Review

Received: 26 January 2017 Revised: 8 June 2017 Accepted article published: 15 June 2017 Published online in Wiley Online Library:

(wileyonlinelibrary.com) DOI 10.1002/ps.4643

Are herbicides a once in a century method of weed control?

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Abstract

The efficacy of any pesticide is an exhaustible resource that can be depleted over time. For decades, the dominant paradigm – that weed mobility is low relative to insect pests and pathogens, that there is an ample stream of new weed control technologies in the commercial pipeline, and that technology suppliers have sufficient economic incentives and market power to delay resistance – supported a *laissez faire* approach to herbicide resistance management. Earlier market data bolstered the belief that private incentives and voluntary actions were sufficient to manage resistance. Yet, there has been a steady growth in resistant weeds, while no new commercial herbicide modes of action (MOAs) have been discovered in 30 years. Industry has introduced new herbicide tolerant crops to increase the applicability of older MOAs. Yet, many weed species are already resistant to these compounds. Recent trends suggest a paradigm shift whereby herbicide resistance may impose greater costs to farmers, the environment, and taxpayers than earlier believed. In developed countries, herbicides have been the dominant method of weed control for half a century. Over the next half-century, will widespread resistance to multiple MOAs render herbicides obsolete for many major cropping systems? We suggest it would be prudent to consider the implications of such a low-probability, but high-cost development.

Supporting information may be found in the online version of this article.

Keywords: pesticide resistance; exhaustible resources; user cost; common pool resource; integrated pest management; herbicide-tolerant crops

1 INTRODUCTION

It has long been recognized that the efficacy of any pesticide, including herbicides, is an exhaustible resource that can be depleted through use over time.[1–3] Long term management of herbicide efficacy is not unlike mineral or petroleum extraction, aquifer management, or management of antibiotic resistance.[4,5] Exhaustible resources are *locally* depleted all the time – oil fields run dry; mines close because ore can no longer be extracted economically. Similarly, use of a particular pesticide will lead inexorably to the evolution of resistance to that pesticide in some pest species. Although a potential problem for local economies, resource depletion often is not a problem for the economy as a whole. New petroleum or mineral deposits are discovered. New technologies make old deposits profitable to tap once again.

An important policy question is, when *does* resource depletion create social, environmental, or economic problems that warrant some public policy response? Resource extraction industries *know* that localized deposits will be depleted, but constant technological change and resource discovery make the 'finiteness' of resources more elastic. The situation may be different for communities relying on an exhaustible aquifer as their sole water source or patients for whom available antibiotics no longer work. For decades, the dominant herbicide resistance paradigm – characterized by beliefs that weed mobility is low, that there is an ample stream of new weed control technologies in the commercial pipeline, and that technology suppliers have sufficient economic incentives and market power to delay resistance – supported a *laissez faire* approach to resistance management emphasizing voluntary actions. Earlier market data bolstered the belief that private incentives and actions were sufficient to manage herbicide resistance.[3,6] The introduction of genetically modified, glyphosate-tolerant (GT) crop varieties in the mid-1990s did not change the *laissez faire* approach to herbicide resistance management as it did with genetically modified Bt crops (reasons for this are discussed later). Where approved, GT crop varieties were widely and quickly adopted. Glyphosate was heralded as a 'once in a century' herbicide.[7] Benefits of GT cropping systems to farmers included simplification of weed-management decisions, convenience, flexibility in timing, reduced crop damage, lower environmental risk, lower management time requirements, and compatibility with conservation tillage.[8]

The rapid and pervasive adoption of GT crops in the western hemisphere led to heavy reliance on glyphosate for weed control, a reduction in the diversity of weed control tactics, and a steady rise in glyphosate resistant weeds.[9] The costs of glyphosate resistant

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weeds in US corn, cotton, and soybeans alone have reached $1 billion per year.[10] The proliferation of weeds resistant to glyphosate and other herbicides would not be cause for concern if industry were introducing new MOAs to replace older, ineffective ones. But, no new commercial herbicide MOA has been discovered in more than 30 years. Industry has responded by developing crop varieties that are tolerant of multiple MOAs. Yet many weed species are already resistant to one (or more) MOAs intended for use with these varieties. So the resistance management benefits of stacking herbicide tolerant traits may be illusory in some cropping systems.

The growing weed resistance problem has drawn the attention of the scientific community and government agencies, as well as chemical/seed industry and farm groups. The US National Research Council (NRC) report on the sustainability of genetically modified crops devoted considerable attention to resistance issues and recommended a national public–private collaboration to develop cost-effective management programs.[11] The 2016 NRC report on the future prospects for genetically engineered crops affirmed the importance of addressing resistance.[12] The Weed Science Society of America (WSSA) and the US Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) collaborated to publish special journal issues on resistance management.[13,14] The Council for Agricultural Science and Technology similarly issued a report outlining the economic and environmental consequences of resistance as well as options to combat it.[15] WSSA and the NRC collaborated to organize two herbicide resistant weed summits in Washington, DC, to bring together stakeholders to develop concrete action items to address resistance.[16] Agricultural input industries and commodity groups have also been active participants in these endeavors in addition to supporting research on grower adoption of resistance management practices. On 15 October 2014 the US Secretary of Agriculture, Tom Vilsack, announced plans for USDA to commit additional resources to address the growing herbicide resistance problem.

This increased attention to herbicide resistance has called into question the dominant paradigm that has been the foundation to a *laissez faire* approach to herbicide resistance management. This article reviews the beliefs underlying this earlier paradigm. We make use of a framework originally developed by Miranowski and Carlson in a National Academy of Sciences report on insect resistance to pesticides to the case of herbicide resistant weeds.[3] This framework represents a more complete treatment of resistance management than those focusing on farm-level management decisions. Miranowski and Carlson explicitly considered the role of a broader set of participants including, 'pesticide manufacturers, formulators, retail firms, custom applicators, pest-control consultants, and farmers (p. 436).' Their framework considered the private incentives and mechanisms that farm input suppliers have to delay resistance as well as public agencies to either regulate chemical use or provide public information (extension) to management resistance. Other key features are the degree of weed mobility, which determines how much control individual farmers have over resistant weeds and third-party costs (externalities) that may be imposed on other members of society. The framework includes normative policy considerations, such as determining under what circumstances public intervention in private markets and decisions *might* be warranted. This framework is useful for understanding why – up until recently – a more *laissez faire*, voluntary approach to herbicide resistance management appeared to be justified.

Next, we re-examine the major assumptions and beliefs underlying the dominant paradigm and find that evidence supporting a *laissez faire* approach is weaker than it was 30 years ago. While some in industry have expressed confidence in the possibility of 'eliminating' resistance by 2050,[17] we consider a more pessimistic possibility. Herbicide use first took off in the 1950s, but near universal use, for example on US planted acres of major crops, was not reached until around 1980.[18] Given that herbicides have been pervasively used for less than 40 years, is it possible that herbicides are a 'once in century' form of weed control? In other words, by 2050 instead of 'eliminating resistance,' will the efficacy of herbicides be eliminated in some major cropping systems? Related questions are, what is the evidence that we are somehow 'running out' of herbicide efficacy? If so, what are the economic implications to farmers if they are forced to switch to more expensive practices and to suffer greater yield losses? What are the scope and limits for private incentives, private actions, and public policies to address this issue? Betting against human capacity to innovate to extend the supply of 'exhaustible' resources is a fraught exercise (see, for example, the Simon–Ehrlich bet).[19] Yet, even a small probability of herbicide obsolescence is as deserving of consideration as an assertion that 'resistance' (i.e. the laws evolutionary biology) will be 'eliminated.'

