A Recent Epizootic of Skunk Rabies and Associated Spillover in Northern Colorado, USA

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ABSTRACT: Rabies is a fatal viral zoonosis that is transmitted by bite contact with saliva of an infected animal. In the U.S., human deaths are rare, but each year over 5,000 rabid animals are reported and over 90% of cases are from wildlife. Multiple species of carnivores and bats are the primary sylvatic reservoirs in the U.S., and several variants circulate independently among these two taxonomic orders. Rabies prevention efforts led by USDA APHIS Wildlife Services using live recombinant vaccine baiting began in 1995 and currently target raccoons and canids, but the territory of the south-central skunk rabies virus variant has been expanding in recent years, leading to incursions into areas previously free of carnivore rabies. Colorado has been one such area, where multiple species of bats were the main rabies reservoir prior to 2007. By 2012, the number of rabid striped skunks exceeded rabid bats in Colorado. Larimer County and Weld County, in Northern Colorado, both witnessed skunk rabies epizootics starting in 2012 that have continued through 2013. Despite spillover events into raccoons, red foxes, companion animals, and livestock during 2012 and 2013, no other host species appears to support independent circulation of the south-central skunk variant in Northern Colorado. Virus isolation from salivary glands of rabid animals will help to quantify the likelihood for secondary transmission from spillover hosts and guide intervention strategies targeting wildlife. We describe the spatiotemporal pattern of the epizootic and predict likely areas of spread along the Front Range of Northern Colorado.

KEY WORDS: disease, epizootic, *Mephitis mephitis*, rabies virus, south-central skunk variant, striped skunk, surveillance, zoonosis

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INTRODUCTION

Rabies is caused by infection with single-stranded negative sense RNA viruses in the genus *Lyssavirus* and globally is responsible for greater than 55,000 human deaths annually. The human burden of disease is greatest in Africa and Asia, and nearly all human rabies cases are caused by rabies virus (RV) and linked to transmission from domestic dogs (Knobel et al. 2005). Although diverse lyssaviruses have been detected in Europe, Asia, and Africa, RV is the only member of the genus that circulates in the Americas (Rupprecht et al. 2011). Programs controlling canine rabies circulation by increasing rates of domestic animal vaccination have been effective in the United States (U.S.) and have dramatically reduced the human case burden to an average of 2 to 4 cases per year (Velasco-Villa et al. 2008). Despite these successes, the circulation and incidence of rabies in wildlife remains significant, and it has been estimated that up to 40,000 persons in the U.S. are exposed to RV annually as a result of sylvatic RV circulation (Christian et al. 2009). In the U.S., several bat and carnivore variants of RV circulate among individual host species, with varying levels of virus spillover infections into other mammalian hosts (Smith et al. 1995). In areas of the U.S. where only bat RV variants circulate, the incidence of spillover infections into other mammals is relatively rare (McQuiston et al. 2001). However, in areas where sylvatic carnivore RV variants are enzootic, the incidence of spillover RV infections into other mammals is much higher (Dyer et al. 2013). The Wildlife Services (WS) program of the United States Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) began a program to mitigate and control the circulation of RV in wildlife after a particularly explosive epizootic of rabies in raccoons (*Procyon lotor*) along the eastern seaboard of the U.S., which was initially sparked by the translocation of an infected animal from an enzootic area in Florida (Rupprecht and Smith 1994, Biek et al. 2007, Slate et al. 2009). The WS oral rabies vaccination (ORV) program delivers live recombinant vaccine baits to wildlife via aerial and ground-based broadcast strategies. Target wildlife species consume the baits, and infection with the recombinant vaccine induces a rabies virus-neutralizing antibody response and subsequent herd immunity at the population level, to create barriers to disease spread on

