ORIGINAL ARTICLE

Risk of injury for occupants of motor vehicle collisions from unbelted occupants

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Objective: Unbelted occupants may increase the risk of injury for other occupants in a motor vehicle collision (MVC). This study evaluated the association between occupant restraint use and the risk of injury (including death) to other vehicle occupants.

Design: A population based cohort study.

Setting: United States.

Subjects: MVC occupants (n = 152 191 unweighted, n = 18 426 684 weighted) seated between a belted or unbelted occupant and the line of the principal direction of force in frontal, lateral, and rear MVCs were sampled from the 1991–2002 National Automotive Sampling System General Estimates System. Offset MVCs were not included in the study.

Main outcome measure: Risk ratios and 95% confidence intervals for injury (including death) for occupants seated contiguous to unbelted occupants compared to occupants seated contiguous to belted occupants. Risk ratios were adjusted for at risk occupant's sex, age, seating position, vehicle type, collision type, travel speed, crash severity, and at risk occupants' own seat belt use.

Results: Exposure to unbelted occupants was associated with a 40% increased risk of any injury. Belted at risk occupants were at a 90% increased risk of injury but unbelted occupants were not at increased risk. Risks were similar for non-incapacitating and capacitating injuries. There was a 4.8-fold increased risk of death for exposed belted occupants but no increased risk of death for unbelted occupants.

Conclusions: Belted occupants are at an increased risk of injury and death in the event of a MVC from unbelted occupants.

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t has been reported that seat belts reduce fatalities and severe injuries from motor vehicle collisions (MVCs) for both front and rear seated occupants. 1-7 However, the effect that seat belt usage affords other vehicle occupants is not well known. Absence of seat belt use may be associated with an increased injury risk to the other occupants. In the event of an MVC, unrestrained occupants may become projectiles within the vehicle and increase injury risk to the other occupants.8-10 The phenomena of unbelted occupants' inertia propelling them within the vehicles interior at the time of impact has become known as the "human collision" and is based on Newton's Laws of Motion.11 Mackay et al suggested that among restrained front seat occupants, up to 12% of fatalities received their injuries from seat belt loading and additional loading from unrestrained rear seat occupants may have been an important feature.8 Wild et al reported that unrestrained front seat occupants had a higher incidence of serious injury when rear seated occupants were present but the association was absent for restrained front seat occupants.9 However, this study considered only the presence of rear seat occupants and not their restraint use.

A recent study reported an increased risk of severe injury and death to belted front seated occupants from unbelted rear seated occupants.¹² A potential limitation to this study was that it included only vehicles where at least two backseat occupants were injured. Given its inclusion criteria, it is possible that the MVCs of belted rear seat occupants were of greater severity than those for unrestrained rear seat occupants. Thus the study's results are difficult to generalize to less severe crashes and the reported associations may be an underestimate of the true risks.

The objective of this population based study was to evaluate the association between occupant restraint use and

the risk of injury (including death) to other vehicle occupants.

METHODS

A cohort study design was used to evaluate the possible association between occupant restraint use and injury risk (including death) to other vehicle occupants. The data for this study were obtained from the National Automotive Sampling System (NASS)—General Estimates System (GES). 13

Subjects selected for the study were MVC occupants seated between the initial principal direction of force (PDOF) and a contiguous occupant. For example, in frontal MVCs, front seated occupants in seat positions 11 (driver) or 13 (front outboard occupant), would be at risk from rear seat occupants in seat positions 21 (left rear occupant) or 23 (outboard rear occupant), respectively (fig 1). In this instance, occupants in seat position 21 or 23 are contiguous to occupants seated in positions 11 or 13, respectively. Figure 1 also demonstrates at risk subjects in lateral (driver's side and passenger's side) and rear MVCs. Occupants at risk were counted only once in the study group since their inclusion was based on PDOF, a single measurement for each vehicle. Occupants not seated between the PDOF and a contiguous occupant and single occupant vehicles were not included.