2 ECONOMIC INCENTIVES AND RESISTANCE MANAGEMENT

Economic studies of resistance management have focused on how resistance alters (or should alter) farm management decisions, focusing on voluntary responses of farmers to private economic incentives. They also have considered whether pest, weed, or disease resistance create special problems that are not adequately addressed by private market responses and warrant some form of public policy intervention. The focus of analysis is usually an individual farmer or groups of farmers. This is because farmers are often the proximate decision makers for on-farm weed management decisions. Yet, many actors influence resistance management.[20] These include crop consultants, custom applicators, and custom machine operators, as well as cooperative extension agents and specialists. The agricultural chemical industry develops new compounds or new seed varieties that complement old ones. Regulatory agencies determine how, and on which crops, chemicals can be used. They also affect how quickly new technologies become commercially available. Universities and other research institutions also develop and evaluate a host of non-chemical methods of weed control. These off-farm actors play important roles in shaping grower attitudes and beliefs about the long-term benefits of resistance management.

In 1984, the US National Academy of Sciences convened a Committee on Strategies for the Management of Pest Resistant Pest Populations and organized conferences and workshops to produce a report on pest resistance, focusing primarily on insect pests, but occasionally addressing herbicide resistant weeds. The subsequent report[21] included a chapter by Miranowski and Carlson[3] on the economics of public and private approaches to preserving pest susceptibility. The framework developed in that chapter considered the roles of private economic incentives and public policies in managing resistance. Now 30 years old, their approach remains highly useful. It explains well more recent developments in resistance management policy brought on by the introduction of genetically modified crops and still provides a useful framework for understanding contemporary resistance problems.

Miranowski and Carlson's framework (hereafter the 'MC framework') included four key elements. First, in line with earlier studies, they characterize the evolution of resistance – either of insects to insecticides, fungal pathogens to fungicides, or weeds to herbicides – as an exhaustible resource management problem.[1,2,19] Through constant use, the efficacy of a pesticide could be depleted just as oil could be from a well or ore from a mine. Greater use of a pesticide in the present speeds the evolution of resistant pests. As with other exhaustible resources, taking steps to conserve the resource today to prolong its use can entail loss of current benefits from using the resource. When resources are finite and exhaustible, current use means that there is less of that resource available in the future. The cost of this future limitation is referred to as a 'user cost'.[1−3] Failure to account for this user cost – ignoring the future consequences of current resource use – will lead to depletion of the resource occurring too soon. By 'too soon,' we mean at a rate that does not maximize long-run returns. Farmers thus face an intertemporal trade-off: steps taken to delay resistance – and maximize long-term benefits – may provide growers with lower short-term profits.

Second, the MC framework (as with previous work[2,22]) considers the critical role of pest mobility. If pests are not particularly mobile,[23] then growers have control over the extent of resistance on their own land. Managing resistance remains a multi-year management problem, but an individual one. If, however, pests are highly mobile, then resistant pests on a farmer's fields may depend on the extent of resistance management by neighbors. Growers have less incentive to adopt costly resistant management practices today if they expect that their neighbors will not manage resistance. Thus, in an area, each grower may believe that managing resistance on their own fields is pointless and that delaying resistance is beyond their own control. Because farmers cannot prevent others from depleting the efficacy of pesticides, they have little incentive to preserve it on their own farms. Thus, attempts to manage resistance can suffer from the 'tragedy of the commons'.[23,24]

Third, departing from previous work, the MC framework explicitly considered the incentives and the role of agricultural chemical companies in resistance management. Companies had an incentive to consider how current product sales could negatively affect future sales and profits via resistance. Patent protection could enhance firms' monopoly control over specific compounds. Such protection could give companies both greater incentives and mechanisms to limit sales to 'conserve' pest susceptibility. Further, a company's behavior would also change depending on its ability (and competitors' abilities) to develop new, substitute compounds.

Fourth, the MC framework considered how different private and public actors might organize to manage resistance. It addressed the questions of, when are private market incentives and voluntary actions sufficient to adequately manage resistance and when *might* public interventions be warranted? We say 'might' because they emphasized that there were costs to any intervention that would not necessarily outweigh any benefits. The MC framework began identifying conditions where private actions by farmers, individual chemical companies, or multiple chemical companies in coordination would be sufficient. Regulatory interventions were only considered as a last resort if private, voluntary actions were insufficiently effective. They concluded from their analysis that, 'development of pesticide resistance is not an argument for resistance management in and of itself. The best group to implement resistance will depend on market and pest mobility conditions (p. 447).'[3]

Although the MC framework focused on insecticide resistance, applying their framework to weeds and herbicides appeared to support a *laissez faire* approach to herbicide resistance management, relying on voluntary actions by private actors. First, they argued that, unlike some insect pests, weeds were not especially mobile. So 'tragedy of the commons' problems were less likely. Second, whether resistance to any one compound represented a significant problem depended on the capacity of the chemical industry to introduce substitute compounds. At the time of their writing, a steady stream of new MOAs was still being developed. Third, patent protection and market power of a concentrated agricultural chemical industry provided firms with both economic incentives and mechanisms to limit current uses to maintain the efficacy of herbicides. Economic theory does *not* imply that resistance should not occur. Indeed, resistance of some weeds to some compounds can develop rather quickly. Multiple weed biotypes evolved resistance to acetolactate synthase (ALS) inhibitors within 5 years of commercial introduction,[25] while resistance of horseweed to glyphosate was observed with 3 years of regular use on soybeans in Delaware.[26] Standard economic theory merely suggests that individual firms have an incentive to manage their resources to maximize long-term returns. It may well be profitable for firms to accept resistance of some weeds to some compounds over time.

Earlier market data also appeared to bolster the belief that private incentives and actions were sufficient to manage herbicide resistance. Miranowski and Carlson[3] argued, 'If new pesticides are not expected to be readily available in the future, we should see higher relative pesticide prices to reflect the increasing scarcity (p. 442).' Yet, at the time of their analysis, herbicide (insecticide and fungicide) prices were rising more slowly than other farm inputs. Based on such evidence, they concluded, 'The aggregate market evidence does not indicate the need for overwhelming concern over future pesticide availability and pest susceptibility (p. 442).'

Public policy regarding herbicide resistance management at the time in the US followed a *laissez faire* approach, where the role of the public sector was limited. Herbicide use was regulated to control external costs (e.g. negative effects on worker safety, water quality, etc.), but not explicitly to address user costs of resistance. Public research and extension provided information to farmers about the intertemporal (i.e. now vs. later) trade-offs associated with herbicide resistance, how to incorporate new MOAs into their production systems, and how to incorporate non-chemical methods of weed control into their production systems.