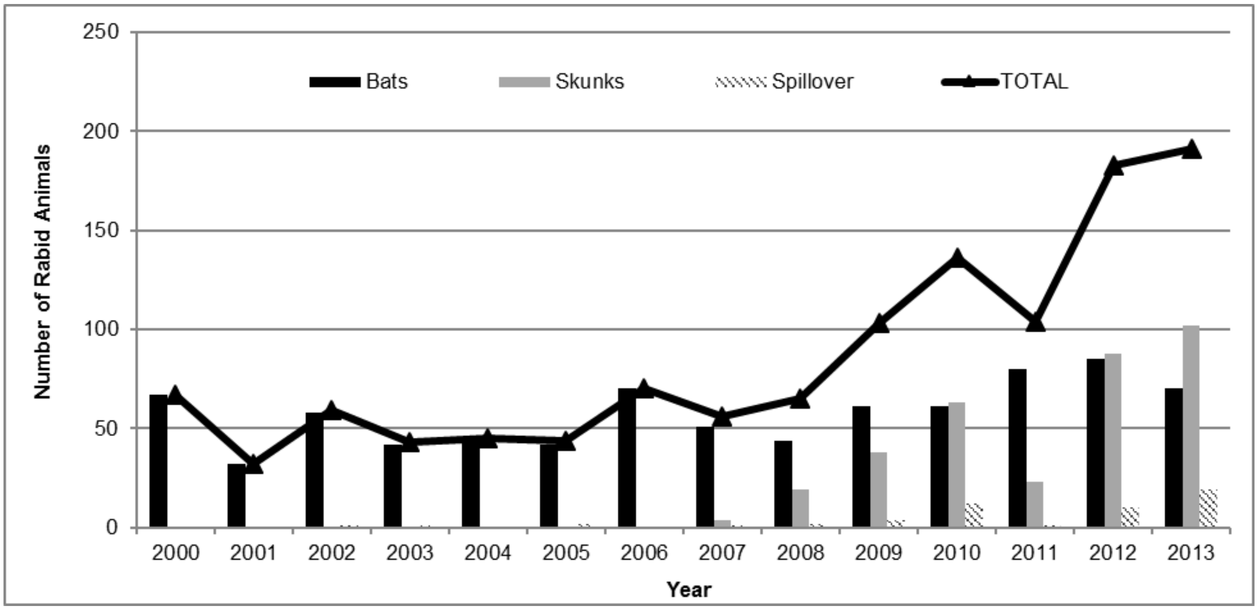


Figure 1. The number of rabid animals reported to the Colorado Department of Public Health and Environment during 2000 to 2013 (CDPHE 2014). (regardless of variants of RV)

the landscape by reducing the number of susceptible animals. The focal targets of this effort have been raccoons, gray foxes (*Urocyon cinereoargenteus*), and coyotes (*Canis latrans*), yet complex issues with delivery and/or uptake of the vaccine baits by striped skunks (*Mephitis mephitis*) has precluded focal efforts to control skunk RV variant circulation in the U.S. (Slate et al. 2009). Where needed, control efforts targeting skunks in the U.S. have typically utilized trap-vaccinate-release strategies (Engeman et al. 2003).