All analyses applied the GES sampling weights using statistical software designed for the analyses of stratified samples (SUDAAN, version 7.5.6). Vehicle and collision

Abbreviations: CI, confidence interval; GES, General Estimates System; MVC, motor vehicle collision; NASS, National Automotive Sampling System; OR, odds ratio; PDOF, principal direction of force; RR, risk ratio

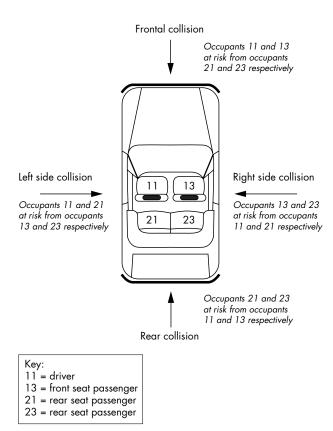


Figure 1 Subjects at risk by occupant seat position and MVC's initial direction of force.

characteristics of exposed and unexposed subjects were compared. Risk ratios (RRs) and 95% confidence intervals (CIs) were used to quantify the strength and precision of the association between injury risk and seat belt use of contiguous occupants. Finally, adjusted RRs and 95% CIs were computed using a multivariable model that adjusted for at risk occupants' age, gender, travel speed, crash severity, vehicle body type, and crash type. Curb weight was highly correlated with vehicle type and thus was not included in multivariable models.

Data

The NASS is composed of two systems—the GES and the Crashworthiness Data System.¹³ Both systems select cases from a national probability sample of light passenger vehicles (passenger cars, light trucks, vans, sports utility vehicles) involved in police reported tow-away MVCs and recorded on police accident reports. The 1991–2002 GES data files were the source of information for this study. The data are derived entirely from police accident reports and therefore focus on MVCs that resulted in injury, death, or major property damage.

Passenger cars, pickup trucks, minivans, and sports utility vehicles were included in this study. Only occupants who were seated in the front driver's, front outboard, rear driver's, and rear outboard seats were included. Occupants in the third row of vehicles such as vans and sports utility vehicles were not included. For lateral impact MVCs, in which there were middle seat occupants, all row occupants were excluded to remove any potential interaction that middle occupants would have with occupants to their side. Approximately 6% of all MVCs in the GES were offset MVC angles (not clearly frontal, lateral, or rear PDOF) and these were excluded

because their inclusion would complicate our definition of at risk and contiguous occupants.

The primary exposure of interest was the seat belt usage among those occupants seated contiguous to at risk occupants and the PDOF (fig 1). Thus, exposed occupants were seated between unbelted occupants and the PDOF and unexposed occupants were seated between belted occupants and the PDOF. Seat belt use was coded according to the GES "restraint system" variable. An occupant was considered restrained if the occupant's GES record reported seat belt restraint by a child seat, lap belt, separate lap and shoulder belt combination, lap and shoulder belt combined, or restraint use but specifics unknown. All other occupants were coded as unbelted. Misclassification of occupant seat belt use as recorded on police accident reports may be a potential source of bias. It has been reported that restraint use recorded in NASS GES (from police accident reports) compared to that recorded in NASS Crashworthiness Data System (from crash investigators, multiple sources not including police accident reports) differed from 11.6% to 36.6% depending on the primary sampling unit.14 However, when at least one fatality occurred seat belt estimates based on police accident reports did not substantially differ to those obtained by trained crash investigators in MVCs.15 If present, the resulting bias would artificially decrease injury risks for belted occupants (by adding non-injured survivors) and increase injury risks for unbelted occupants (by excluding non-injured survivors). Thus, RRs would be an overestimation of the true effect.

Outcomes of interest were the occurrence of an MVC related injury as indicated by the GES injury severity variable. GES does not collect information on specific types of injury. We did not count as injured subjects classified as "possible injured" by GES. Finally, for those subjects with injury reported as unknown (0.75%), imputed values included in the GES data file were used.

Other information obtained from the GES files included occupants' demographic (that is, age and gender) and vehicle characteristics (that is, body type). Vehicle damage severity was used as a proxy for collision severity with vehicles classified as having "minor" or "moderate/severe" damage. If information on vehicle damage was missing, information on whether or not the vehicle required towing from the scene was used. Vehicles towed were coded as having moderate/severe damage and those not towed as having minor damage. In addition, vehicles' travel speed was used as another variable to characterize collision severity. Vehicle curb weight information is not available in GES. However, this information is available in the NASS Crashworthiness Data System file and was obtained by linking make, model, and model year information between the two NASS files.

