Mass Chemoprophylaxis for Control of Outbreaks of Meningococcal Disease

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Appendix

Table S1. Cases before and after mass chemoprophylaxis reported in thirty-three meningococcal disease outbreaks. Key characteristics of the outbreak, population, and intervention are included.

Ref	Serogroup	Setting	Population N	Cases before mass prophylaxis	Time from last case to prophylaxis	Primary Antibiotic	Coverage (%)	Cases after mass prophylaxis	Time from mass prophylaxis until next case	Vaccination*	Additional details
Rifampicin and minocycline chemoprophylaxis for military outbreaks											
Beam et al. 1971[1]	C	Military	1635	10	10 days	Rifampicin	98	1	3 months	NR	1 case also occurred during the 3 months after chemoprophylaxis in a control population not experiencing an outbreak. **Carriage**: 65% prior to rifampicin prophylaxis; 10% four days after administration (N=1599 at each time point). No rifampicin-resistant meningococci were detected among those carried prior to rifampicin administration; however, 4 days after rifampicin treatment more than 73% of the carried meningococci were rifampicin-resistant.
Gaunt and Lambert 1988,[2] Gaunt 1988[3]	C	Military	~2200	3	NR	Rifampicin	37**	0	N/A	Yes; serogroup A/C polysaccharide vaccine provided 1 week after first round of prophylaxis.	Base screened for carriage and rifampicin provided only to carriers (37% of base). Six weeks after the last case, ciprofloxacin chemoprophylaxis was provided to all base residents. **Carriage**: 37% before prophylaxis; 19% one week after prophylaxis, 8% with rifampicin-resistant meningococci.
Guttler and Beaty 1972[4]	C	Military	8954	7**	Simultaneous	Minocycline	97	8**	4 weeks	Yes; serogroup C polysaccharide vaccine provided to new recruits after 13th case.	6 initial cases; an additional case occurred in an untreated recruit during the time period of minocycline administration. Population experienced rapid turnover during outbreak as new recruits entered training. Four weeks after initial chemoprophylaxis, 61% of recruits at the base were new recruits who had arrived after the prophylaxis regimen was administered. After six additional cases, a second round of mass chemoprophylaxis plus

											serogroup C polysaccharide vaccination occurred but targeted only new recruits. Two additional cases occurred in recruits who had received the initial chemoprophylaxis treatment but not the second round of antibiotic or vaccine. **Carriage**: Meningococcal carriage was reduced from ~65% to less than 30% after the first round of chemoprophylaxis. No resistance to minocycline was observed among carried isolates.
Rifampicin chemoprophylaxis for organization and community outbreaks											
Sáez-Nieto et al. 1984[5]	C	Nursery	206	7	<10 days	Rifampicin	66	4	<10 days	Yes; serogroup C polysaccharide vaccine provided to children at the nursery after last 4 cases (68% coverage).	Chemoprophylaxis targeted all nursery attendees and staff. Additional chemoprophylaxis provided to carriers of the outbreak strain after last 4 cases. **Carriage**: Unspecified subset of daycare attendees/staff/contacts assessed for carriage prior to intervention (N=222): 8·1% had carriage, 2·5% carried the strain causing the outbreak. Several weeks after chemoprophylaxis carriage was 10%; 4% carriage of outbreak strain; and at least one rifampicin-resistant isolate (N=219).
O'Donovan et al. 2000[6]	C	Nursery	72	2	Same day	Rifampicin	100	3	1 day	Yes; serogroup A/C polysaccharide vaccine provided two days after initial rifampicin prophylaxis.	All cases after mass chemoprophylaxis were in family members of nursery students (family members were not initially targeted for prophylaxis) and occurred within 3 days. Antibiotic prophylaxis and A/C polysaccharide vaccine provided to all household contacts of nursery attendees after 5th case.
Katz et al. 2007[7]	B	Nursery	61	3	NR	Rifampicin	100	1	"Within 2 weeks"	No	First case was in a daycare attendee; second in a sibling of a daycare attendee; third in the daycare-attending sibling of the second case. After chemoprophylaxis of all children attending the nursery, fourth case occurred in an adolescent visited by a girl whose sister attended the daycare. Additional round of rifampicin provided to

