
1.5	67	$6,651	$15,382
2	75	$8,868	$18,070
2.5	80	$11,085	$19,600

Increasing monitoring intensity reduced the development of resistance (Figure 6.13).

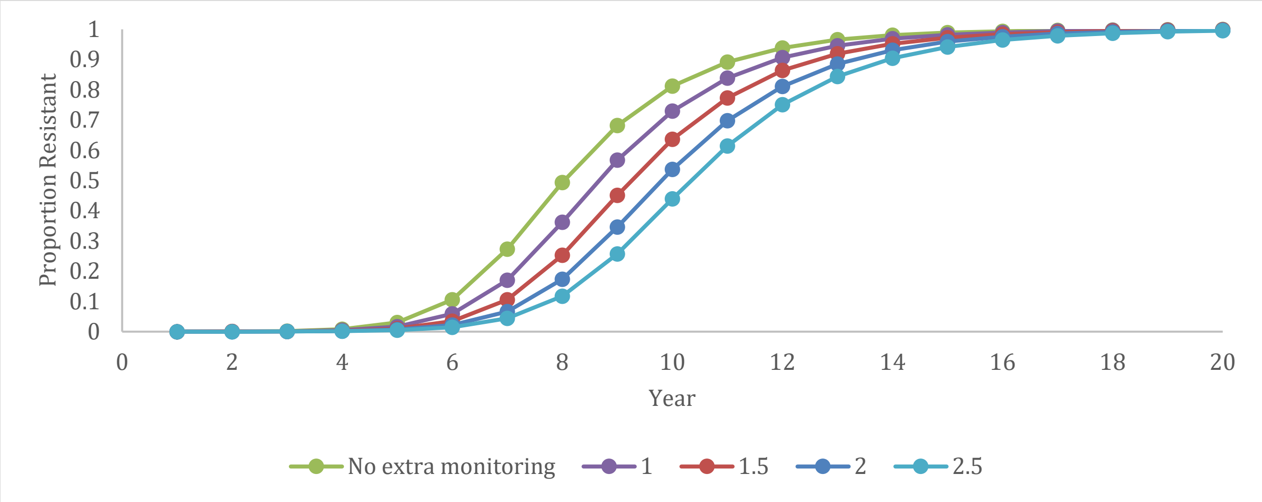

Figure 6.13. Resistance development in gene 2 over 20 years as the monitoring intensity varied. Treatment was one application of CyS on the 3rd of November each year.

When one application of CyS was used each year, the total costs for the first seven years were higher for extra monitoring. This occurred because strike costs were low due to treatment, so reduction in strike costs due to monitoring was less valuable. Over time, as resistance developed there were higher total costs as a result of 'no extra monitoring' (Figure 6.14).

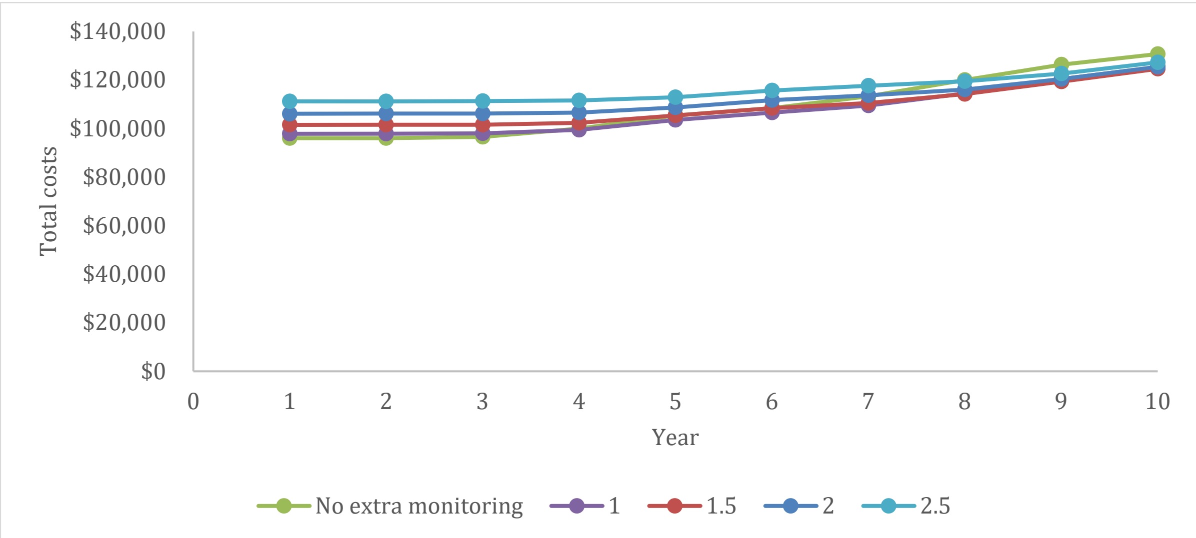

Figure 6.14. Treated flock: Total costs due to flystrike each year for 10 years as the monitoring intensity varies. Treatment was one application of CyS each year.