Many variables necessary for the selection of the study population and/or the statistical analysis contained a substantial number of missing values; a problem noted by other reports based on NASS data.16 For example, 12.1% of subjects were missing data for restraint use, 26.9% for vehicle damage severity, and 14.4% for travel speed. In order to address this problem, multiple imputation was used to create values for this missing information using a Markov Chain Monte Carlo method.¹⁷ The imputation process generates information for missing values based on the values of other, known variables using actual information from subjects who have a similar pattern of information in the dataset. Values were imputed using known values for restraint use, vehicle damage, speed, seat position, year and weekday of MVC. Finally, GES supplied multiple imputed variables were used for age, injury severity, and gender.

	Exposed (unbelted)	Unexposed (belted)	Total (%)	p Value
N				
Number of sample subjects (%) Weighted number of subjects (%) Occupant	28429 (18.7) 3060029 (16.6)	123762 (81.3) 15366655 (83.4)	152191 (100) 18426684 (100)	
Age in years, mean (SE) Gender (%)	27.5 (0.25)	28.8 (0.25)	28.6 (0.23)	<0.001 <0.001
Male	55.7	47.9	49.2	
Female	44.3	52.1	50.8	
Seating position (%)				< 0.001
Driver	42.7	40.0	40.4	
Front seat outboard	42.2	37.8	38.6	
Row 2 driver's side and outboard	15.2	22.2	21.1	
Seat belt use (%)				< 0.001
Belted	35.0	94.5	84.6	
Unbelted	65.1	5.5	15.4	-0.001
Injury (%)	17/	7.0	0.0	< 0.001
Any injury	17.6 10.2	7.2 4.6	8.9 5.5	
Non-incapacitating Incapacitating	6.1	2.2	2.9	
Death	0.7	0.1	0.2	
Vehicle	0.7	0.1	0.2	
Vehicle type (%)				< 0.001
Automobile	75.9	72.3	72.9	
Sports utility vehicle	5.1	7.7	7.2	
Van/minivan	6.5	9.5	9.0	
Pickup truck	7.4	7.6	7.6	
Other	5.0	3.0	3.3	
Curb weight in lbs (%)				< 0.001
<2500	26.0	22.3	22.8	
2500–3000	26.9	28.3	28.1	
>3000	47.1	49.5	49.1	
Collision				
Crash type (%)				< 0.001
Frontal	41.9	24.5	27.4	
Side	50.0	58.1	56.8	
Rear	8.1	17.4	15.9	-0.003
Collision severity (%)	31.6	27.7	24.7	< 0.001
Minor	31.6 68.4	37.7	36.7	
Moderate/severe Mean (SE) travel speed in mph	68.4 26.9 (0.43)	62.3 23.2 (0.40)	63.3 23.8 (0.40)	< 0.001

RESULTS

Table 1 presents occupant, vehicle, and collision characteristics for at risk occupants by exposure group. Those exposed (contiguous to an unbelted occupant) and unexposed (contiguous to a belted occupant) varied significantly in all characteristics examined. Exposed subjects were younger $(27.5 \ v \ 28.8 \ years)$, more likely to be male, more likely to be seated in the driver or front seat outboard positions, less likely be restrained (35.0%), and more likely to be occupants of passenger cars and other vehicles. Finally, exposed subjects were more likely have been involved in a frontal MVC and be

involved in moderate/severe collisions with a higher mean travel speed.

Figure 2 presents injury risks stratified by subjects own belt use. For subjects who themselves were belted, there was a substantial increase in injury risks in both frontal and lateral MVCs but only moderate increased risk in rear MVCs. In opposition to this finding, injury risks were similar or slightly less for those subjects who were unbelted. However, unbelted subjects had greater injury risk in rear MVCs. Overall, for both belted and unbelted subjects, exposure increased risks

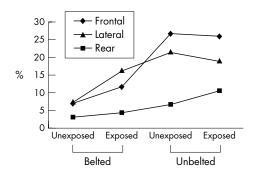


Figure 2 Injury risk by principal direction of force for belted and unbelted occupants by exposure to unbelted occupants.