											all 370 in community (100% coverage) after 4th case. **Carriage**: Serogroup B carriage was 21·3% prior to first round of chemoprophylaxis; 4·9% two weeks after second round of chemoprophylaxis (following 4th case); 31·1% 3 months later. N=61 at each time point. Rifampicin resistance not assessed.
Stewart et al. 2013[8]	B	Nursery	176	2	4 days	Rifampicin (ciprofloxacin for most staff)	73	0	N/A	No	Cases occurred within a 5-day period. All children and staff at nursery given prescriptions for chemoprophylaxis.
González de Aledo Linos et al. 2000[9]	B	Pre-school and school	99 (pre-school), 795 (school)	1	NR	Rifampicin (ciprofloxacin for staff)	NR	5	<2 weeks	No	First case occurred in a preschool student; rifampicin was then administered to children in the pre-school and ciprofloxacin to adult workers. After 3 additional cases (2 in pre-school students who had received rifampicin; one in a child at the school), an additional round of prophylaxis was attempted with azithromycin for daycare attendees (coverage not specified) and ciprofloxacin for older children and adults (coverage ≥89%). However, 2 additional cases occurred in the following 2 months (patient ages not specified).
Zangwill et al. 1997[10] (cluster 8***)	C	Elementary school	NR	3	NR	Rifampicin	NR	0	N/A	Yes; vaccine (type not specified) provided to entire school, close contacts, and parents of children attending assemblies after 3rd case.	Cases occurred within 3 days. Chemoprophylaxis provided to entire school, parents, and siblings of students who attended parties or assemblies.
Zangwill et al. 1997[10] (cluster 20***)	C	Elementary and secondary school	276	3	<3 days	Rifampicin	93	0	N/A	NR	Cases spanned a week.
Jackson et al. 1996[11]	B	Middle school	900	6	1 day	Rifampicin	>90	0	N/A	No	**Carriage**: 9·7% before chemoprophylaxis (3·4% outbreak strain; N=351); 2·6% 3 weeks after chemoprophylaxis (1·0% outbreak strain; N=196).

											Rifampicin resistance detected after prophylaxis.
Zangwill et al. 1997[10] (cluster 1***)	C	Secondary school	NR	4	2 days	Rifampicin	NR	0	N/A	Yes; all students, staff and siblings vaccinated concurrently with chemo-prophylaxis (vaccine type not specified).	Cases occurred over 13 days. Chemoprophylaxis and vaccination provided for students, staff, and siblings.
Zangwill et al. 1997[10] (cluster 10***)	C	Secondary school	1289	3	7-10 days	Rifampicin	89	0	N/A	Yes; vaccine (type not specified) provided during mass chemo-prophylaxis campaign.	Cases occurred within 3 days. Approximately 260 contacts provided chemoprophylaxis 4 days after 3rd case.
Zangwill et al. 1997[10] (cluster 16***)	C	Secondary school	NR	3	NR	Rifampicin	NR	0	N/A	NR	All cases occurred in a 4-day period.
Zangwill et al. 1997[10] (cluster 22***)	B	Secondary school	NR	4	2 days	Rifampicin	NR	0	N/A	No	Cases occurred in a 31-day period.
De Wals et al. 2004[12]	C	Secondary school	3034	4	"Immediately"	Rifampicin	~80	0	N/A	Yes; serogroup C polysaccharide vaccination (89% coverage).	Cases occurred within a 9-day period.
CDC 1998[13]	B	Hotels	730	3	NR	Rifampicin	66	2	"5 weeks after first cluster"	No	Initial 3 cases occurred in a 2-day period in a guest of one hotel and two siblings staying at a second hotel but who had visited the first hotel to play with other children. Rifampicin then offered to all guests and employees at both hotels. Fourth case 5 weeks later occurred in a person who had provided child care at the first hotel shortly before symptom onset; fifth case occurred in a child who had been cared for by the fourth case-patient (secondary case). The fifth patient and her family had received prophylaxis after the first three cases. Second round of chemoprophylaxis occurred after last two cases, but details not specified.
Pearce et al. 1995[14]	C	Community	~1250	12	1-2 weeks	Rifampicin	75	0	N/A	Yes; serogroup A/C	**Carriage**: 8·4% overall, 3·1% serogroup C, 2·3% epidemic