A monitoring intensity of 1 was more cost-effective than no extra monitoring. Increasing monitoring intensity was less cost-effective as the extra cost of labour outweighed the savings from struck sheep (Table 6.8).

Table 6.8 NPVs for monitoring intensity. Treatment was one application of CyS on the 3rd of November each year.

Monitoring intensity	NPV over 10 years
No extra monitoring	$560,370
1	$572,406
1.5	$557,750
2	$532,142
2.5	$500,195

Shearing

Shearing dates were tested with once-a-year treatment of CyS. The default shearing was winter shearing, but spring, summer and autumn shearing were used for testing purposes. For each fixed shearing date the optimum treatment dates were calculated using the Strike Treatment Optimiser (Table 6.9).

Table 6.9 Optimised treatment dates for each shearing date.

Shearing season	Shearing date	Treatment date
Spring shearing	1st of November	19-Jan
Summer shearing	1st of January	12-Oct
Autumn shearing	1st of March	3-Nov
Winter shearing	1st of July	3-Nov

Spring shearing reduced the development of resistance (Figure 6.15), whereas summer shearing increased the rate of development of resistance.

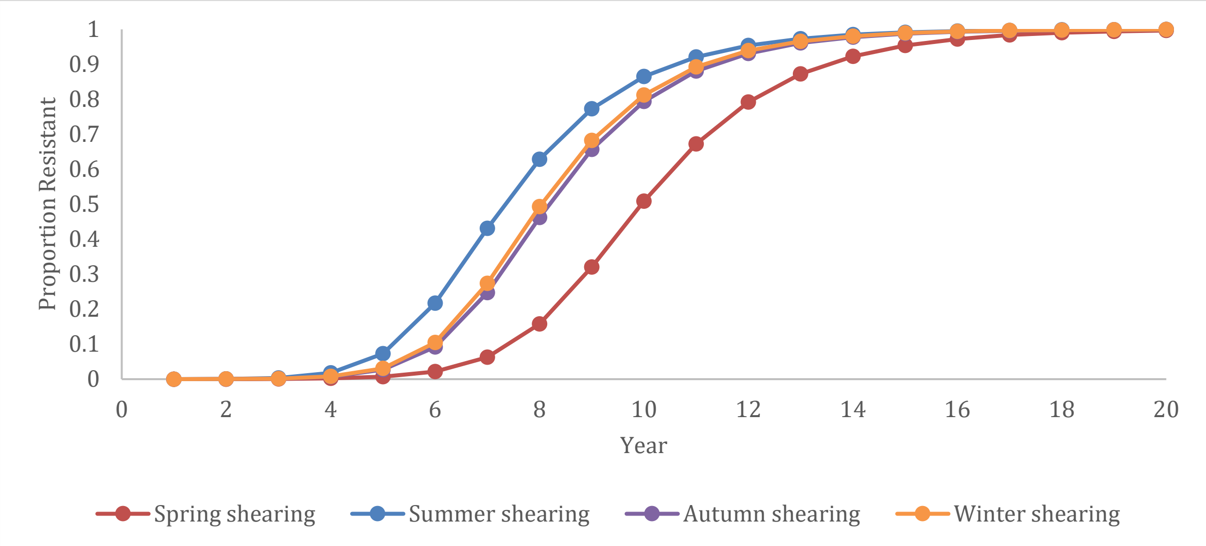

Figure 6.15. Resistance development in gene 2 over 20 years for spring, summer, and autumn shearing. Treatment was one application of CyS on the optimised treatment date.

Winter shearing had the highest flystrike risk, determined by measuring the area under the no treatment curve, as it was the only shearing date that did not reduce the length of the flystrike season (Figure 6.16).