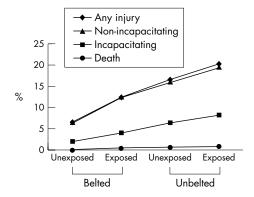


Figure 3 Injury severity for belted and unbelted occupants by exposure to unbelted occupants.

Table 2 Crude and adjusted risk ratios and 95% confidence intervals for the association between contiguous occupant seat belt use and injury by at risk occupants seat belt use and seating position

	Belted		Unbelted		Total	
Seating position	RR (95% CI)	RR (95% CI)*	RR (95% CI)	RR (95% CI)*	RR (95% CI)	RR (95% CI)*
All	1.9 (1.8 to 2.2)	1.9 (1.7 to 2.1)	1.3 (1.1 to 1.4)	1.0 (0.9 to 1.1)	2.6 (2.3 to 2.9)	1.4 (1.3 to 1.5)
Driver	1.7 (1.6 to 2.0)	1.8 (1.6 to 2.0)	1.1 (1.0 to 1.3)	1.2 (1.0 to 1.4)	2.5 (2.2 to 2.8)	1.5 (1.4 to 1.6)
Passenger	1.9 (1.7 to 2.1)	1.9 (1.7 to 2.2)	0.8 (0.7 to 1.0)	0.9 (0.8 to 1.0)	2.4 (2.2 to 2.7)	1.3 (1.2 to 1.5)
Row 2 driver's and passenger's side	1.9 (1.5 to 2.6)	1.9 (1.5 to 2.5)	1.7 (1.3 to 2.2)	1.2 (0.9 to 1.5)	2.9 (2.4 to 3.5)	1.3 (1.1 to 1.6)

^{*}Adjusted for at risk occupant's age, seating position, vehicle type, collision type, travel speed, and crash severity (and at risk occupants' own seat belt use for total).

for any injury, non-incapacitating injuries, incapacitating injuries, and death (fig 3).

Exposure was associated with a 1.4-fold (95% CI 1.3 to 1.5) increased risk of injury when adjusted for age, seating position, vehicle type, travel speed, crash severity, and at risk subjects' own seat belt use (table 2). However, subjects' own seat belt use modified this association. Among belted subjects, a 1.9-fold increased risk of injury was observed (95% CI 1.7 to 2.1) whereas among unbelted subjects, no association was observed (RR 1.0, 95% CI 0.9 to 1.1). This pattern of effect modification was consistent for all seating positions. For belted at risk occupants', regardless of seating position, exposure significantly increased the risk of injury. For unbelted at risk occupants', adjusted RRs were all near the null.

Belted subjects contiguous to unbelted occupants were at greatest injury risk in lateral MVCs (RR 2.1, 95% CI 1.8 to 2.4) and at least injury risk in rear MVCs (RR 1.5, 95% CI 1.0 to 2.2) (table 3). However, the greatest injury risk for unbelted subjects was in rear MVCs (RR 1.4, 95% CI 1.0 to 1.9) and near null in both frontal and lateral MVCs.

Similarly, for non-incapacitating injuries, belted subjects had an elevated risk (RR 1.8, 95% CI 1.7 to 2.0), whereas unbelted occupants' risk was null (table 4). For the overall association, additional adjustment for subjects' own seat belt use resulted in an association, intermediate to that of belted

and unbelted subjects (RR 1.3, 95% CI 1.2 to 1.4). RRs were virtually unchanged for incapacitating injuries. However, the risk of death increased dramatically for belted at risk occupants (RR 4.8, 95% CI 3.3 to 7.0), but null for unbelted at risk occupants (RR 0.9, 95% CI 0.6 to 1.3).

DISCUSSION

The results of the present study indicate that occupants involved in MVCs and seated between unbelted occupants and the PDOF are at increased risk of injury, including death. This association was consistent across seating positions but limited to belted at risk occupants when adjusted for significant confounders. For belted at risk occupants, the greatest increases in risk were seen for death and injury resulting from lateral impact collisions.

Interesting findings of the current study include that the increased injury risks noted for unbelted occupants in figs 2 and 3 were for the most part removed when significant confounders were adjusted for in multivariable analysis. In this group, there was an exception for rear MVCs were increased risks were maintained after adjustment.