3 ENTER HERBICIDE-TOLERANT CROPS

The introduction of genetically modified, glyphosate-tolerant (GT) crop varieties in the mid-1990s did not change the *laissez faire* approach to herbicide resistance management as it did with genetically modified Bt crops. GT varieties came right at the time when a number of economically important weeds had developed resistance to the most economical herbicide MOAs. Herbicide tolerant (HT) crops were not a new herbicide MOA. Rather, they expanded the applicability of existing ones. While genetically modified, insect resistant Bt crops were subject to explicit resistance management regulation, such as EPA-mandated refuge planting requirements, resistance management for HT crops relied on voluntary measures.

There were a number of reasons for the difference in approach.[27] While Bt crops incorporated an insecticide into a crop, HT crops did not. Glyphosate had already been commercially approved and its toxicological and chemical properties had been more thoroughly studied. Moreover, there was concern (and active lobbying by) organic crop producers concerned about whether the new Bt crops would lead to widespread resistance to the Bt foliar sprays that they relied upon. Here, there was a more obvious, potential external cost that users of Bt cotton or corn could be imposing on organic producers that would warrant some form of intervention.

Some of the insects Bt crops controlled were highly mobile, suggesting that attempts at individual, private resistance management strategies would lead to tragedy of the commons problems and rapid resistance evolution. Yet, weeds were still characterized as relatively immobile.[28,29]

In contrast to environmental concerns over Bt crops, there was some evidence of environmental *benefits* of the shift to GT crops.[30] Compared to many competing herbicides, glyphosate has certain desirable environmental characteristics. It degrades relatively quickly in the environment. Unlike water-soluble herbicides (e.g. atrazine), it is less likely to reach groundwater sources. Further, it has a lower EPA toxicity rating than many other herbicides; widespread adoption of GR soybeans was predicted to lead to significant reduction in the overall acute mammalian toxicity of herbicides used.[27] Studies also found evidence that adoption of GT crops encouraged adoption of conservation tillage methods.[31,32] Conservation tillage can reduce soil erosion and attendant water pollution as well as carbon emissions from passes over the field.[11,33]

Patent protections for new herbicide tolerant crop varieties appeared to give chemical–biotechnology firms both incentives and the market power to limit resistance. At first, it was even questioned whether glyphosate resistant weeds would become a problem. Some argued that glyphosate had been in commercial use for many years (though to a much more limited extent) with little sign of resistance developing and that evolution of weeds to glyphosate in field conditions was 'unlikely'.[34]

In sum, a constellation of beliefs – what we refer to as the 'dominant paradigm' – buttressed continuance of a *laissez faire* approach to herbicide resistance management in North America. These included beliefs that weed mobility was not a significant problem, that the possibility of glyphosate resistance was remote, that GT crops were associated with environmental benefits (such as lower toxicity and greater use of conservation tillage), and that firms supplying the new herbicide-seed technology packages had adequate incentives and means to limit resistance.

4 CHALLENGES TO THE DOMINANT PARADIGM

Increasingly, facts on the ground have challenged the dominant paradigm underlying herbicide resistance management. First, within a year of a publication claiming that field evolved resistance of weeds to glyphosate was unlikely, articles confirming glyphosate resistance in rigid ryegrass (*Lolium rigidum* Gaudin) in Australia were published.[35,36] In Delaware, in the US, for some farms 'within 3 years of using only glyphosate for weed control in continuous glyphosate-resistant soybeans, glyphosate failed to control horseweed in some fields.'[26] In 1995, before the introduction and widespread adoption of GT crops, there were no reported GR weed species in the US today there are 16, with one or more GR weed species reported in 38 of 50 US states.[37] The dramatic reduction in the diversity of weed control tactics that accompanied GR crops – including reduced reliance on non-chemical control methods and a reduction in the diversity of MOAs used – contributed to the rise in GR weeds.[9] Worldwide, the number of weed species rose from zero in 1995 to 34 by 2015.[37] The growth of herbicide resistant weeds is not confined to glyphosate resistant weeds in the United States. Globally the *growth rate* in unique resistant cases of weeds of all types rose sharply after the late 1980s.[37]

The evolution of resistance by particular weeds to particular MOAs need not be a severe economic problem so long as new, substitute MOAs (or effective non-chemical control methods) are being continually developed. From the mid-1950s, when herbicide use started to take off in North America, until the early 1980s, new MOAs were being introduced at a rate of roughly one per year.[37] Yet no new commercial herbicide MOA has been discovered in more than 30 years.[37,38] The success and dominance of GT crops masked the lack of new MOAs. Today companies are introducing multiple-tolerance transgenic seed varieties, tolerant of old chemistries such as glyphosate, glufosinate, dicamba, and 2,4-D. Yet these are not new MOAs, rather just new ways of using (and depleting the efficacy of) existing ones. Further, many weed species are already resistant to one (or more) MOAs to be used with these varieties.[37] This means that the purported resistance management benefits of stacking herbicide tolerant traits may be illusory in some cropping systems.[39]

There is further concern that GR weeds will undercut some of the environmental benefits of GT crops. Some of the older chemistries (such as 2,4-D and dicamba) to be used in stacked trait crop varieties have less benign environmental profiles than glyphosate. It has been estimated that a switch away from GT crops because of GR weeds would lead to increases in the acute mammalian toxicity of herbicides used on soybeans and cotton.[40] There are also concerns that herbicide resistant weeds could discourage continuation of conservation tillage in many areas.[15,41] Soil disturbance from tillage generally causes higher erosion with sediment, nutrient and pesticide-laden runoff, and more carbon dioxide emissions from oxidizing soil particles. Dis-adoption of conservation tillage has not appeared to be a problem in Australia as, 'Few farmers chose to revert to a cultivation-based farming system. The benefits of zero tillage in the Australian environment are too great to make a return to cultivation attractive (p. 2).'[42] In the US there is little evidence, based on USDA's Pest Management Surveys, of declines in conservation tillage in corn and soybean production. For cotton, however, the share of cotton acreage practicing no-till or minimum till declined from 54% in 2007 to 47% in 2015.[43]

There is also growing evidence that the mobility of resistant weeds is a greater problem than previously appreciated. Resistant weed seed can be transported great distances via movement of farm equipment or hay shipments.[44] Palmer amaranth seed can spread via irrigation and other water flows, with the movement of animals, and through plowing, mowing, harvesting and spreading compost, manure, or cotton gin trash.[45] Resistant alleles can also be transferred great distances to susceptible populations through movement of pollen and seed or other propagules.[46,47] In addition to any physical realities of mobility, there is evidence that growers *believe* their neighbors affect their own weed resistance and that resistant weeds are the result of factors beyond their individual control.[48]

Weed mobility problems will vary by weed species and cropping system. A landscape-scale empirical study[49] found no evidence of spatial contagion (i.e. increased infection probability due to proximity to infected fields) of herbicide resistant common waterhemp (*Amaranthus tuberculatus*). In contrast, a bioeconomic modeling exercise[50] found potential for common pool resource problems with resistant horseweed (*Conyza canadensis*) in continuous soybean production systems, but not for continuous corn or corn–soybean rotations. In Australia, common pool resource issues in pesticide resistance are viewed by some to be relatively unimportant. This stems in part from the very rapid evolution of resistance to different selective herbicides by annual ryegrass. Pannell *et al.*[42] note: 'in the case of ryegrass resistance to selective herbicides in Australia, the external cost of resistance spread has been minor in most cases. The reason is that almost all farmers were using similar herbicides intensively, so they were evolving resistance on their farms at approximately the same rate. Spread of resistant weeds from one farm to another is a minor issue if the second farm was on the verge of generating a resistant weed population internally anyway. (p. 138).'