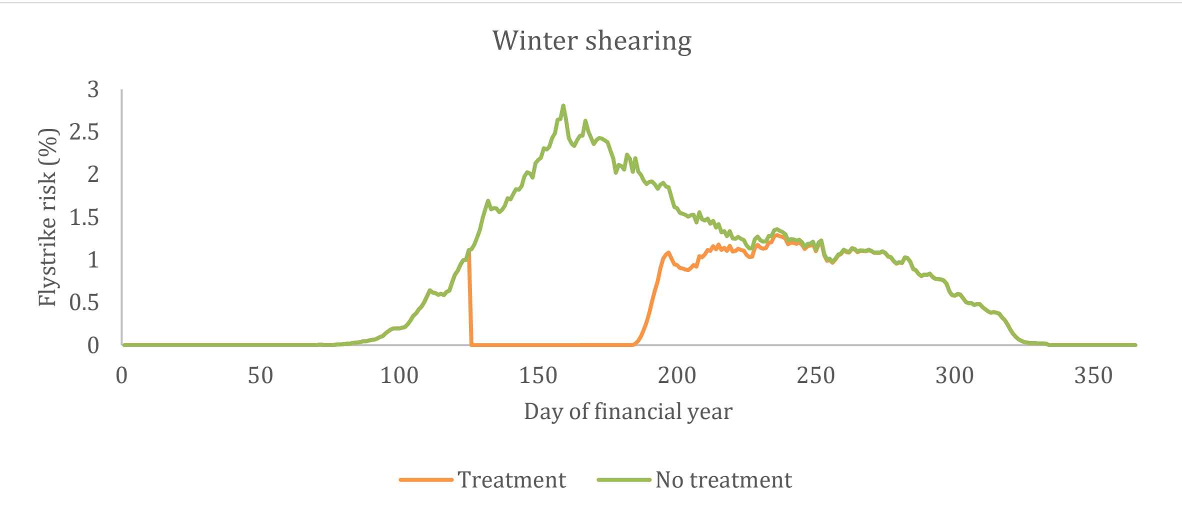

Figure 6.16. Flystrike risk over one year for winter shearing. Treatment was one application of CyS on the 3rd of November.

Spring shearing delayed the beginning of the flystrike season (Figure 6.17). Summer shearing split the flystrike season into two periods (Figure 6.18). The shearing followed closely after the end of effective treatment, so the fly population would have been low for a long time after the period of selective advantage for resistant flies. This may have maintained a high proportion of resistant flies for the rest of the fly season. The other shearing dates allow time for the fly population to increase after treatment, which could dilute the resistant population with non-resistant flies. Autumn shearing reduced the length of the flystrike season by cutting it short (Figure 6.19).

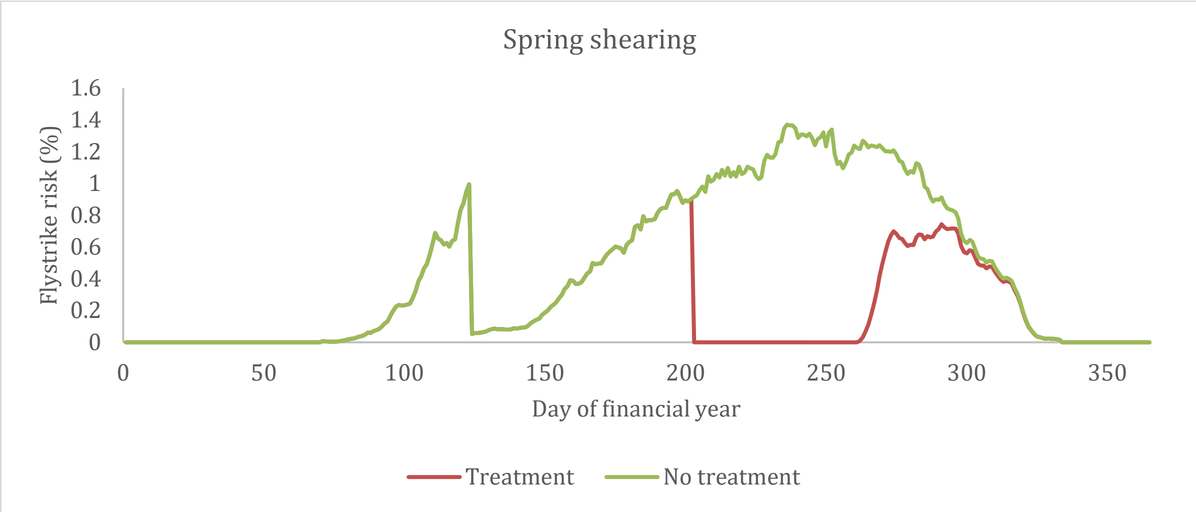

Figure 6.17. Flystrike risk over one year for spring shearing. Treatment was one application of CyS on the 19th of January.