These findings are consistent with the hypothesis that unbelted occupants in MVCs become projectiles within the vehicle and increase the risk of injury to other occupants. Belted at risk occupants absorb the force of the unbelted occupant seated contiguous to them whereas the unbelted at

Table 3 Adjusted* risk ratios and 95% confidence intervals for the association between injury risk and contiguous occupant seat belt use by collision type and occupants' seat belt use

	At risk occupants' seat belt use		
Collision type	Belted	Unbelted	Total
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Frontal	1.8 (1.6 to 2.0)	1.0 (0.9 to 1.1)	1.5 (1.4 to 1.7)
Lateral	2.1 (1.8 to 2.4)	0.9 (0.8 to 1.0)	1.3 (1.2 to 1.5)
Rear	1.5 (1.0 to 2.2)	1.4 (1.0 to 1.9)	1.5 (1.1 to 1.9)

^{*}Adjusted for at risk occupant's sex, age, seating position, vehicle type, travel speed, and crash severity (and at risk occupant seat belt use for total).

Table 4 Adjusted* risk ratios and 95% confidence intervals for the association between injury risk severity and contiguous occupant seat belt use by occupants' seat belt use

	At risk occupants' seat belt use			
Injury severity	Belted RR (95% CI)	Unbelted RR (95% CI)	Total RR (95% CI)	
Any injury	1.9 (1.7 to 2.1)	1.0 (0.9 to 1.1)	1.4 (1.3 to 1.5)	
Non-incapacitating	1.8 (1.7 to 2.0)	0.9 (0.8 to 1.1)	1.3 (1.2 to 1.4)	
Incapacitating	1.8 (1.6 to 2.1)	1.0 (0.9 to 1.2)	1.3 (1.2 to 1.5)	
Death	4.8 (3.3 to 7.0)	0.9 (0.6 to 1.3)	1.6 (1.1 to 2.3)	

^{*}Adjusted for at risk occupant's sex, age, seating position, vehicle type, collision type, travel speed, and crash severity (and at risk occupant seat belt use for total).

Key points

- Unbelted occupants increase the risk of injury for other
- Belted occupants had the greatest increased risk of injury.
- Unbelted occupants were not at increased risk of

risk occupant experiences little additional adverse effect from the unbelted occupant.

Past research has supported this theoretical mechanism. Bodiwala et al reported that most injuries to rear seated occupants were due to contact with the front seat, glazing materials, or other parts of the car.18 Christian and Bullimore reported that unrestrained rear seated occupants have a much greater risk of vehicle ejection compared with restrained rear seated occupants.5 Mackay et al suggested that up to 12% of fatalities among restrained front seat occupants were from seat belt loading, and that loading from unrestrained rear seat occupants may be an important feature.8 Finally, Lowenhielm and Krantz reported that belted front seat occupants sustained a higher injury risk with an unrestrained rear seat occupant in the vehicle.10 Thus, previous research has recognized the potential for unrestrained intravehicle movement by unbelted occupants and that this might increase risk of injury to other occupants. However, to date few studies have explicitly tested this hypothesis.

More recently, Ichikawa et al reported odds ratios (ORs) by seat position for front seat occupants, stratified by their own seat belt use.12 Compared to the present study, they reported similar results for severe injury and death for belted drivers (OR 1.93, 95% CI 1.61 to 2.30) and belted front passengers (OR 1.99, 95% CI 1.62 to 2.44) but dissimilar results for unbelted drivers (OR 1.88, 95% CI 0.92 to 3.84) and unbelted front passengers (OR 3.32, 95% CI 1.23 to 9.00). This result was in opposition to ours, where little to no increased risk was seen for unbelted at risk occupants. Some of the differences in inclusion criteria may explain the discrepancy

As in the current study, Ichikawa et al examined frontal, lateral and rear MVCs separately but only front seat occupants were at risk for severe injury and death. Compared to the present study they reported similar results for frontal and lateral collisions but reported near null associations for rear collisions. This difference is probably because in the present study's rear collisions only rear seated occupants were at risk from unbelted front seated occupants.