										polysaccharide vaccination provided to children 1-15 years of age (93% coverage) after first 4 cases.	strain before chemoprophylaxis (N=237). Two months after mass prophylaxis all carriers were retested and all were negative. Six months after chemoprophylaxis population carriage was reassessed (N=779): 4·0% overall, 0·64% serogroup C, and 0·51% epidemic strain carriage was detected; one isolate was rifampicin-resistant.
Perrocheau et al. 2000[15]	B	Community	3000	4	3 weeks	Rifampicin	93	0	N/A	No	Cases occurred during a 1-month period. Two patients attended the same kindergarten and two attended the same secondary school.
Perrocheau et al. 2005[16]	B	Community	8000	7	NR	Rifampicin	86	0	N/A	No	Cases occurred over 18 days among children in a neighborhood. Some patients were part of a single extended family, but exact number not specified.
Ciprofloxacin chemoprophylaxis for organization and community outbreaks											
Chatt et al. 2014[17]	B	Nursery	111	5	~2 weeks	Ciprofloxacin	NR	0	N/A	No	Three cases occurred in nursery students in a 5-month period; retrospective review of community cases then identified two additional cases caused by the nursery outbreak strain. One of these two cases had an epidemiologic link to the nursery but one did not. **Carriage**: 1·5% prior to prophylaxis, 0 carriers of outbreak strain; not assessed after prophylaxis.
Ngo et al. 2010[18]	B	High school	3100	2	Same day	Ciprofloxacin	92	0	N/A	No	Investigators' intent was to target close contacts, but ultimately most students and staff at the school received prophylaxis.
CDC 1998[13]	B	Nursing home	218	3	1 day	Ciprofloxacin	99·5	1	4 days	No	Initial 3 cases in staff and residents occurred within 5 days. 4th case occurred in only nursing home resident who did not receive prophylaxis.
Barker et al. 1999[19]	C	University	~1100	5	Simultaneous	Ciprofloxacin	92	1	5 days (until death)	Yes; serogroup C polysaccharide vaccination also offered to target	Initial five cases occurred within 4 days among university students residing in a group of 3 nearby residence halls. Population N is for the 3 residence halls initially targeted

										group at time of prophylaxis.	for prophylaxis. 6th case was in student outside of original target population. After 6th case wider chemoprophylaxis and vaccination was instituted among ~4100 first-year students plus all staff and students in halls of residence.
Burke and Burne 2000[20]	NR	University	4253	2	NR	Ciprofloxacin	75	NR (assume 0)	N/A	NR	Population N is first-year students only (population targeted for prophylaxis).
Round et al. 2001[21]	C	University	750	5	Simultaneous	Ciprofloxacin	99	1	2 days	Yes; serogroup A/C polysaccharide immunization offered along with chemo-prophylaxis.	Four cases occurred among residents of a single residence hall and one in a close contact of a residence hall resident within 3 days. Population N is just the residence hall associated with the outbreak. Sixth case was in another resident of the residence hall; not specified whether this patient had received prophylaxis. **Carriage**: 19·4% prior to chemoprophylaxis, 0 with outbreak strain; not assessed after prophylaxis.
O'Connor et al. 2015[22]	B	Extended family	123	8	~1 month	Ciprofloxacin	98	0	N/A	Yes, serogroup B vaccine (MenB-4C) provided at or up to 1 month after chemo-prophylaxis, 70% coverage	Outbreak occurred over a 3-year period in an extended family of Irish Travellers. Vaccination targeted only persons aged 2 months–23 years as well as close contacts of the 8th case. **Carriage**: 13% carriage, including 6% carriage of outbreak strain, detected at time of chemoprophylaxis. Not assessed after prophylaxis.
Perrett et al. 2000[23]	C	Community	NR	5	Simultaneous	Ciprofloxacin	NR	3	1 day	Yes; serogroup C polysaccharide vaccine provided concurrently with ciprofloxacin.	Prophylaxis and vaccination provided only to school attended by first two cases and a "family and friends" group of the first 3 cases. However, prior to the intervention an additional case occurred in a district resident with no epidemiologic links to the first 3 cases; a 5th case occurred in a second unconnected district resident on the same day as chemoprophylaxis administration. The additional 3 cases were also in district residents not associated with the high school; all occurred within