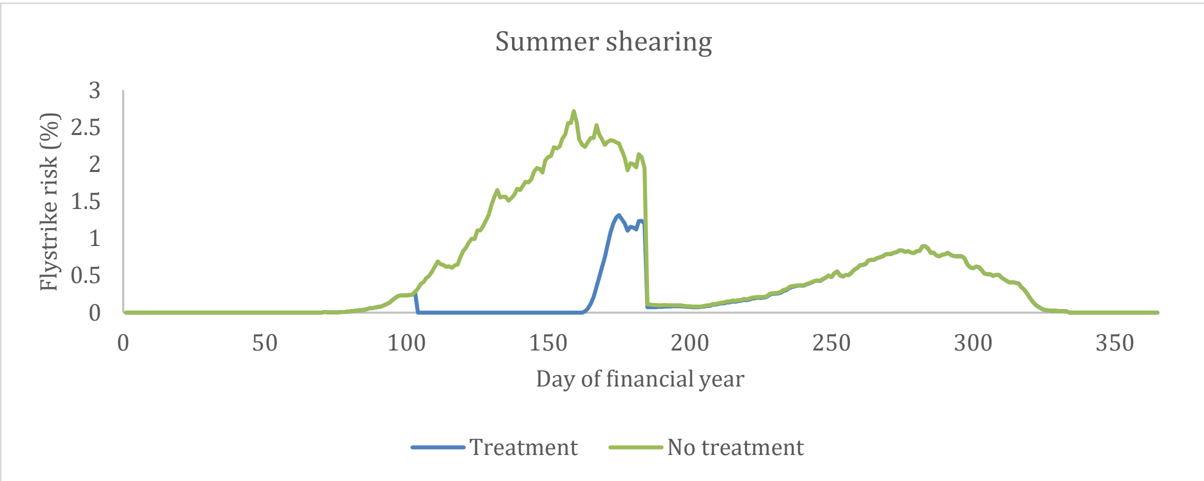

Figure 6.18. Flystrike risk over one year for summer shearing. Treatment was one application of CyS on the 12th of October.

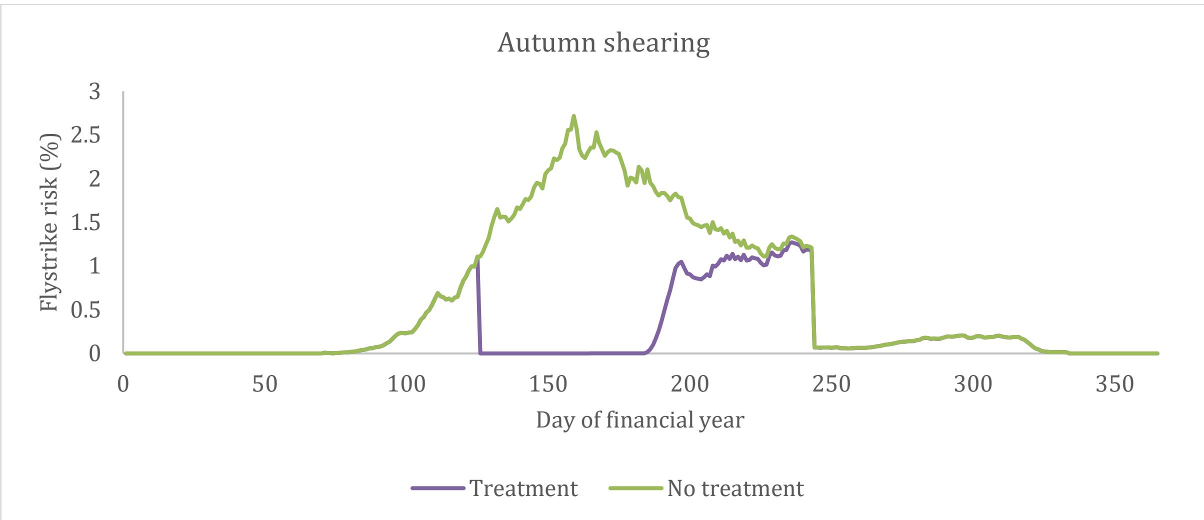

Figure 6.19. Flystrike risk over one year for autumn shearing. Treatment was one application of CyS on the 3rd of November.

Spring shearing was the most cost-effective shearing date, but all alternative shearing dates were more cost-effective than the default winter shearing date (Table 6.10).

Table 6.10. NPVs for spring, summer, and autumn shearing. Treatment was one application of CyS each year on the optimised treatment date.

Shearing	NPV over 10 years
Winter shearing	$560,370
Spring shearing	$887,208
Summer shearing	$779,089
Autumn shearing	$821,047

Crutching

Crutching dates were tested with once-a-year treatment of Dic (breech only), as Dic was the only treatment where breech-only treatment was recommended and crutching only removes wool from the breech. Spring crutching was conducted on the 1st of November, summer crutching on the 1st of January and autumn crutching on the 1st of March. The optimum treatment dates for these crutching dates were calculated using the Strike Treatment Optimiser (Table 6.11).