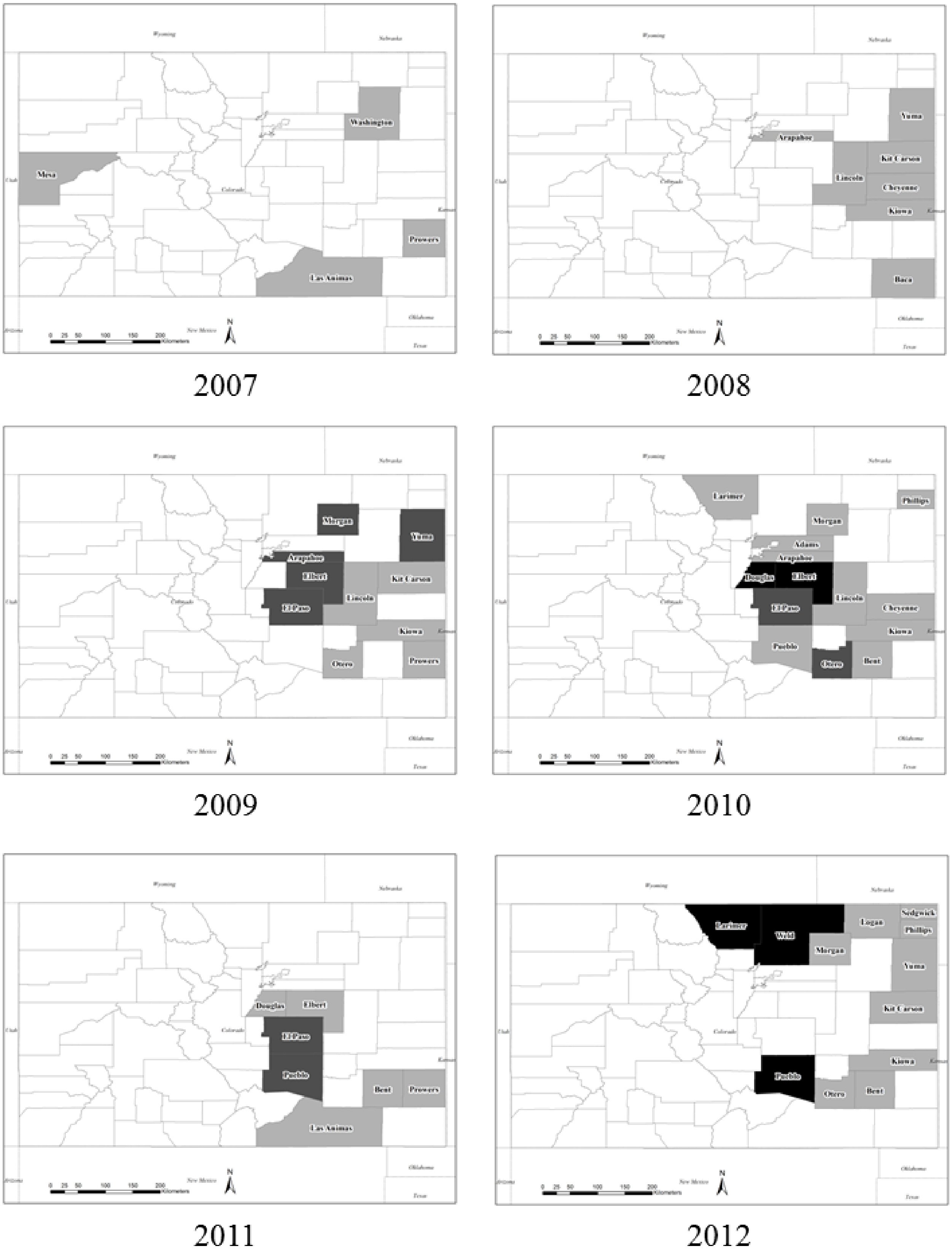
The south-central skunk (SCSK) variant of RV is one sylvatic RV lineage maintained by striped skunks, and historically shares a common ancestor with raccoon, Mexican skunk, and bat RV lineages in the Americas. In contrast, the north-central skunk and California skunk RV lineages, also maintained by striped skunks, share common ancestry with canine lineages, indicating a different source of historical spillover (Kuzmin et al. 2012). Based on genetic studies, it has been demonstrated that the historical source and greatest diversity of the SCSK variant circulates in Texas, and appears to have been present in wildlife in this area since the early 1800s (Davis et al. 2013, Kuzmina et al. 2013). Kuzmina et al. (2013) also demonstrated that the spread of this variant has increased through time since the 1800s, with directional signatures and greatest spread in a northerly direction. As the geographic distribution of the SCSK RV cycle in striped skunks has expanded into areas where only bat RV lineages circulated previously, the incidence of RV in other terrestrial wildlife has also increased. The incursion of SCSK RV into Colorado was first detected in 2007 and, though it has not persisted in all counties where incursions have been documented, the number of skunk rabies cases in Colorado has steadily increased since 2007 (Figure 1) (CDPHE 2014). Genetic studies have suggested that the incursions of the SCSK RV lineage into Colorado likely originated from SCSK RV cycles in skunks in Nebraska and Kansas, as cases in all 3 states form a highly supported clade that has been termed the Great Plains sub-lineage of SCSK RV (Davis et al. 2013, Kuzmina et al. 2013).