Yet, as one reviewer has pointed out, this is exactly what one could expect in a common-pool setting. The authors concede, further, that, 'It appears likely that the speed of development of glyphosate resistance will be more variable amongst farms. If so, the potential for external costs from weed spread will be greater (p. 139).' In Australia, the Office of Gene Technology Regulator has approved use of glyphosate tolerant crop varieties for only one crop, canola. Australia also has much larger farms than in the United States or the European Union. This naturally limits the spread of weeds across ownership boundaries.

Finally, the scope of chemical-seed companies to exercise market power to delay resistance may also be less than earlier believed. In 2000, glyphosate went off patent. The rise in generic glyphosate products led to share reductions in glyphosate prices, increases in use, and acceleration in the evolution of resistant weeds. Ten more herbicides are scheduled to go off patent in the coming years.[51] The original patent holders will have less scope to control supplies (and hence slow resistance).

The MC framework modeled chemical companies as a sole owner with the objective of maximizing long-run company profits. This approach, common to other studies of exhaustible resource extraction, treats a monopolistic firm as governed by a single decision maker, with the single objective of maximizing long-run company profits. This presumption, though, is just that – a presumption. Corporations are not monolithic, and the short-term economic incentives of their officers are not always in concert with long-term profit goals. There is a growing body of empirical business literature identifying problems of 'short-termism' among corporate executives.[52,53] In one survey of corporate executives, respondents were asked to choose between two 5-year projects.[53] The first project had a higher net present value (i.e. greater long-run returns), but negative cash flows in the first 2 years. The second program had positive short-run cash flows in each year, but its net present value (long-run returns were lower than the first project. Researchers found, 'A surprising 41% of respondents said they would choose the NPV-inferior project (p. 22).'[53] In another survey of 401 corporate chief financial officers (CFOs), more than 80% of respondents said they would cut expenditures on R&D and marketing to meet quarterly earnings targets, even if this would hurt long-term company value.[52]

5 SORTING OUT PRICE SIGNALS

Examining agricultural input trends from the late 1960s to early 1980s, Miranowski and Carlson noted that herbicide (and other pesticide) prices were rising more slowly than other agricultural input prices.[3] They argued that the lack of price increases suggested that market actors were not concerned about future availability of pest susceptibility. They noted, however, that market prices are affected by market features (such as patents and market power), environmental regulations, and energy costs also affect pesticide prices. An applied econometric model was developed[6] to test whether common property resource problems existed for pesticides and herbicides or whether individual growers had control over the level of resistance on their own farms. The model provided evidence of increasing resistance and common pool resource problems for insecticides, but 'no resistance buildup or common property characteristics for herbicides (p. 45)'. The data for this analysis, however, covered the United States from 1950 to 1984. This preceded the sharp rise in herbicide resistant weeds that occurred subsequently in the US. Up to 1984, there were 36 reports of state/site of action/weed species combinations in the US.[37] Since then, this number has grown to 156 combinations. US herbicide prices still rose more slowly than agricultural production items as a whole from 1990 to 2010.[27]

Pesticide resistance has continued to evolve steadily for fungicides,[54] insecticides[55,56] and herbicides.[37] Yet contrary to expectations, if the cost of resistance was being factored into pesticide price, the inflation-adjusted market price of most pesticides has not increased over the past 15 years.[50] Instead, insecticide prices have decreased (Fig. 1a; $\text{slope}_{\text{year}} = -1.24$, $p < 0.001$), fungicide prices have remained constant (Fig. 1b; $\text{slope}_{\text{year}} = -0.10$, $P = 0.25$), and herbicides have decreased (Fig. 1c; $\text{slope}_{\text{year}} = -0.11$, $P < 0.01$) (Supporting Information, Methods). For weeds, a comprehensive database of unique resistance events has been compiled for all major sites of herbicide action, going back to the mid-20th century.[37] When these data are integrated with public records of herbicide and seed prices for 1990 through 2015, the patterns revealed are striking. Although cumulative unique resistance events increased for all sites of herbicide action (Fig. 2a), herbicide prices remained constant over the same period (Fig. 2b; $\text{slope}_{\text{resistance}} = -3.0$, $P = 0.38$).

If the number of herbicide resistant weeds continue to grow and no new MOAs have been discovered in the past 30 years, why are we not seeing increases in herbicide prices? There are many possible explanations. As Miranowski and Carlson noted, many other factors influence prices besides resource exhaustion.[3] First, the price of glyphosate dropped dramatically once it went off patent in 2000, while patents for several other herbicides have also expired. This led to the entry of generic herbicides into the market, depressing overall herbicide prices.[57] One would expect a transition from a monopoly pricing regime (via patent protection) to a more competitive price regime (with the introduction of generics) to lower overall herbicide prices. Next, inflation adjusted crude oil prices have fallen 64% over the last five years. Energy price modeling exercises suggest reductions in fossil fuel costs would exert downward pressure on pesticide prices of 6%.[58]

Third, price trends for exhaustible resources do not in and of themselves measure actual physical resource scarcity. Rather, they reflect people's *beliefs* about physical scarcity, which may or may not turn out to be correct.[59] There is evidence that farmers (at least in the United States and Australia) have maintained a high degree of confidence that chemical companies will be able to deliver new products to address resistance problems.[60–62] Farmers have formed such expectations based on the past record of chemical companies providing new chemistries that address immediate resistance problems. Following development of triazine-resistant weeds, farmers were able to switch to acetolactate synthase (ALS)-inhibiting and ACCase-inhibiting herbicides. When weeds evolved resistance to ALS-inhibitors and ACCase-inhibitors, the introduction of glyphosate-resistant crop varieties allowed farmers to switch to glyphosate.[9] In addition, chemical industry officials have also expressed confidence in addressing resistance.[17] There