Table 6.11. Optimised treatment dates for each crutching date.

Crutching date	Treatment date
Spring crutching	28-Nov
Summer crutching	3-Aug
Autumn crutching	26-Sep

Crutching in spring, before the start of the flystrike season, reduced resistance development (Figure 6.20), whereas autumn and summer crutching increased the rate of development of resistance.

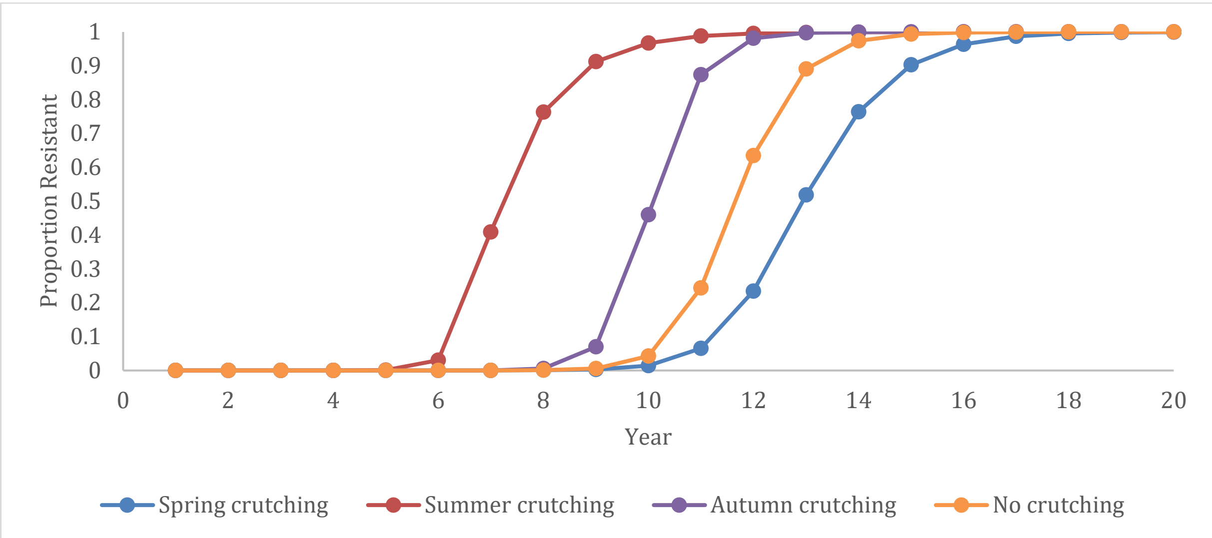

Figure 6.20. Dic (breech only): Resistance development in gene 3 as the crutching date varies. Treatment was one application of Dic (breech only) on the optimised treatment date for each crutching time. Shearing was the 1st of July.

The most cost-effective crutching time was spring crutching. An inclusion of a crutching in spring or autumn was more cost-effective than not crutching, but summer crutching was not cost-effective (Table 6.12).

Table 6.12. NPVs for crutching dates. Treatment was one application of Dic (breech only) each year. All shearing dates were the 1st of July.

Crutching	NPV over 10 years
No crutching	$873,896
Spring crutching	$889,060
Summer crutching	$539,699
Autumn crutching	$882,986

7. Discussion

Strike Treatment Optimiser

The Strike Treatment Optimiser optimised the method and date of application for each chemical based on cost and did not account for resistance development. This would give the same results as using the FlyBoss Tool to determine the optimum treatment dates. The date of treatment application recommended by the Strike Treatment Optimiser was not necessarily the date of treatment application that resulted in the least amount of resistance development. It should be noted that changing the date of treatment alone would influence resistance development, but this study assumed that users followed the standard advice.

Chemical costs had to exceed $41/sheep before chemical treatment was no longer cost-effective. Chemical prices reaching this height is extremely unrealistic, with chemical prices currently fluctuating between $0.30 and $2 per sheep. This lends weight to the advice that preventative chemical treatment should be used in areas with a risk of flystrike.

Extremely valuable ewes (high price for culled sheep) or extremely high wool value changed the recommended treatments, resulting in more treatment and therefore a faster development of resistance. However, very high value sheep would be monitored more closely, so that flystrike would be detected at a very early stage, and treatment of struck sheep could include killing all maggots on the sheep, preventing any increase in resistance.