											3 days of ciprofloxacin administration. Overall community size and antibiotic coverage for community not specified.
Shehab et al. 1998[24]	B	Community	~11600	13	<1 year	Ciprofloxacin (ceftriaxone for children under 5)	97	12	<1 month	No	Outbreak spanned 6 years. Mass prophylaxis administered over a period of several days. First case after prophylaxis was in a person who refused treatment; next case occurred 7 months later. Despite temporary lull in cases, average annual incidence of meningococcal disease following mass prophylaxis was similar to incidence prior to intervention. **Carriage**: In sample of 1036 at each time point, carriage was 8·3% (3 outbreak strain) before mass prophylaxis and 1·3% (1 outbreak strain) six weeks later. Antibiotic resistance not assessed.
Irwin et al. 1997,[25] Irwin et al. 1998,[26] Neal et al. 1998[27]	C	Community	16,900	8	1 day	Rifampicin and ciprofloxacin	NR	1	1 month	Yes; serogroup C polysaccharide vaccine provided in conjunction with prophylaxis. 95% vaccination coverage achieved.	Initial 8 cases occurred over 35 days in persons aged 1-75 years in south Rotherham and north Nottinghamshire, England. Rifampicin was provided to persons 2-10 years, ciprofloxacin to persons 11-18 years; vaccine provided to both age groups. Staff at a priority school which was attended by 2 patients also received prophylaxis; antibiotic not specified. Administration spanned 1 week. Target population includes only persons aged 2-18 years. Case after chemoprophylaxis was in a person with documented antibiotic and vaccine receipt as part of the outbreak response; serologic testing showed this patient had suboptimal immune response to the vaccine. **Carriage**: 6 months after the intervention, carriage among targeted 11-18 year olds was 2.4% compared with 8.5% among 1-18 year olds outside the target area; by 11 months

											post-intervention the two groups had comparable carriage prevalence. No rifampicin- or ciprofloxacin-resistant isolates were identified.
Chemoprophylaxis with other agents for organization and community outbreaks											
CDC 2012[28]	C	Primary and secondary school complex	1850	5	Simultaneous	Ceftriaxone (intramuscular; rifampicin for faculty)	46	0	N/A	Yes; quadrivalent meningococcal conjugate vaccine offered to full population 1 week after first round of prophylaxis – 68% coverage.	Chemoprophylaxis targeted to students and faculty at the elementary school as well as high school students who had contact with elementary school students (n=893 total). Coverage was 95% in target population but 46% in school complex. Additional round of chemoprophylaxis occurred 4 days later but details and target population not specified.
Gilja et al. 1993[29]	B	University	397	3	NR	Ofloxacin	20	0	N/A	No	Only individuals testing positive for carriage targeted for chemoprophylaxis. **Carriage**: 99% of students, teachers, and staff (n=392) swabbed; 21·4% of population carried *N. meningitidis*. Thirty-three days later carriage had been reduced to 3·7%.
Macchiavello et al. 1954[30]	Unknown	Community	10,394	293	Simultaneous	Sulfadimidine and penicillin	51	115	<= 10 days	No	Chemoprophylaxis provided to 4 villages in Sudan during 1952 epidemic season; 2 villages received sulfadimidine and 2 received penicillin. Coverage varied from 33–93% of each village. Cases prior to intervention occurred in late January to late March; after intervention cases quantified through early May. After the intervention, incidence was lower among prophylaxis recipients (486 per 100,000) than among those who did not receive prophylaxis (1,768 per 100,000). Note that case counts would be expected to decline in April–May in the absence of an intervention as this represents the end of meningitis season in the African meningitis belt.

NR: Not reported

*For serogroup C and unknown serogroup outbreaks, vaccination is recorded as NR if the outbreak report(s) does not mention vaccination but does not specifically state that vaccination was not used. For serogroup B, it was assumed that vaccination did not occur as no licensed serogroup B vaccines were available at the time of these outbreaks.

**See Additional Details

***Reference 10 describes multiple outbreaks and clusters of meningococcal disease. These notes indicate which of the clusters in reference 10 is described in each line.

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