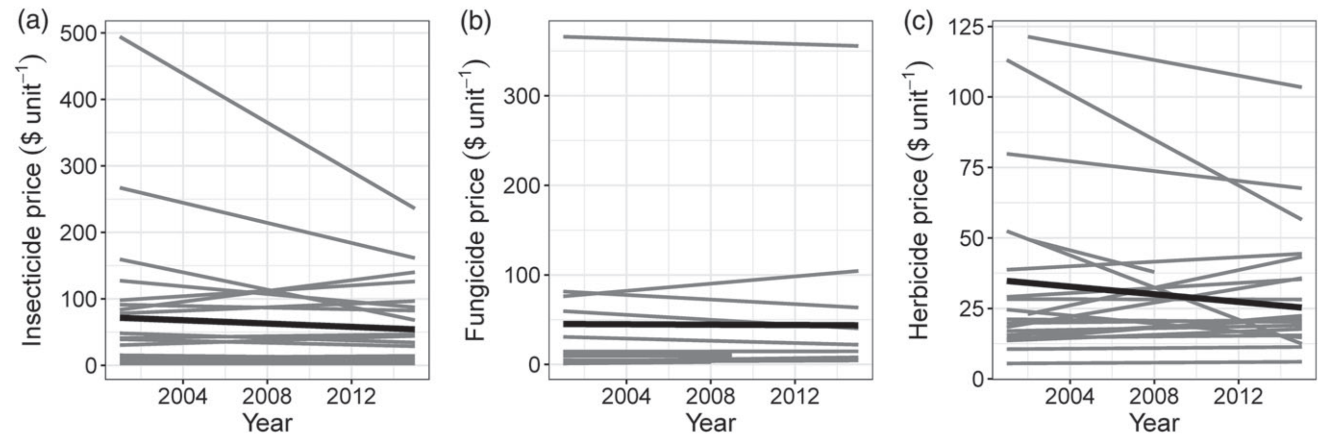

Figure 1. Pesticide prices have remained constant or decreased for (a) insecticides, (b) fungicides and (c) herbicides over the past 15 years. Grey lines represent best linear unbiased predictors for individual pesticide classes, generated from linear mixed effects models of pesticide price over time. Black lines represent the population-level response. See supplemental information for pesticide classes included in the analyses. Source: USDA NASS.

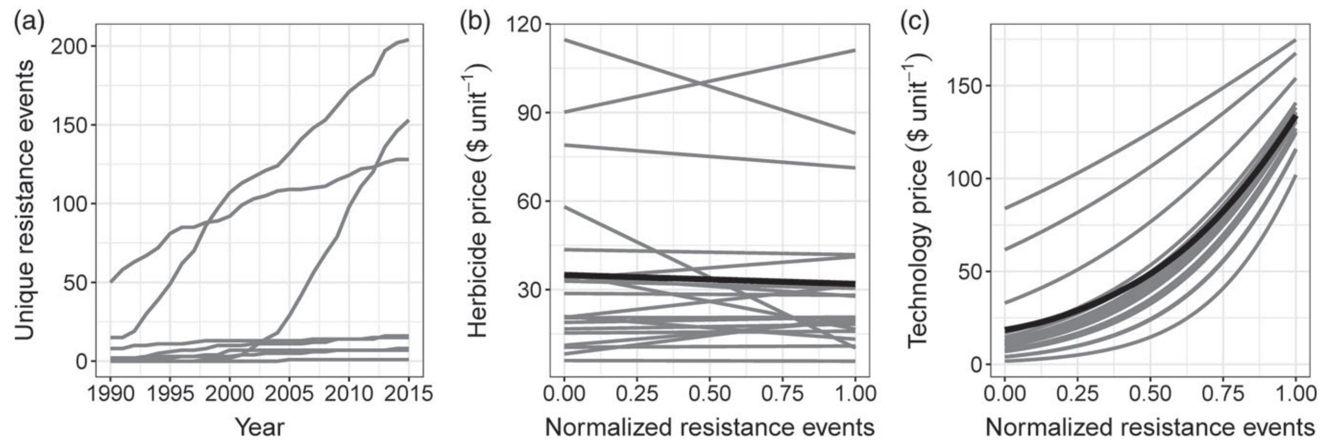

Figure 2. Cumulative unique herbicide resistance events (a) have increased over the 1990 through 2015 period in the US for most herbicide modes of action common used in maize and soybean production. The price of herbicide resistance (normalized from 0 to 1) was not reflected in the market price of the herbicides during this period (b), but was positively associated with the cost of technology bundles (c) that include both seed and herbicide cost. Grey lines represent best linear unbiased predictors from linear mixed effects models for individual herbicide MOA; black lines represent the population-level response. Source: USDA NASS.

is also some evidence that farmers who believed that new herbicides would be available soon were less likely to adopt resistance management practices.[63] Thus, farmers may see no need to switch to more costly practices that might bid up herbicide prices if they expect solutions to resistance problems to be forthcoming.

One final reason that trends in herbicide price series are not signaling scarcity of herbicide efficacy is that herbicide prices may not be accurately reflecting the total costs of weed control. When companies introduced herbicide-resistant crop varieties, these seeds came with technology fees (price premiums) attached to the seed, rather than their associated herbicides (predominantly glyphosate). Herbicide tolerant crops now dominate acreage of corn, soybeans, cotton, and canola in North and South America, and weed control is achieved via a seed-herbicide 'technology bundle.' The costs of weed control now hinge on the price of seed as much as the price of herbicides. While it is true that herbicide prices have risen more slowly than production inputs overall, seed prices have risen much faster. From 1995 to 2016, herbicide prices rose 25% while the price index for all production inputs doubled. Over this same time though, seed prices tripled.[43] Seed prices also include technology fees embodied for insect resistant Bt traits, but Bt price premiums have been falling since 1996. When the price of the entire commodity bundle (seed technology fee plus herbicide price) is taken into account, it is strongly associated with the increase in resistance events from 1990 to 2015 (Fig. 2c; logistic model fixed effects: asymptote = 402, $P < 0.0001$, xmid = 1.2, $P < 0.0001$, scale = 0.40, $P < 0.0001$).

6 RECENT TRENDS IN WEED MANAGEMENT

Recent trends in weed management point to an upsurge in the quantity of herbicides used, a decline in herbicide productivity (the amount of crop produced per herbicide input), and an increase in farm-level costs to deal with herbicide resistant weeds. Here we use an example from the US, since the time series data are comprehensive and publicly available.[37,43]

Herbicide use in the US first took off in the 1950s, but near universal use on planted acres of major crops was not reached until around 1980, when farmers applied more than 400 million pounds of herbicide active ingredient (a.i.).[18] Usage dropped, then fluctuated between 300 million and 350 million pounds a.i. from the mid-1980s to mid-1990s. Starting in the mid-1990s total a.i. fell further, as reductions in older herbicides exceeded increased glyphosate use. From 2002 onward, use of other compounds has

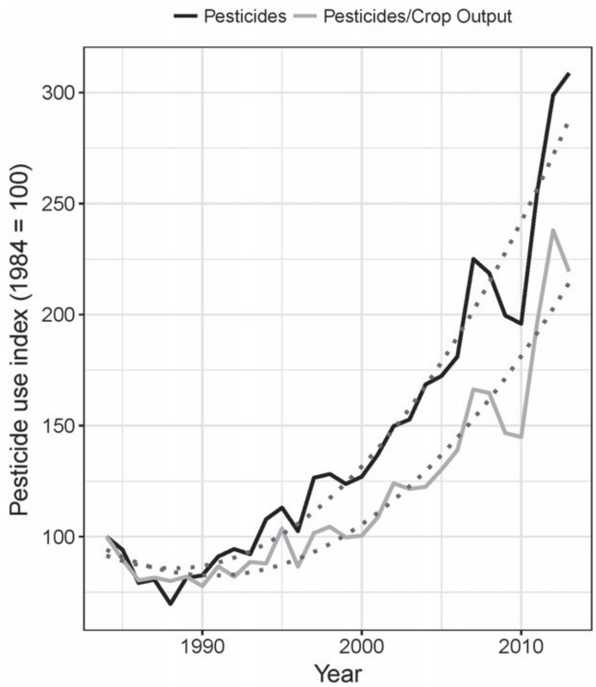

Figure 3. Aggregate index of pesticide use increased, both as an absolute measure (black solid line) and in relation to crop productivity (grey solid line), over the 1984 through 2014 period in the US Dotted lines represent quadratic regression models (pesticide use $= 0.33x^2 - 1301x + 10^6$, $R^2 = 0.95$; pesticide use/crop productivity $= 0.26x^2 - 1050x + 10^6$, $R^2 = 0.92$). Source: USDA ERS.