Breech only vs body + breech treatment

Dic was the only chemical were breech-only treatment was recommended and applying Dic to the breech instead of the breech and body delayed resistance development. When treating only the breech, blowflies striking the body aren’t exposed to the insecticide, and therefore resistance is not being selected for in these blowflies – reducing the rate of development of resistance in the fly population (Heath and Levot 2015). For the first five years, treating only the breech resulted in more flystruck sheep each year than breech and body treatment (due to body strikes when only breech was treated). After five years, resistance to Dic resulting from both breech and body treatment was almost at 100%, and the number of sheep flystruck each year increased if Dic treatment continued unchanged. As resistance increases, treatment becomes less effective, resulting in reduced protection periods and more strikes (Levot 2001). Subsequently, after six years of the same treatment, the risk of flystrike was considerably higher for breech and body treatment than for breech treatment alone. This method of reducing the development of resistance, by allowing some sheep to be struck can only be recommended where the risk of flystrike is very low.

Fly variables

The starting resistance level had a considerable influence on resistance development and was an important setting in the model. It can be assumed that at higher frequency of resistance genes in the starting population the subsequent resistance development will be greater. The true starting resistance level cannot be known, but an estimation of 0.001% appears to be reasonable (Yen *et al.* 1996).

Although rare, *L. cuprina* has been reported to breed off the sheep, for example on possum carcasses (Lang *et al.* 2006) and the model accounts for this. Increasing the unselected flies multiplier increases the number of flies reproducing off the sheep. However, increasing the unselected flies multiplier also decreases resistance development, as the flies reproducing off the sheep are not exposed to chemical treatment. An unselected flies multiplier of 1 was chosen and resulted in an off-sheep development of 1.07%. Although there was sparse literature to suggest an appropriate value, an emergence of <1% of *L. cuprina* from possum carcasses reported by Lang *et al.* (2006) supported this decision. As this assumption affected resistance development and off-sheep reproduction, it was an important assumption in the model.

Requirement for Cyr resistance to express Dic resistance

The model requires existing Dic resistance before Cyr resistance can develop, in acknowledgement of recent findings from Sales *et al.* (2020). During experimentation, the model was updated so that Cyr resistance was required before Dic treatment could cause resistance development in gene 3. This dependence of resistance in one gene for resistance to develop in another delayed the onset of resistance.

This finding raises the question of whether resistance to other insecticides may involve more than one gene and highlights an area of research that is yet to be explored. NN was also given cross-resistance but was only briefly tested due to its high cost per sheep and therefore lack of recommendation by the Strike Treatment Optimiser. However, when used in a mixture with Dic and ML, resistance remained negligible at 0.0045% after 20 years of treatment, suggesting that if time permitted that this would have been an interesting insecticide to research further.

Resistance factors

With limited reported cases of in-field resistance development for the majority of the chemicals used, it was difficult to decide if the chosen resistance factors were resulting in the expected rate of resistance development. ML and NP resistance development in the model was a concern, as resistance developed rapidly when using these chemicals. Although literature suggested that a resistance factor of 8 was reasonable during the beginning stages of resistance (Levot *et al.* 2014), this resulted in a very rapid increase in resistance in testing. As a result of these preliminary tests the resistance factors for ML and NP were reduced to 6 in an attempt to slow resistance development. No other resistance factors were changed throughout experimentation. An unselected flies multiplier greater than 1 could have been used to decrease the rate of resistance development for ML or NP but was not chosen since this is not consistent with the assumption that almost all *L. cuprina* reproduction occurs on the sheep (Lang *et al.* 2006).

Continuous use of same treatment

As expected, continuous use of the same treatment resulted in more resistance development in comparison to the utilisation of rotations. Also as expected, two or more treatments a year will result in more resistance development than one treatment a year. Simulating continuous use of the same treatment resulted in high levels of resistance within 3 to 9 years, depending on the chemical. This is not unexpected, as historically chemicals have become ineffective in short periods of time once resistance had been detected (Levot 2001; Heath and Levot 2015). For example, 70% of flies were resistant to dieldrin four years after resistance was detected (Hughes and McKenzie 1987). Interestingly, since the cessation of dieldrin treatment for flystrike and subsequent lack of selection pressure, dieldrin resistance dropped to 2-3% by 1995 (Levot 1995). This decrease in cyromazine resistance frequency suggests an effect of gene lethality, which was explored here through the use of gene 1. Through continuous use of the same treatment and rotations, it can be seen that lethality decreases the proportion of that resistance gene over time. When comparing CyS and CyJ resistance development, it was evident that jetting resulted in more resistance development than spraying on Cyr. This is because CyJ has a slower day reduction (log linear relationship between chemical concentration and the number of days since treatment was applied), therefore there is a longer period where only resistant flies survive. The chemical with the slowest resistance development was Spn, which is only used for protection for short periods (approximately 4 weeks) and was not a major focus of research as short-term protection is less advantageous than long-term protection (Levot *et al.* 2014).