METHODS

Rabies case reports for terrestrial mammals were reviewed and summarized from the online database of the Colorado Department of Public Health and Environment (CDPHE 2014). Higher resolution case data were obtained with permission from Larimer County, Weld County, and Boulder County Health Departments, respectively, spanning 2012 and 2013. County aggregate and high resolution case data were mapped using ArcMap, version 10.1 (Environmental Systems Research Institute, Redlands, CA).

RESULTS AND DISCUSSION

The SCSK RV lineage originally invaded Colorado in 2007, and affected 3 eastern counties with a single case in each county. In 2008, cases were recorded in 7 counties, all of which were along the Kansas and Nebraska border, though no more than 4 cases were reported for any single county. It continued to spread to 10 counties in 2009 and 14 counties by 2010, with 2 counties being heavily affected in 2010 (10 and 20 cases respectively). It appears that the 2 heavily affected counties in 2010 exhausted the supply of susceptible hosts that year, as only single cases were reported from either county in 2011, and only 7 counties were affected and no counties reported 10 or more cases in 2011. However, a resurgence was observed in 2012, where 12 counties were affected and 3 counties reported 10 or more cases, including Larimer (n = 35) and Weld County (n = 21) (Figure 2) (CDPHE 2014). Epizootics continued in Weld and Larimer County in 2013, and a total of 13 counties were affected, with 3 counties reporting 10 or more cases.



2007 2008

2009 2010

2011 2012

Figure 2. The distribution of counties in Colorado reporting rabid skunks during 2007 to 2012 to the Colorado Department of Public Health and Environment (CDPHE 2014). Counties are shaded according to the number of reports of rabid skunks each year: no cases (white), less than 5 cases (light gray), 5 to 9 cases (dark gray), and 10 or more cases (black). One skunk case from Denver County in 2008 that typed as a bat RV variant was excluded.

