Abstract: Understanding how population dynamics respond to landscape-scale disturbance and disease are crucial for effective wildlife management and conservation. Two new potential stressors on greater sage-grouse (Centrocercus urophasianus) populations in the Powder River Basin of Montana and Wyoming are coal-bed natural gas (CBNG) development and West Nile virus (WNv). I first examined how CBNG development, habitat, and other landscape features influenced trends in the abundance of displaying males and the status of sage-grouse leks. Second, I used rates of WNv-induced mortality and seroprevalence from radio-marked birds to estimate rates of WNv infection. Third, I studies the influence of female characteristics, season, and environmental variables on nest, brood, and female survival. I then used population models to estimate potential impacts of WNv on population growth. From 2001-2005, numbers of males on leks in CBNG fields declined more rapidly than leks outside CBNG. Of leks active in 1997 or later, only 38% within CBNG remained active by 2004-2005, compared to 84% of leks outside CBNG. By 2005, leks in CBNG had 46% few males per active lek than leks outside CBNG. Persistence of 110 leks was positively influenced by proportion sagebrush habitat with 6.4 km of the lek and negatively affected by CBNG development at multiple scales. Prohibiting CBNG development within 0.4 km of sage-grouse leks is inadequate to ensure lek persistence. From 2003-2005, minimum WNv-related mortality rates from 1 July -15 September ranged from 2.4-13.3% and maximum possible rates ranged from 8.2-28.9%. In spring 2005 and 2006, 10.3% and 1.8% respectively, of newly-captured females tested seropositive for neutralizing antibodies to WNv. Annual WNv infection rates were lower in habitats without CBNG development. Summer mortality from WNv occurred every year, decreased annual female survival rates by 0-27% per year, and reduced estimates of population growth by 7-10% per year. Changes in epizootiology of WNv and in distribution and management of surface water from CBNG development will play an important role in long-term impacts of WNv on greater sage-grouse populations in the Powder River Basin. Management should focus on eliminating man-made water sources that support breeding mosquitos known to vector the virus.