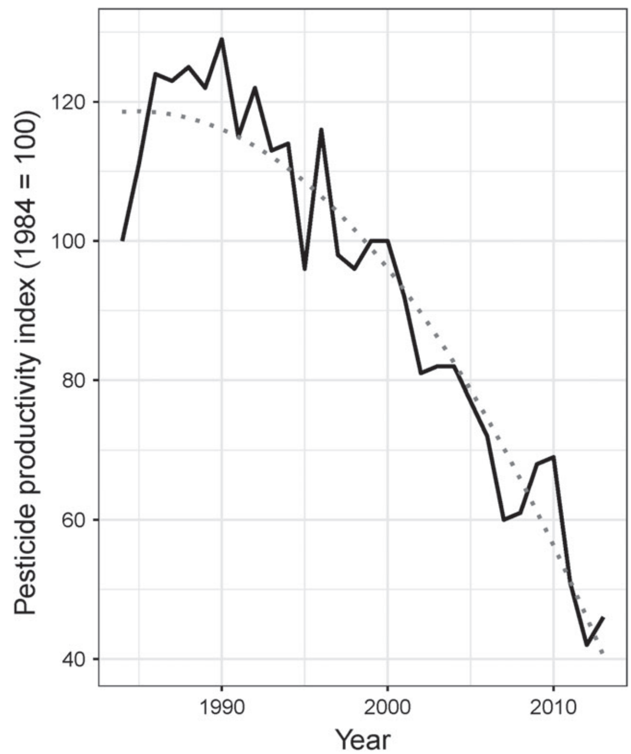

Figure 4. Aggregate index of pesticide productivity (crop productivity per unit of pesticide use) decreased over the 1984 through 2014 period in the US. Dotted line represents a quadratic regression model (crop productivity per unit pesticide use $= 0.098x^2 - 391x + 3.8 \times 10^5$, $R^2 = 0.92$). Source: USDA ERS.

stabilized while glyphosate use continued to increase. Total a.i. once again exceeded 400 million pounds a.i. While the sharp rise in herbicide use in the 1970s was attributable to more acres where herbicides were applied, the recent sharp increase in herbicide use is attributable almost entirely to more use per acre.

The total amount of a.i applied is not necessarily good measure of the quantity of herbicides used or the environmental impacts of that use.[64] To create a US national aggregate index of pesticide use requires adjusting pounds of a.i., by quality characteristics such as pesticide potency, hazardous characteristics, and persistence in the environment. Figure 3 uses such an index to show trends in US pesticide use and use per aggregate unit of crop production since 1984. This represents the period where herbicide use was firmly established on major field crop acres and herbicides dominated overall pesticide use. US pesticide use per crop output remained relatively constant from the mid-1980s to the mid-1990s. More recently, though, pesticide use per unit of output has risen more sharply reaching levels double those of the mid-1990s. Figure 4 presents this data as a partial productivity measure – US crop output per unit of pesticide input. US pesticide productivity has declined significantly (by more than 50%) over the past 30 years. In a study weighting herbicides by toxicity,[64] herbicide use intensity was shown to increase for maize, cotton, rice and wheat over the last 25 years. Analyzing data from a large plot-level, representative sample of US maize and soybean farmers from 1998 to 2011 provided 'clear evidence of increasing herbicide use by GT variety adopters over time for both soybeans and maize, a finding that we attribute in part to the emergence of glyphosate weed resistance.'[65]

Herbicide resistant weeds have begun to prove costly to US farmers. One survey of weed specialists placed costs of managing resistant weeds (using additional herbicides and/or hand weeding) as high as \$35/acre for corn, \$42/acre for soybean, and \$100/acre for cotton.[66] A large-scale survey cotton growers found the proportion of growers with weed control costs of \$50/acre or more nearly doubled with the emergence of HR weeds on their farms.[67] Farmers have reported heavy yield losses, with complete acreage abandonment in some cases.[68] A USDA study found that growers reported fields had been infested with GR weeds on 4.5 million US corn acres in 2010, while farmers reported a decline in the effectiveness in glyphosate applications on 32.5 million soybean acres in 2012.[69] Controlling for other factors, corn growers reporting a GR-weed infestation had economic returns that were \$67.29/acre lower than for other growers. For soybean growers reporting a decline in glyphosate effectiveness, returns were \$22.53/acre lower than for growers who did not report declining effectiveness.[69] These losses (which combine higher weed control costs and yield losses) on the acres involved and combined with estimated resistance in US cotton[68] suggest that glyphosate resistant weeds are costing US corn, cotton, and soybean growers more than \$1 billion per year.[12]

7 THE END OF HERBICIDES? AN ARGUMENT FOR 'PRICING IN' THE RISK

In contrast to the multi-faceted integrated pest management approaches that are increasingly common in management of disease and insect pests,[70,71] producers have been slow to adopt best management practices for herbicide stewardship, leading to calls for economic incentives and regulations for conserving weed susceptibility to herbicides.[72] The accelerating evolution and spread of herbicide resistant weed genotypes, with the imminent loss of chemical control in some locations and systems, offers an advance warning for other forms of pest management.

We believe that the costs of herbicide resistance are undervalued because the underlying risk model does not fully capture the magnitude of the situation. In comparison to pathogen and insect pest evolution of resistance to fungicides and insecticides, in which local stocks of susceptibility are often renewable through immigration and multiple pest generations per season, pest-compound relationships are highly specific, and numerous alternate pesticidal compounds exist,[28,73] weed evolution of resistance to herbicides within a local population appears to be cumulative and unidirectional, due to the low dispersal range of many weeds and low fitness costs of many herbicide resistance alleles.[49,74] In the absence of selection by herbicides, the standing allele frequency of resistance genes with low fitness penalties does not decrease in the soil seedbank.[74] Rather, it remains more or less constant, ready to be enriched by the next round of selection. Over time, this results in an inexorable increase in the proportion of herbicide resistant individuals in a population.