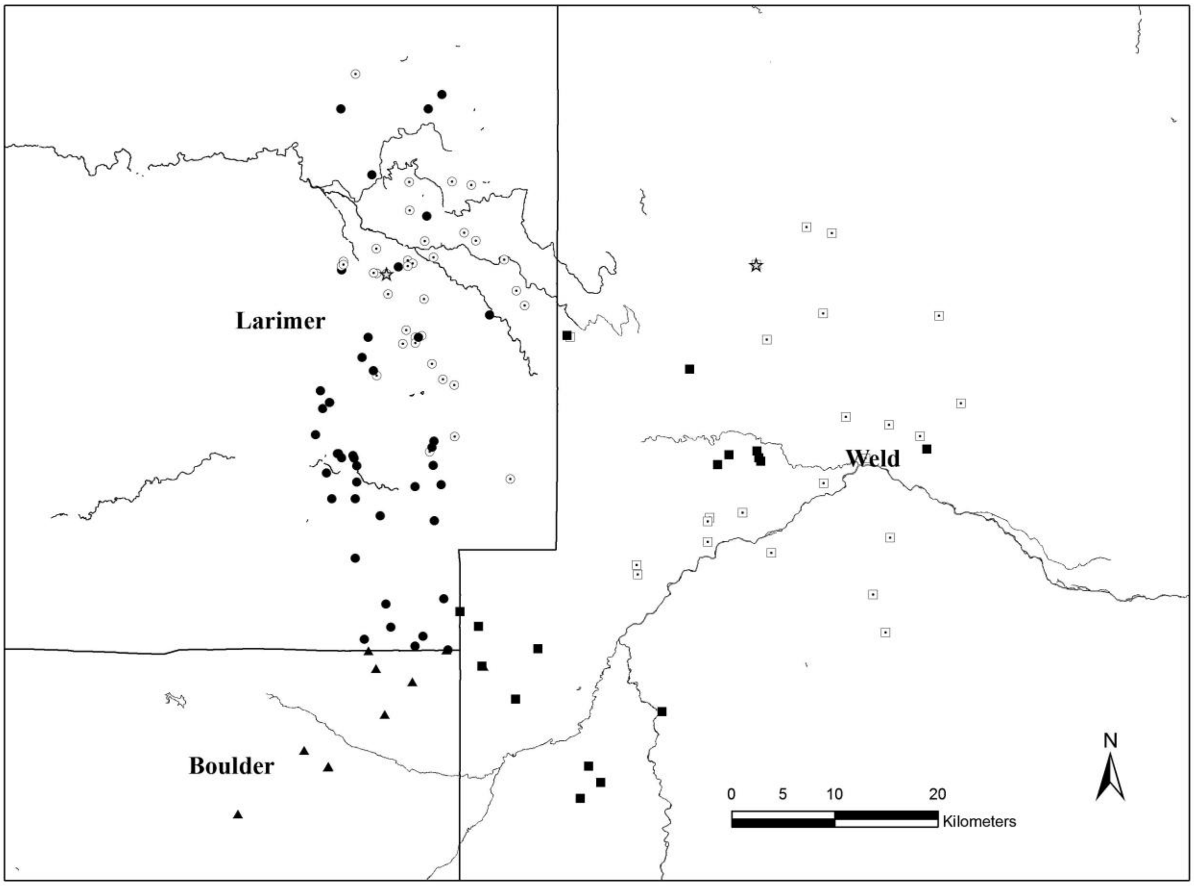


Figure 3. The distribution of positive rabies cases in terrestrial mammals reported by Larimer (circles), Weld (squares), and Boulder (triangles) County Health Departments during 2012 (dotted symbols) and 2013 (black symbols). Index cases in 2012 from Larimer and Weld County are shown with gray stars.

Why certain counties (e.g., Pueblo, Douglas, Elbert) appear to exhaust the supply of susceptible skunk hosts and others do not (e.g., Larimer, Weld) may relate to differences in the population size and density of skunks in these areas, although sparse information exists currently to evaluate this hypothesis. The fluctuating distribution of affected counties across years along the Kansas and Nebraska border with Colorado suggests that RV incursions are not occurring each year (or there is imperfect detection by passive surveillance), and broadening the geographic scope of a virus genetic survey could yield additional insight into the spatiotemporal relationship of infection cycles resulting from incursions in Colorado during 2007 to 2013.

Regarding the epizootics in Larimer and Weld County, the leading edge of the wave front has been traveling south (Larimer) and southwest (Weld) at a rate of at least 25km/yr, with these fronts merging in Boulder County by mid-2013 (Figure 3). At this rate of directional spread along the Front Range, the wave front is likely to affect Jefferson County in 2014 and could reach Denver County by 2015. Spillover cases represented 4% of submissions in Northern Colorado, and affected wild carnivores [e.g., red foxes (*Vulpes vulpes*) and raccoons], companion animals, and livestock; thus, there are clear implications for public and veterinary health, especially for the metro Denver area.

Forecasting the dynamics of spread and associated public and veterinary health impacts is critical to evaluate interventions for mitigation and control, as well as the economic costs associated with the SCSK skunk rabies epizootic. A Bayesian diffusion model of rabies spread (Smith et al. 2002, Hooten and Wikle 2010) in skunks is being applied to the cases in Larimer, Weld, and Boulder Counties and will allow improved prediction of future spread across the landscape to neighboring counties, as well as the relative contributions of local and long-distance spread and impact of landscape features on the rate of spread.

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