The current study is strengthened by its clear definition of the at risk population. At risk occupants were defined based on a combination of information that accounted for the PDOF and restraint usage of the occupant in the contiguous seating position. For analysis, we were able to include subjects who were clearly at risk of injury within the constraints of the hypothesized mechanism. Thus, within the constraints of the study's definitions, the reported increased RRs for injury risk are compelling. Nonetheless, MVCs result in a number of different forces and varying angles of impact and so study results may not reflect all MVCs.

Another study strength was the use of multiple imputations for missing values of restraint system use. Potentially, missing values for this variable would influence study eligibility and inclusion and may have resulted in selection bias if subjects with incomplete data were different by seat belt use and injury status. However, a sensitivity analysis restricted to study subjects for whom complete information was available indicated that measures of association were not noticeably different from those reported.

Limitations of the current study included an inability to define post-initial impact forces. Although middle seat occupants were excluded as both at risk and contiguous occupants, there were relatively few middle seat occupants and their inclusion represented methodological challenges because in side impact MVCs they would potentially be both at risk and contiguous to other at risk occupants. Other limitations included not considering the potential effect that airbags might have.

The results of this study add to previous research supporting the efforts of various public health and safety organizations in their advocacy of mandating seat belt restraints for all vehicle occupants.

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REFERENCES

- 1 Kahane CJ. Fatality reduction by safety belts for front-seat occupants of cars and light trucks: update and expanded estimates based on 1986-99 FARS data. DOT report number HS 809 199. Washington, DC: National Highway Traffic Safety Administration, 2000.
- Kendall IG, Bodiwala GG. The effect of legislation on injuries sustained by rear seat car occupants. J Accid Emerg Med 1994;11:49–51.
 Mucci SJ, Eriksen LD, Crist KA, et al. The pattern of injury to rear seat occupants involved in automobile collisions. J Trauma 1991;31:1329–31.
- 4 Bodiwala GG, Thomas PD, Otubushin A. Protective effect of rear-seat restraints during car collisions. Lancet 1989;i:369-71.
- 5 Christian MS, Bullimore DW. Reduction in accident injury severity in rear seat occupants using restraints. Injury 1989;20:262-4.
- 6 Campbell BJ. Safety belt injury reduction related to crash severity and front seated position. J Trauma 1987;27:733-9.
- 7 Chorba TL, Reinfurt D, Hulka BS. Efficacy of mandatory seat belt use legislation. The North Carolina experience from 1983 through 1987. JAMA 1988;260:3593–7.
- 8 Mackay GM, Cheng L, Smith M, et al. Restrained front seat car occupant fatalities—the nature and circumstances of their injuries. Accid Anal Prev
- 9 Wild BR, Kenwright J, Rastogi S. Effect of seat belts on injuries to front and rear seat passengers. BMJ 1985;290:1621–3.
- 10 Lowenhielm P, Krantz P. The effect of the unrestrained back seat passenger on the injuries suffered by drivers and front seat occupants in head-on collisions. Z Rechtsmed 1984;**92**:199-204.
- King AI, Yang KH. Research in biomechanics of occupant protection. J Trauma 1995;**38**:570–6.
- 12 Ichikawa M, Nakahara S, Wakai S. Mortality of front-seat occupants attributable to unbelted rear-seat occupants in car crashes. Lance 2002;**359**:43-4.
- 13 National Automotive Sampling Survey (NASS). General Estimates System (GES) analytical user's manual, 1988–2001. Washington, DC: National Highway Traffic Safety Administration, Available at: http://wwwnrd.nhtsa.dot.gov/pdf/nrd-30/NCSA/GES/01GESAUM.pdf (accessed December 2003).
- 14 Greenberg L. Police accident report (PAR) quality assessment project. DOT report number HS 808 487. Washington, DC: National Highway Traffic Safety Administration, 1996.
- 15 Cummings P. Association of seat belt use with death: a comparison of estimates based on data from police and estimates based on data from trained crash investigators. *Inj Prev* 2002;**8**:338–41.

 16 **Rivara FP**, Koepsell TD, Grossman DG, *et al*. Effectiveness of automatic shoulder belt system in motor vehicle collisions. *JAMA* 2000;**283**:2826–8.
- Schafer JL. Analysis of incomplete multivariate data. London: Chapman and
- 18 Bodiwala GG, Thomas PD, Otubushin A. Protective effect of rear-seat restraints during car collisions. Lancet 1989;i:369-71.