Rotations

Overall, rotations reduced the rate of development of resistance of the individual products used. Rotation simulations were repeated for multiple chemicals with all rotations proving to slow resistance development, lending credibility to these findings and the functionality of the model. Rotations with two chemicals did not perform as well as rotations with three chemicals. Treating with one chemical for 10 years before changing to another chemical for 10 years proved of little value in slowing resistance development, as resistance reached 100% before the end of the 10-year period.

A potential limitation when comparing NPVs was the number of years for which the NPVs were calculated. When comparing rotations, NPVs were usually calculated over 12 years, which may have been too long as resistance could reach 100% by this point (with genetic disadvantage rotations as an exception). ML and NP rotations run over six years instead of 12 suggested that there was not much difference in cost-effectiveness between the three types of rotations. It should be noted that rotating a chemical was more cost effective than using that chemical continuously. However, differences in NPV were relatively small. Annual rotation of two or three chemicals did not ultimately provide a longer period of protection than using each of the two or three chemicals continuously until they failed. If there is no disadvantage for the resistant genes then there is no recovery when not using the product, so rotation alone does not prevent resistance from developing. However, rotation does provide a longer period of effective control of flystrike in the first few years, resulting in a lower NPV, since this favours the near future over the distant future.

Rotating treatment of three different chemicals was more effective at decreasing the rate of resistance development than rotating treatment of two different chemicals.

When there was a disadvantage for the genes for resistance, rotations were more effective, potentially providing some protection over many years, with the frequency of resistance genes falling when the relevant product was not in use. However, the actual disadvantage, if any, is not known, except for one of the genes of cyromazine resistance, which is known to be lethal.

Mixtures

Using mixtures substantially reduced resistance development. This was as expected, as it is statistically less likely that a fly would be carrying resistance genes to both chemicals. If the fly was only carrying resistance genes to one chemical, it would still be killed by the other chemical (Cloyd 2010). Ultimately, simulated mixtures proved more beneficial in delaying the onset of resistance than using individual insecticides continuously. This was in agreement with conclusions from Mani (1985), whose two-locus resistance model showed that insecticide mixtures slowed resistance. Although mixtures are recommended for internal parasite resistance management (Dobson *et al.* 2001), they are not yet registered for flystrike control. The ML and NP mixture was by far the most cost-effective and most successful in reducing resistance development in comparison to continuous use of the same treatment and rotations. This may have been related to the fact that ML and NP had similar properties. including Dic in a mixture with ML and MP did not have any influence on the rate of resistance development in gene 2.

Monitoring

Routine monitoring results led to the conclusion that a moderate level of monitoring should be implemented in order to reduce flystrike related costs and resistance – and ultimately reduce welfare issues surrounding severe strikes. Increasing the monitoring level and therefore increasing the time spent per week surveying the flock for flystrike allows producers to identify and treat flystruck sheep while the strike is still in early stages, avoiding the loss in productivity that is associated with severe stages of flystrike (Horton *et al.* 2018).

Implementing an extra form of monitoring where maggots detected were removed and killed successfully delayed the onset of resistance

Increasing routine monitoring from an average level or increasing extra monitoring from an intensity of 1 resulted in labour costs that may outweigh the benefit of better monitoring. Further work would need to be conducted before ruling out a certain level of monitoring on the assumption that it is not cost effective. The costs of monitoring used here may not be realistic on all farms.

Shearing and crutching

It is known that shearing during the flystrike season reduces the risk of flystrike as sheep are less likely to be struck when in short wool (Cole and Heath 1999). Spring shearing and summer shearing were more cost-effective than winter shearing, even though summer shearing increased the rate of resistance development. When shearing in summer, treatment was applied early in spring before flies began reproducing. Any flies reproducing once the flystrike season began had withstood treatment and were therefore at least partially resistant. These resistant flies bred and produced more resistant flies while the fly population was very low due to the sheep having short wool from shearing. This is why the rate of resistance development for summer shearing was increased. Spring shearing was effective at decreasing the rate of resistance, whereas autumn and winter shearing had almost identical resistance development over 20 years. This was possibly due to the fact that the optimum date of treatment for autumn and winter shearing dates was the same. Shearing was only tested using CyS and it would have been of interest to run these calculations with other products and observe whether these trends still held. It would also be useful to test a range of periods between the end of spring treatment and the date of the summer shearing.