The lack of diversity of chemical options for weed control is another key feature of the additional threat posed by herbicide resistance. Currently, there are a few dozen commonly used herbicides registered for use in US soybean production,[75] representing 11 herbicide modes of action and 13 physiological sites of action. When considering the chemical control of a single weed species, the number of available compounds drops precipitously. In the case of *A. tuberculatus*, a dioecious summer annual forb that is currently the dominant weed in soybean production systems of the north central region of the US,[76,77] herbicides from only six sites of action receive fair or better ratings for selective control in soybean.[78] The low fitness cost of resistance traits, combined with the obligate outcrossing typical of this species, have resulted in recurrent, independent evolution of *A. tuberculatus* genotypes with multiple resistance, ranging from two to five of the relevant sites of action.[79,80] Alarmingly, an *A. tuberculatus* population in central Illinois has evolved five-way multiple resistance, with only glyphosate remaining available for chemical control; many of the neighboring farms have glyphosate resistant *A. tuberculatus* populations, raising the possibility that a six-way multiple resistant population will evolve, precluding chemical control of this species in a corn–soybean rotation.[80] Extension weed scientists from across the southern and central US relay similar reports of genotypes of dioecious Amaranthaceae, including *A. tuberculatus* and *Amaranthus palmeri*, with multiple resistance to several sites of action.[79,81]

The confluence of steadily increasing resistance levels due to low weed mobility and low fitness costs of some resistance, greater prevalence of multiple resistant weed genotypes, and the absence of new herbicide chemistries in the research and development pipeline for the foreseeable future represent a perfect storm of risk to agricultural producers. It is not a matter of if, but when, multiple resistant weed genotypes evolve that are completely resistant to chemical control for a particular cropping system. Under such a scenario, the cost of herbicide resistance is not simply an incremental increase due to use of a more expensive herbicide, but a categorical shift to non-chemical weed management, with all the attendant costs and risks. For this reason, we speculate that catastrophic risk modeling should be used to conceptualize and quantify the risks associated with herbicide resistance, rather than simply considering resistance to be the depletion of a natural resource under a common pool resource scenario.

8 TAKING ACTION ON THE LONG-TAILED RISK OF HERBICIDE OBSOLESCENCE

Preparing for catastrophic risks is a fundamental aspect of agricultural production that takes many forms. Some current products available to producers already include remedies for problems specifically related to pesticide resistance. When a farmer hires a custom agricultural pesticide applicator, the agreement often includes a clause that entitles the customer to a repeat application of the same pesticide should the first application fail.[82] Crop insurance, in contrast, usually covers weather-related losses. It also covers losses from insects and plant pathogens, but 'not damage due to insufficient or improper application of pest control measures.' Damages from weeds are not included in insurable causes of loss.[83] Innovations in crop insurance may be one vehicle to protect farmers against resistant pests. One possible implementation would be a compulsory, actuarially-priced resistance insurance product that would accompany each pesticide sale. Pesticides highly prone to resistance would become more expensive, and pesticides less prone to resistance would decline in price. A potential downside of such an approach is the problem of 'moral hazard'; if growers are insured against risks of resistant pests, they have less incentive to guard against it. Indeed, there is evidence that in some circumstances, crop insurance lowers farmer expenditures on pest control.[84,85]

As discussed in the previous section, risk of the evolution of herbicide resistance is at a critical state, with rapidly accelerating problems unmet by commensurate mitigation measures, and the increasing likelihood that certain production regions and cropping systems will be left without chemical control options. How should such an event be priced?

The recent experience of insurers of natural disasters indicates that there is a tendency to underestimate the losses associated with low-probability, high impact events. Prior to Hurricane Andrew, which left a wide swath of destruction in coastal Florida in 1989, risk models were based on retrospective analyses of previous events, and the low number of hurricane landfall events and direct hits of urban centers suggested that losses from a single storm would not likely exceed $7 billion. Hurricane Andrew did make landfall near Miami, and eventual losses exceeded $15 billion,[86] leaving many insurers in financial ruin. This event prompted the insurance industry to adopt more advanced, prospective risk modeling focused on better estimating tail risk for catastrophic events.[87] Even so, there is still reluctance among insurers to include worst case scenarios in their risk models, and among homeowners to pay for such insurance, potentially leaving both financially overexposed.[86] As we consider how to price the long risk tail of pesticide resistance, we would do well to consider the experience of the property insurance industry, and choose risk models that do not systematically underestimate tail risk.

Quantifying the maximum probable losses under different scenarios of the evolution of pesticide resistance is a challenging problem that will require the cooperation of pest management scientists, natural resource economists, risk modelers and actuaries. Because the loss of chemical weed control is already imminent in some areas, this may form a meaningful test case for beginning to assign monetary costs to the loss of control. The economic consequences of loss of chemical weed control may span a wide range, and compiling data on the variety of impacts will be useful. One weed species in particular, *Amaranthus palmeri*, is making clear what types of costs can be incurred as growing numbers of multiple herbicide resistant genotypes evolve and spread throughout the grain production regions of the southern and central US.[88]

Because of its rapid growth, enormous fecundity and high competitive ability, *A. palmeri* has forced many farmers to acknowledge the extreme risks posed by unchecked evolution of herbicide resistance. In contrast to its congeneric, *A. tuberculatus*, which can cause yield losses of around 30% in soybean, *A. palmeri* infestations can result in crop yield losses greater than 75% and interfere with harvest.[88] On farms where glyphosate resistant *A. palmeri* genotypes have become established, there is a substantial increase in the use of physical weed control methods such as hand weeding and tillage, as well as heavily increased use rates of other herbicides[89] resulting in greatly increased production costs. Increased dependence on rescue weed control tactics causes economic losses by increasing production costs and reducing net returns to management. But *A. palmeri* can cause even more extreme forms of economic loss: some farms where multiple herbicide resistant genotypes of this weed have spread over entire fields have not been able to recover and have been forced out of business (J. Norsworthy, personal communication). Infestations of this magnitude are likely to reduce the rental value of such land, and should be considered in risk models as well. While such cases are currently isolated and few in number, this is the level of financial loss that should be accounted for in tail risk scenarios. Integrated weed management strategies for herbicide resistant *A. palmeri* can be successful if they implement multiple tactics from different control categories,[90] but they will be precipitously less cost-effective if no chemical tools are available for integration.[91]

Tools for coping with catastrophic risk associated with pesticide resistance should include a diversified portfolio of financial and agronomic strategies. Some tools may be insurance policies, offering compensation should a grower be faced with an unmanageable pest genotype. Some resource economists have suggested that 'it may be better to indemnify crop losses with insurance rather than try to prevent or mitigate them through the use of pesticides…'.[92] Other risk mitigation instruments may use a system of advance payment by taxpayers to create a fund supporting proactive pest management strategies.[93] An early detection and rapid response framework has been proposed for the detection and eradication of noxious invasive weeds of wildland areas before they become entrenched and too costly to manage.[94] A similar approach could be taken with the weeds of field crops, with self-reporting by producers and custom-applicators of a particularly problematic multiple resistant weed genotype triggering an eradication response, in which a crop is baled and burned prior to harvest, and the producer is compensated for the crop loss. Prevention funds could also be used to support 'chemical of last resort' strategies, similar to those taken by medical organizations to fight multiple resistant disease organisms.[95] A compound that is currently performing well, without large amounts of resistance, could be held in reserve for use only in emergencies. The producer of the herbicidal compound would be reimbursed by the reserve fund while the compound is still under patent. Producers with multiple herbicide resistant genotypes with no commonly available chemical options left would be permitted to use the reserve compound for a period of 3 years, during which the producer would be required to adopt additional non-chemical weed management strategies.