The default shearing date in the model was winter shearing, as this was the only shearing date that did not have an interaction with any treatment being tested. If there was an interaction between shearing and treatment, then a range of shearing dates would have been required for all other testing. Winter shearing is common for spring lambing, as pre-lambing shearing results in better lamb survival and better wool quality (Pullin and Tipples 2008).

Dic (breech only) treatment was chosen to test crutching dates as Dic was the only insecticide where breech only application was recommended by the Strike Treatment Optimiser and crutching only removes wool from around the breech. Only spring crutching reduced the rate of resistance development. An inclusion of summer crutching was much less cost-effective than not crutching at all, since it increased resistance, similar to the increased resistance seen with summer shearing.

8. Impact on Wool Industry – Now and in 5 years' time

The results of using the model of fly resistance can be used immediately to fine-tune the advice to wool producers in order to limit the further development of resistance of flies to pesticides. This will result in lower resistance in the future, thereby prolonging the use of existing methods of prevention of flystrike.

Further studies using the model can be used to examine some scenarios more closely, such as the combination of treatment with time of shearing and crutching to ensure the optimum control of flystrike, while avoiding an increased rate of development of resistance.

Some additional studies could be made on the genetics of the resistance genes, to clarify whether there is any disadvantage for flies carrying those genes, and whether there are interactions between genes for different chemicals and chemical groups.

9. Conclusions and Recommendations

FlyBoss advises that if two treatments a year is required, to use two insecticides from different chemical groups each year. Over 12 years, alternating between ML one year and NP the next year was a better rotation than treating with both chemicals each year. However, when calculated over six years the difference in cost between these two rotations was negligible, suggesting either rotation could be recommended. Producers are currently advised not to rotate chemicals from the same chemical group, as in the case of Dic and Cyr. However, even with cross-resistance between Dic and Cyr, rotating these chemicals slowed resistance development and increased cost-effectiveness.

Similarly, producers are advised not to use mixtures of insecticides for flystrike management, even though mixtures are an established practice in the management of other livestock parasites. These results also question whether this advice is outdated, and if research into mixtures for flystrike management is required as the threat of resistance grows.

FlyBoss advises that monitoring should be conducted to allow for early therapeutic treatment after detection of struck sheep and advises that maggots on struck sheep should be killed. FlyBoss also suggests spring and autumn shearing to shorten the flystrike season or summer shearing to split the flystrike season into two. Summer shearing resulted in more resistance development and should not be recommended for flystrike resistance management, without further studies on the optimum timing of treatment and shearing.

This study has contributed to flystrike resistance management by demonstrating how rotations, shearing/crutching and monitoring have the potential to delay the onset of resistance development using a model. Through the development of the model, areas of this discipline that need further research have been highlighted – particularly off-sheep blowfly reproduction, current resistance levels in the field and characteristics of the resistance genes (such as partial dominance). Consequently, developing a model was not without limitations. The model assumes that all neighbouring properties are also adopting the same management strategy, therefore not accounting for flies entering from other properties. Another limiting factor was that the model was only tested for one location (Gunning) and therefore lacked validation from other locations with different flystrike risk. Future use of the model could utilise weather data from other locations in Australia to ensure that recommendations in this thesis are applicable nationwide. Additionally, interactions between preventative chemical treatment and the chemicals used as a dressing to treat struck sheep and/or for lice control were not considered. Further work could focus on examining whether using a dressing or lice treatment and a preventative treatment from the same chemical group in the same flystrike season increases the rate of resistance development. The combination of multiple flystrike resistance management strategies was not explored in this thesis. Further work could combine rotations with spring shearing or extra monitoring and compare the rate of resistance development to using either flystrike resistance management strategy individually. Similarly, shearing and crutching was explored individually, but further work could determine the effect of shearing in the flystrike season with one or more crutchings throughout the year on the rate of resistance development.

Although rotations can decrease the rate of resistance development, producers should not rely solely on chemical rotation to prevent resistance development. An integrated management approach should be adopted with non-chemical strategies such as shearing, crutching, and monitoring to slow down the rate of resistance development. For example, rotating chemicals may only provide a certain number of additional years before the insecticide is ineffective, but if during that time the sheep were bred to be resistant to blowflies then insecticide resistance would be less important.

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11. List of Abbreviations and/or Glossary

Table of chemical abbreviations.

Abbreviation	Chemical
DHi	Dicyclanil extra
Dic	Dicyclanil
DLo	Dicyclanil low dose
Cyr	Cyromazine
CyS	Cyromazine spray-on
CyJ	Cyromazine jet
NN	Neonicotinoid
ML	Macrocyclic lactone
NP	New Product
Spn	Spinosyn

NPV Net Present value