Aside from innovations in insurance markets, there are also more standard regulatory approaches to resistance management. The US Environmental Protection Agency (EPA) recently released Draft Pesticide Registration Notice 2016-XX providing guidance on herbicide resistance management.[96] This guidance begins by restating that herbicide registrants are legally required to report resistance events to EPA under FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act). This is just a restatement of existing law. The guidance also notes that resistance problems could render existing labels 'misleading' and that 'Flaws or inadequacies in the labeling could lead EPA to cancel the product' under section 6(b) of FIFRA. Again this is just restatement of current law and amounts to saying that EPA has authority to cancel registration of a product that is no longer working as labeled. In which case, though, growers are not likely to continue using it.

What *is* new about the guidance are more substantial information requirements for herbicide product labels. Information requirements ramp up based on the perceived risk of resistance evolution. Herbicide MOAs are grouped into low, moderate, and high 'concern' categories. The high concern category requires the greatest level of detail concerning resistance to an MOA and methods to address it. The high concern category has additional measures that could include, 'mandatory crop rotation or time-limited registration (p. 12).'[96] An example of time-limited registration might be to register use of a particular active ingredient on a crop in alternating years, with its use prohibited in alternating years. The new generation of genetically-modified crop varieties with tolerance to multiple herbicides are designed for use with MOAs that are all on EPA's 'high concern' list – glyphosate, glufosinate, dicamba, and 2,4-D.

Because agricultural production is so diffuse, centralized regulatory approaches can have high monitoring and enforcement costs, as well as being difficult politically to implement.[97] There is a substantial body of literature studying how local groups have successfully managed common property resources, avoiding both the tragedy of the commons and top-down, centralized regulation.[98] Several types of these institutions deal with insects and invasive weeds in agriculture.[97] These include grower-led area-wide insect control programs, insect eradication programs, area-wide invasive weed control programs, weed districts, and cooperative pest management areas. Specifically, the insect pest control initiatives often arose in response to pest resistance problems. A common feature of these programs is active involvement with government and university scientists and a high degree of self-governance. Often it is the growers themselves that determine limits on behavior, with the government in the background, enforcing the resource management rules on which the growers collectively agree. An example of a highly successful area-wide cooperative pest management group can be found in the Australian cotton industry, in which growers coordinated to use best management practices for preventing the population growth and spread of insect pests prior to the development of Bt cotton, as well as best management practices for use of Bt cultivars to avoid evolution of Bt resistance.[99]

Recent concern over herbicide resistance has grown because no new MOAs have been developed in more than 30 years and no new MOAs appear to be in the pipeline. This raises questions about what changes in R&D might hasten the development of new, effective weed control technologies. Some have attributed reductions in private R&D investment to develop new MOAs to reductions in herbicide prices resulting from chemicals coming off patent, the dominance of glyphosate-resistant crop varieties and glyphosate use, and increasing regulatory (and other) costs to develop new herbicides.[57] Others have noted that it can take 7–10 years between the time when a compound is first patented and when in can clear regulatory hurdles and come to market.[100] This delay cuts the US patent length of 20 years effectively in half and may be a disincentive for private R&D. Innovations in weed control do not necessarily need to be new chemicals. Industry is exploring various mechanical innovations such as harvest weed seed control, drones, and robotics.[101,102] Some non-chemical resistance management tactics – such as use of cover crops or crop rotations – are not patentable inventions. Gaining better scientific understanding of how such tactics may be integrated profitably is of social value, but this value is difficult to capture by the private sector. Because of this, there will tend to be private underinvestment in these tactics and there is thus a role for the public sector in conducting R&D into these tactics.

Another possibility for policy innovation would be in the Conservation Title of the next US Farm Bill, scheduled for 2018. In the past, 'compliance' programs have required farmers to adopt conservation practices on working lands (to protect wetlands or reduce soil erosion) as a condition for access to crop insurance or other USDA program payments.[103] In principle, similar compliance provisions could be applied to require growers to adopt certain resistance management practices in order to qualify for crop insurance or other USDA programs.[92] A less punitive approach might offer growers reductions in crop insurance premiums for adopting resistance management practices. The Conservation Title has historically included subsidies for farmers adopting conservation practices (such as the Environmental Quality Incentive Program (EQIP), the Conservation Reserve Program [CRP, and the Conservation Stewardship Program (CSP)]. These programs might be adapted to include payments to growers planting cover crops or adopting crop rotations designed to delay herbicide resistance.

Ultimately, we must view long-term sustainable pest management as the management of evolution itself, regardless of the pest or cropping system.[73,104] This is why talk of 'eliminating resistance' is quite literally, nonsense. There is also confusion about what is meant by 'managing resistance.' In a number of contexts, this appears to mean developing alternative weed control strategies *after* resistance to a specific MOA has become an economically significant problem. Farmers certainly need alternatives once resistance to a specific MOA has become economically important. Yet resistance is not a binary variable, determined simply in terms of presence or absence of it. As Coble[105] notes, 'From the management perspective, one must assume that all fields have resistance present. That resistance may not have manifested itself yet in an actual plant and may not have been selected for yet, but because genes have many ways of moving around, proper management dictates that assumption (p. 15).' Hurley and Frisvold[8] note regarding herbicide resistance management (HRM), 'HRM is more than adjusting weed management to the presence of particular resistant weeds once they appear. In this framework, shifting from overuse of an herbicide with one mode of action (MOA) to overuse of an herbicide with a different MOA is not HRM. Rather, HRM is explicitly forward looking, considering how management decisions made today affect the likelihood of resistance in the future (p. 585).'

Pest managers can plan ahead across appropriate time horizons for a given crop/pest-complex to assemble integrated pest management systems that effectively shift control tactics over time and space. If they do, they can avoid having to respond to sequential resistance crises as different MOAs, one-by-one, lose effectiveness. Proactively planning and implementing such practices while there are still viable control tactics from all management categories (i.e. chemical, physical, cultural, biological) represents an extraordinarily valuable investment in the future of agriculture that no insurance policy can replace. As Benjamin Franklin famously noted, 'an ounce of prevention is worth a pound of cure.' It is up to us to recognize that the time for pesticide stewardship is now. To imbue this societal responsibility with the necessary urgency, we must quantify the catastrophic costs of inaction so that the comparatively modest price of stewardship is fully appreciated for the bargain it is.

ACKNOWLEDGEMENTS

Many thanks to the USDA-ARS Area-Wide Pest Management Program for funding this work, and to Dr Ian Heap for curating, and providing access to, the International Survey of Herbicide Resistant Weeds database.[37] USDA-ARS is an equal opportunity employer.

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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